American Society for Nutrition
Webinar Series
National Nutrition Research Roadmap
2016–2021: Advancing Nutrition Research to Improve and Sustain Health

Webinar 1:
The National Nutrition Research Roadmap:
Basic Science and Epidemiology of Nutrition
A Few Reminders

CPE Credit

- ASN designates this educational activity for a maximum of 1 CPEUs. Dietitians and Dietetic Technicians, Registered should only claim credit commensurate with the extent of their participation in the activity.

- To claim credit, please take the post webinar evaluation to be emailed after the webinar.

This webinar is being recorded.
Please mute your phone and/or computer microphone.
Questions & Answers

- Please use the “questions” box on your “Go To Meetings” screen to submit questions to our presenters.

- Please submit your questions at any time during today’s webinar.
Faculty

Speakers

- **Paul M. Coates, PhD**
  Director, Office of Dietary Supplements
  National Institutes of Health
  Co-Executive Secretary to the Interagency Committee on Human Nutrition Research

- **Patrick J. Stover, PhD**
  Professor & Director
  Division of Nutritional Sciences, Cornell University

Moderator

- **Marian L. Neuhouser, PhD, RD**
  Cancer Prevention Program, Fred Hutchinson Cancer Research Center
  President, American Society for Nutrition
Learning Objective

At the end of this program, attendees will be able to:

- Describe research gaps and opportunities, including the open funding opportunity announcements, training activities, and research resources related to the basic science and epidemiology of nutrition, as found in the National Nutrition Research Roadmap.
NIH Research Activities
Addressing the National Nutrition Research Roadmap, 2016-2021

Paul M. Coates, Ph.D.

American Society for Nutrition Webinar Nov 2016
## Disclosures for Paul Coates

<table>
<thead>
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Agenda

• How does the NIH address nutrition research topics?
• Examples
• A plan
• Website for NNRR

Organizing Questions

- Question 1: How can we better understand and define eating patterns to improve and sustain health?
- Question 2: What can be done to help people choose healthy eating patterns?
- Question 3: How can we engage innovative methods and systems to accelerate discoveries in human nutrition?
<table>
<thead>
<tr>
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<td>1. How do we better understand and define eating patterns to</td>
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<td>improve and sustain health?</td>
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<td>2. What can be done to help people choose healthy eating patterns?</td>
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<td>Assessing Dietary Exposures</td>
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NIH Human Nutrition Research

- Many of the 27 NIH ICs and Offices support nutrition-relevant research; ~4-5% of the total NIH budget

- Initiatives, Funding Opportunity Announcements, supplements to existing grants

- Common Fund programs on microbiome and on metabolomics

- Intramural research programs, including the Clinical Center

- Training and career development

- Public health information emerging from NIH-supported research
Let’s use an example…

Question 1. How do we better understand and define eating patterns to improve and sustain health?

• Topical Area 1. Health Promotion and Disease Prevention and Treatment
Enhance optimal development and reduce the risk of chronic disease

- What’s the evidence? What’s the gap?
  - Systematic reviews
  - Workshops
- Study designs
- Variability in individual responses
- Role of the microbiome
- Translational efforts
- Collaborative research
- Frame research around public health needs, e.g., Dietary Reference Intakes, NNRR areas of interest
- Big data
There are plenty of others…

- Establish the causal relationship between nutrition and disease pathophysiology
  - e.g., FOAs related to the microbiome

- Understand how nutritional status affects response to different types of physical activity across the lifespan
  - e.g., nutrigenetics/nutrigenomics approaches; molecular transducers of physical activity

- Examine the role of nutrition, physical activity and other health habits during pregnancy/gestation and early childhood to enhance health
  - e.g., maternal nutrition and pre-pregnancy obesity: effects on mothers, infants, and children
• Workforce development (examples)
  • Cancer Prevention Fellowship Program
  • Loan Repayment Programs
  • John A. Milner Fellowship Program
  • Mary Frances Picciano Dietary Supplement Research Practicum
  • T, F, K Awards at various stages of career development
  • Short-term experiences at NIH

