

Agenda — Monday, September 15

OBJECTIVES

- To highlight the most critical and actionable gaps in understanding of non-prescription, ingested interventions used to improve sleep in generally healthy populations.
- To identify key considerations in the prioritization of research to address the knowledge, methodology and resource gaps identified.
- To explore opportunities for generating new insights into sleep and circadian biology through this research, including through the application of new approach models.
- To identify new areas where trans-disciplinary collaboration is needed and approaches to support those collaborations.
- To communicate the state of the science and forward-looking discussions to the research community and beyond through the peer-reviewed biomedical research literature and beyond, as appropriate.

WORKSHOP CO-CHAIRS

- Michael A. Grandner, PhD, MTR, Director, Sleep and Health Research Program, University of Arizona
- Eva S. Schernhammer, MD, DrPH, Channing Division of Network Medicine, Brigham and Women's Hospital, Harvard T.H. Chan School of Public Health, Head, Department of Epidemiology, Medical University of Vienna

NATIONAL INSTITUTES OF HEALTH (NIH) CO-ORGANIZERS

- Barbara C. Sorkin, PhD, Office of Dietary Supplements, NIH
- Maria C. Canino, PhD, ORISE Postdoctoral Fellow supporting the NIH
- Shilpy Dixit, Ph.D., National Center for Sleep Disorders Research, NIH National Heart, Lung and Blood Institute, NIH

Session 1: **Scope of the Problem: Prevalence, Causes, and Consequences of Poor Sleep Health**

Moderator: Eva Schernhammer

1100–1120 **Welcome and Opening Remarks**

- Andrew A. Bremer, MD, PhD, MAS, Director, Office of Nutrition Research (ONR), NIH, Acting Director, Office of Dietary Supplements (ODS), NIH
 - Marishka K. Brown, PhD, Director, National Center for Sleep Disorders Research
 - Barbara C. Sorkin, PhD, Co-Director, Consortium Advancing Research on Botanicals and Other Natural Products, NIH
- Review of workshop objectives and format
 - Day 1: Landscape; current knowledge and critical knowledge gaps.
 - Day 2: What new approaches could enhance our ability to address the knowledge gaps and enhance our understanding of sleep and circadian or other biology?

- 1120–1135 [What do we mean by “sleep health?” The big pictures](#)
Dan Buysse (University of Pittsburgh)
- 1135–1150 [Sleep Health and Cardiometabolic and Cognitive Health](#)
Orfeu Buxton (The Pennsylvania State University)
- 1150–1205 [Sleep and the Human Immune System](#)
Aric A Prather (University of California, San Francisco)

- 1205–1220 **Discussion**
Which gaps in knowledge are most pressing, what would be needed to address them?

Session 2: Ashwagandha to Zinc and Outside the Bottle: Strategies People Use to Improve Sleep

Moderator: Todd Horowitz, National Institute on Aging, NIH

- 1220–1235 Overview of strategies used to improve sleep
• Michael Grandner (University of Arizona)
- 1235–1250 [Sleep from the field? The role of herbal products in insomnia and related disorders](#)
• Michael Heinrich (University College London)
• Rachael Frost (University College London)
- 1250–1305 Nutritional sleep interventions: an overview
Michael Grandner (University of Arizona)
- 1305–1315 [Use of Alcohol as a sleep aid by healthy adults: effects and potential harms](#)
• Todd Arnedt (University of Michigan)
- 1315–1325 Cannabis and sleep: subject-reported outcomes, controlled trials, and the road ahead
• Christopher Scott Colwell (University of California, Los Angeles)
- 1325–1335 [Kratom as a Potential Sleep Aid](#)
• Mary F. Paine (Washington State University)

Melatonin mini-session

- 1335–1340 [An examination of melatonin use in children in the US](#)
• Judith A. Owens (Harvard Medical School)
- 1345–1355 [Melatonin for sleep](#)
• Jeanne F. Duffy (Brigham and Women’s Hospital)

Lightning product proposals

- 1355–1400 [Kava kava](#)—Chengguo Xing (University of Florida)
- 1400 - 1405 Magnesium—Commander J. Kent Werner (Uniformed Services University and Walter Reed National Military Medical Center)

1405–1430 Discussion

1. What are key factors to consider in prioritizing natural products, ingested sleep interventions for further research?
2. For different research phases (in vitro/NAMs, preclinical in vivo models, early or later phase clinical trials)?

1430–1500 BREAK

Session 3: Overview of Mediators, Mechanisms and Targets for Sleep Interventions

Moderator: Shilpy Dixit

1500–1515 Sleep Reactivity as a Macro-target: From the Individual to the Environment

- Philip Cheng (Henry Ford Health)

1515–1530 [Drugs that promote sleep](#)

- William Wisden (Imperial College London)

1530–1540 Brain Fatty-Acid Binding Protein as a Nutraceutical Target to Mediate Sleep and Cognitive Function

- Jason Gerstner (Washington State University)

1540–1555 Sleep and the gut

- Dragana Rogulja (Harvard Medical School)

1555–1630 Discussion

1. What is known, what are the knowledge gaps for mediators and molecular targets for non-prescription ingested and for behavioral and environmental interventions? What NAMs are available for known targets?
2. Are new biomarkers or measures for sleep sufficiency/fatigue or circadian timing needed?