• Public-private partnerships (examples)
  • Biomarkers of Nutrition for Development (BOND)
  • National Collaborative on Childhood Obesity Research (NCCOR)
  • Vitamin D Standardization Program (VDSP)

• Big Data (examples)
  • NIH Big Data to Knowledge (BD2K)
  • NIH Health Care Systems Research Collaboratory Program
  • Environmental Influences on Child Health Outcomes (ECHO)
  • Precision Medicine Initiative (PMI)
Too much information?

- Only a sample of the large array of opportunities
- Basic, clinical, and population research
- A bit daunting???
- How to get started>>>>>>>>>>>>>>>>>>>>>>>>>
Contact Program Director

• Contact the Program Office at early stages!

• Before submission
  • How? Pick up the phone and call!
  • E-mail a short precis (draft title, abstract, specific aims).
  • Follow up phone call or email.
    o Funding mechanisms (research, training, early-stage eligibility)
    o Review venues (study sections)
    o Responsiveness to IC general interests and solicitations
    o Relevance to the NNRR

• After submission
  • Tea and sympathy as a prelude to…..
  • Post-review guidance and strategies for resubmission
  • Appeals, restorations, other adjustments (sometimes)
The ICHNR National Nutrition Research Roadmap
Q1T1 – Health Promotion and Disease Prevention and Treatment
Selected NIH Funding Opportunities (1 of 3 slides)

- Advancing Mechanistic Probiotic/Prebiotic and Human Microbiome (R01) – PA-15-135
- Ancillary Studies to Major Ongoing Clinical Research Studies to Advance Areas of Scientific Interest within the Mission of the NIDDK (R01) – PAR-16-034
- Behavioral Interventions to Address Multiple Chronic Health Conditions in Primary Care (R01) – PA-14-114
- Capturing Complexity in the Molecular and Cellular Mechanisms Involved in the Etiology of Alzheimer’s Disease (R01) – PAR-15-358
- Diet and Physical Activity Assessment Methodology (R01) – PAR-15-170 and (R21) – PAR-15-171
Food Specific Molecular Profiles and Biomarkers of Food and Nutrient Intake, and Dietary Exposure (R01) – PAR-15-024

Maternal Nutrition and Pre-pregnancy Obesity: Effects on Mothers, Infants and Children (R01) – PA-15-100

Obesity and Asthma: Awareness and Self-Management (R01) – PA-14-316


Pilot and Feasibility Clinical Trials in Diabetes, and Endocrine and Metabolic Diseases (R21) – PA-15-176
Revision Applications for Validation of Mobile/Wireless Health Tools for Measurement and Intervention (R01) – PA-16-043

Secondary Analysis in Obesity, Diabetes and Digestive and Kidney Diseases (R21) – PA-15-169

The National Institutes of Health Big Data to Knowledge (BD2K)

The BRAIN Initiative

Understanding Factors in Infancy and Early Childhood (Birth to 24 months) That Influence Obesity Development (R01) – PA-16-169
The ICHNR National Nutrition Research Roadmap

Q1T2 – Individual Differences Including Omics

Selected NIH Funding Opportunities

- Advancing Mechanistic Probiotic/Prebiotic and Human Microbiome Research (R01) – PA-15-135
- Early-Stage Preclinical Validation of Therapeutic Leads for Diseases of Interest to the NIDDK (R01) – PAR-16-121
- Food Specific Molecular Profiles and Biomarkers of Food and Nutrient Intake, and Dietary Exposure (R01) – PAR-15-024
- High Impact, Interdisciplinary Science in NIDDK Research Areas (RC2) – PAR-16-126
- Secondary Analyses in Obesity, Diabetes and Digestive and Kidney Diseases (R21) – PA-15-169
- Precision Medicine Initiative (PMI)
- Selected Common Fund Programs
  - Big Data to Knowledge (BD2K)
  - Epigenomics
  - Human Microbiome Project (HMP)
  - Metabolomics
The ICHNR National Nutrition Research Roadmap
Q1T3 – Population-Level Monitoring
Selected NIH Funding Opportunities