Closing Discussions and Summary of Day 1

Session Chair and Session Organizers

1630–1700 Discussion

1. What do we know about sleep health across age and other population subgroups, and factors (causal?) associated with poor sleep health? What are the most critical gaps in this information, what would be priority approaches to address them?
2. What are key factors to consider in prioritizing non-prescription ingested interventions for efficacy clinical trials? What supporting knowledge and evidence base is important to optimize the information obtained from such trials, what outcomes should be studied? Which, if any, strategies have sufficient evidence and mechanism of action information to be prioritized towards clinical trials?
3. What are key considerations for prioritizing interventions for preclinical, translational or early phase clinical trials (e.g., safety, dose-response, PK/PD, product and outcome optimization)?

Agenda — Tuesday, September 16

Looking Forward to Getting Better Sleep: Innovative Approaches to Accelerating Our Understanding of Ingested Strategies

1100–1110 **Day 1 Recap; Day 2 Introduction**

Session 1: Epidemiological, Nutritional and Ethnobotanical: Exploring Application of 21st Century Methods and Traditional Uses to Query Gaps in Knowledge of Potential Sleep Remedies

Moderator: Dana Schloesser, Office of Behavioral and Social Sciences Research, NIH

1110–1120 Botanical identification matters: traditional plant remedies for sleep among Caribbean and Mexican communities in NYC

- Ina Vandebroek (University of the West Indies, Mona)

1120–1130 Ethnobotany and pharmacognosy of American Southwest medicinal plants used for improving sleep

- C. Benjamin Naman (San Diego Botanic Garden)

1130–1140 **Discussion**

1. Exploring traditionally used natural products: opportunities, challenges, ethical issues

1140–1155 Office of Data Science Strategy, NIH, AI/ML and large data sets, opportunities, caveats, FAIR, data standards and harmonization; NIH resources; How many participants in a data set to detect true signals?

- Steve Tsang (Office of Data Science Strategy, NIH)
- Jeran Stratford (RTI International)

1155–1205 [From small signals to big data: the genomics of sleep in transition](#)

- Angus C. Burns (Brigham and Women's Hospital, Harvard Medical School)

Relevant clinical data sets

1205–1210 [Leveraging NHANES for sleep and nutrition research: Opportunities for population health insights](#)

- Jaime Gahche (ODS, NIH)

1210–1215 [An introduction to the Military Health and Nutrition Examination Study \(MHANES\)](#)

- Claire Berryman (Pennington Biomedical Research Center)

1215–1220 Relevant clinical data sets: Nutrition for Precision Health

- Holly Nicastro (ONR, NIH)

1220–1225 Opportunities for research on sleep in the Environmental Influences on Child Health Outcomes (ECHO), NIH cohort

- Clay Mash (ECHO Program Office, NIH)

- 1225–1235 Data on sleep and diet in the Adolescent Brain Cognitive Development (ABCD) study
• Gayathri Dowling (National Institute on Drug Abuse [NIDA], NIH)
~~Healthy Brain and Child Development (HBCD) study~~
~~• Christopher Sarampote (NIDA, NIH)~~
- 1235–1300 **Discussion**
Gaps and needs: What are the caveats, what controls are needed to ensure validity and limit false positives? What new resources would support this approach?
- 1300 –1330 **BREAK**
- Session 2: Preclinical Approaches: Exploring Application of New Approach Models to Gaps in Knowledge of Over-the-Counter Products Used for Sleep**
Moderator: Barbara C. Sorkin
- 1330–1450 **What higher throughput translational models are available or might be developed to screen interventions for potential efficacy?**
- 1330–1345 1. [Quantitative IVIVE applications for botanical products: bridging in vitro models and clinical predictions](#)
Yitong Liu (FDA Human Foods Program)
- 1345–1400 2. Development of human brain organoids for sleep studies
Alysson R. Muotri (University of California, SD, Gene Therapy Initiative)
- 1400–1415 3. [Connecting metabolites and phenotypes: multi-omic strategies for identifying bioactive constituents in dietary supplements](#)
Roger Linington (Simon Fraser University)
- 1415–1430 4. [Can non-mammalian models be used for studying interventions that improve sleep?](#)
Doris Kretzschmar (Oregon Health & Science University)
- 1430–1450 **Discussion**
1. How might agnostic approaches to screening support discovery of new biomarkers for clinical trials?
2. What new resources would support these approaches?
- Session 3: Approaches to Accelerate Learning from Clinical Trials**
Moderator: Michael Grandner
- 1450–1505 1. Dose response, dose expansion, platform, adaptive/Bayesian, other?
Chris Coffey (University of Iowa)
- 1505–1520 2. Target trial emulation—WHI vs nurses' health outcome—e.g., w melatonin users
Miguel Hernán (Harvard T.H. Chan School of Public Health)

- 1520–1535 3. [Large-scale Decentralized Trials to Rapidly Generate Precision Evidence for Sleep Interventions](#)
Jeff Chen (RadicleScience)
- 1535–1550 **Discussion**
1. What interventions or groups of interventions might benefit from some of these types of clinical trials?
 2. What biomarkers or outcome measures are needed or need further development and/or validation?
- 1550–1630 **What Next? Putting it All Together**
- What factors and new approaches should be considered in prioritizing clinical research on safety, efficacy/effectiveness of non-prescription, ingested approaches to better sleep.
 - Where are the most pressing needs for research, new resources, methods, measures that could be combined to more effectively assess which interventions are most promising and more efficiently move them into informative clinical studies
 - Strategize ways to apply new approaches, pursue new opportunities to address key research needs.
- Overall**
- What are critical criteria in prioritizing different problems affecting sleep health?
 - What are critical criteria in prioritizing research on strategies to address these problems?
 - What are critical criteria in prioritizing gaps in methods, measures, resources, data harmonization?
- 1630–1645 **Closing Discussions and Summary of Workshop**
Co-Chairs
- Next steps
 - Anticipated timeline for publications
- 1645 Adjourn