- Diet and Physical Activity Assessment Methodology (R01) – PAR-15-170 and (R21) – PAR-15-171
- Obesity Policy Research Evaluation (R01) – PA-16-165
- Revision Applications for Validation of Mobile/Wireless Health Tools for Measurement and Intervention (R01) – PA-16-043
- The National Institutes of Health Big Data to Knowledge (BD2K)
- Time-Sensitive Obesity Policy and Program Evaluation (R01) – PAR-15-346
- Understanding Factors in Infancy and Early Childhood (Birth to 24 months) That Influence Obesity Development (R01) – PA-16-169
The National Nutrition Research Roadmap: Basic Science and Epidemiology of Nutrition

“Scientific Premise of Individual Variances in Nutritional Status and Response to Diet”

Patrick J. Stover, PhD
Professor & Director, Division of Nutritional Sciences, Cornell University
## Disclosures for Patrick Stover

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"I expect that in the year 2005 (when the entire human genome is scheduled to be mapped and sequenced), on the back of our foods, there are going to be a lot of things like that, because we are going to know a lot more about ourselves. And I think the field of nutrition, which, in my own opinion now, has not benefited from the advances in molecular genetics, will be a completely different field. That will be the most revolutionized field in the year 2005. And the reason is that we will know lots more, we will actually know something about nutrition so you won't pick up one day and say fat is good for you and the next day fat is bad for you. Because we will know that some people it is good for and some people it is bad for.

"We will be able to know what people can metabolize and what some people can't metabolize. ....We're going to have a new definition of what it means to be healthy."

The Human Genome Project: Part Two: Ushering in a new era of molecular medicine. Date of Publication: 1998

http://www.laskerfoundation.org/rprimers/hgp2.html
American Society for Nutrition
Nutrition Research Priorities

Variability in Responses to Diet & Food
Achieving personalized nutrition with dietary recommendations tailored to each person’s needs.

Healthy Growth, Development and Reproduction
Understanding how nutrition during critical, early periods of development (including pregnancy) impacts future health.

Health Maintenance
Improving health with noncommunicable disease prevention and weight maintenance.

Medical Management
Slowing disease progression through nutrition with improved responses to therapy and survival rates.

Nutrition-Related Behaviors
Understanding how the human brain influences food choice and nutrition-related behaviors.

Food Supply & Environment
Realizing the potential of the food environment to improve diet and lifestyle choices.

Responders vs. Non-responders
### National Nutrition Research Roadmap 2016–2021

**Question 1: How can we better understand and define eating patterns to improve and sustain health?**

**Question 1 Topic 1 (Q1T1):** How do we enhance our understanding of the role of nutrition in health promotion and disease prevention and treatment?

**Question 1 Topic 2 (Q1T2):** How do we enhance our understanding of individual differences in nutritional status and variability in response to diet?

**Question 1 Topic 3 (Q1T3):** How do we enhance population-level food- and nutrition-related health monitoring systems and their integration with other data systems to increase our ability to evaluate change in nutritional and health status, as well as in the food supply, composition, and consumption?

**Question 2: What can be done to help people choose healthy eating patterns?**

**Question 2 Topic 1 (Q2T1):** How can we more effectively characterize the interactions among the demographic, behavioral, lifestyle, social, cultural, economic, occupational, and environmental factors that influence eating choices?

**Question 2 Topic 2 (Q2T2):** How do we develop, enhance and evaluate interventions at multiple levels to improve and sustain healthy eating patterns?

**Question 2 Topic 3 (Q2T3):** How can simulation modeling that applies systems science in nutrition research be used to advance exploration of the impact of multiple interventions?

**Question 2 Topic 4 (Q2T4):** How can interdisciplinary research identify effective approaches to enhance the environmental sustainability of healthy eating patterns?

**Question 3: How can we develop and engage innovative methods and systems to accelerate discoveries in human nutrition?**

**Question 3 Topic 1 (Q3T1):** How can we enhance innovations in measuring dietary exposure, including use of biomarkers?

**Question 3 Topic 2 (Q3T2):** How can basic biobehavioral science be applied to better understand eating behaviors?

**Question 3 Topic 3 (Q3T3):** How can we use behavioral economics theories and other social science innovations to improve eating patterns?

**Question 3 Topic 4 (Q3T4):** How can we advance nutritional sciences through the use of research innovations involving Big Data?

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[https://www.google.ch/?gfe_rd=cr&ei=Og8SWOLrLcHCaNn8gOAN#q=national+nutrition+roadmal](https://www.google.ch/?gfe_rd=cr&ei=Og8SWOLrLcHCaNn8gOAN#q=national+nutrition+roadmal)
National Nutrition Research Roadmap 2016–2021

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https://www.google.ch/?gfe_rd=cr&ei=Og8SWOLrLcHCaNn8gOAN#q=national+nutrition+roadmap
Research and Resource Initiatives

*Short-term Initiatives:*

- Support collaborative, interdisciplinary research for understanding the effects of dietary and physical activity patterns and individual variability on biologic measures related to the epigenome, microbiome, metabolome, and proteome.

- Collate existing data in an effort to establish the relationship between eating patterns, individual variation, healthy development, and disease.

- Develop tissue-on-a-chip models including linked system models that incorporate human-like food metabolism to elucidate the effects of dietary components at a molecular and tissue level.

https://www.google.ch/?gfe_rd=cr&ei=Og8SWOLrLcHCaNn8gOAN#q=national+nourishment+roadmap
Short-term Initiatives (Continued):

• Support research in humans to understand the effects of diet-induced changes in the microbiome, and other omics (e.g., epigenome, metabolome) on subsequent changes in biologic processes and health.

• Support research to understand the potential health effects of consuming nutrients (i.e., pre- or probiotics) that alter the gut or oral microbiome.

• Characterize the absorbable nutrient contributions of the gut microbiome under various conditions and with diverse populations.

https://www.google.ch/?gfe_rd=cr&ei=Og8SWOLrLcHCaNn8gOAN#q=national+nutrition+roadmal
Research and Resource Initiatives

Long-term Initiatives

- Characterize individual differences in “omics” using randomized controlled trials and other research designs as appropriate.

- Utilize adaptive and other controlled trial designs to test the potential for individualized nutrition and lifestyle interventions (i.e., physical activity) based on “omic” signatures to affect specific health outcomes.

- Support research to identify genetic characteristics related to differences in nutritional requirements and metabolism.

https://www.google.ch/?gfe_rd=cr&ei=Og8SWOLrLcHCaNn8gOAN#q=national+nutrition+roadmap
NIH plans to enhance reproducibility

Francis S. Collins and Lawrence A. Tabak discuss initiatives that the US National Institutes of Health is exploring to restore the self-correcting nature of preclinical research.
What does "scientific premise" mean for a grant application?

- The scientific premise will be reviewed as part of the Significance criterion for research grant applications.
- Concerns the quality and strength of the research base used to form the basis for a proposed research question.
- Consideration of general strengths and weaknesses to include attention to the rigor of the previous experimental designs, as well as relevant biological variables and authentication of key resources.

http://grants.nih.gov/reproducibility/faqs.htm#II
“Today, as we learn more about the complexity of living organisms, both successful and failed attempts to replicate a given study can provide valuable insights into biological processes.”

https://www.faseb.org/Portals/2/PDFs/opa/2016/FASEB_Enhancing%20Research%20Reproducibility.pdf
It is important to recognize that variations in experimental results may signal unexpected phenomena leading to new scientific understanding. Lack of reproducibility, generalizability, and translatability are distinct from and do not imply error or scientific misconduct.

Researchers should articulate the rationale for the choice of an animal model as well as its value and limitations in recapitulating human disease and its treatment.
Two Examples

Origins of
Individual Variation in Response to Diet
Human Genome Project (1990-2003)

- Assemble & understand cellular networks
- Manipulate cellular networks for benefit
  - Pharmaceuticals & Nutrients

http://www.ornl.gov/sci/techresources/Human_Genome/home.shtml
Food Intolerances
Dietary Requirements
Susceptibility to Metabolic Disease

Genome Primary Sequence
- *in utero* viability
- mutation rate
- selection

Genome Programming
Gene Expression

Human Genome

Nutrition and Evolution

Dietary Components

Food Intolerances
Dietary Requirements
Susceptibility to Metabolic Disease

Dietary change was a driving force in human evolution.

By William R. Leonard
MTHFR 677C>T SNP modifies folate metabolism

5,10-CH₂-THF  →  5-CH₃-THF

DNA Synthesis  DNA Repair

MTHFR
677C>T
1298A>C

FAD

Cellular Methylation

-Diminished folate status
-Moderate hyperhomocysteinemia
-Altered risk of folate related diseases
-~ 12% of US population with 677TT genotype
## Allelic Frequency of the MTHFR 677 C->T Polymorphism

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<td>Tuscanian (Italy)</td>
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<td>Yemenite Jews</td>
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<td>Muslim Arab Israelis</td>
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<td>Caucasians</td>
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Connections Between Birth Defects and Cancer

Benefit and Risks of MTHFR Polymorphism

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<th>Protein Sequence</th>
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**In utero Risk**

“T” allele

- Low folate status
- Higher folate requirement
- Birth defects
- Miscarriage

**Adult Benefit**

“T” allele

- Physician’s Health Study – Colon Cancer Risk

![Graph showing odds ratio for different MTHFR genotypes](image)
MTHFR 677TT genotype markedly affects biomarkers of folate status in men consuming the folate RDA

Solis et al. JN 2008

**Folate Treatment with 400 μg DFE/d**

**Deficient (<6.8 nmol/L)**
- 34% TT (10 of 29)
- 16% CC (5 of 31)

**Deficient (>14 μmol/L)**
- 79% TT (23 of 29 men)
- 7% CC (2 of 31 men)
**Epigenetic Mechanisms**

Are affected by these factors and processes:
- Development (in utero, childhood)
- Environmental chemicals
- Drugs/Pharmaceuticals
- Aging
- Diet

**Health Endpoints**
- Cancer
- Autoimmune disease
- Mental disorders
- Diabetes

**DNA Methylation**

Methyl group (an epigenetic factor found in some dietary sources) can tag DNA and activate or repress genes.

**Histone Modification**

The binding of epigenetic factors to histone “tails” alters the extent to which DNA is wrapped around histones and the availability of genes in the DNA to be activated.

Histones are proteins around which DNA can wind for compaction and gene regulation.
Choline is an essential nutrient that plays a key role in fetal development.
Supplementing the maternal diet with extra choline may ease baby’s stress by changing production of the stress hormone, cortisol.

Supplementing the diet with extra choline

“Choline” Baby

Effect of maternal choline intake (930 vs. 480 mg/d) on maternal and fetal cortisol.
This lower production of cortisol in “choline” babies may reduce risk of stress-related diseases.

- Hypertension
- Obesity
- Diabetes
- Depression

- Memory
- Learning
- Attention

# National Nutrition Research Roadmap 2016–2021

## Q1T2 Glossary

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Questions & Answers

Please submit your questions to via the “questions box” on your screen.
Thank you for joining us!

Make plans to participate in our next webinar:

The National Nutrition Research Roadmap: Measuring and Monitoring Individual Dietary Intake and the Food Environment

Wednesday, January 18, 2017
3:00 pm - 4:00 pm (ET)

Visit www.nutrition.org for details.
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