DEPARTMENT OF HEALTH AND HUMAN SERVICES NATIONAL INSTITUTES OF HEALTH NATIONAL CENTER FOR COMPLEMENTARY AND INTEGRATIVE HEALTH NATIONAL ADVISORY COUNCIL FOR COMPLEMENTARY AND INTEGRATIVE HEALTH Minutes of the Eighty-Third Meeting January 20, 2023

NACCIH Members Present Virtually

Dr. Helene Benveniste, New Haven, CT* Dr. Todd Braver, St. Louis, MO Dr. Per Gunnar Brolinson, Blacksburg, VA* Dr. Nadja Cech, Greensboro, NC Dr. Robert Coghill, Cincinnati, OH Dr. Daniel Dickerson, Los Angeles, CA* Dr. Roni Evans, Minneapolis, MN Dr. Margaret (Meg) Haney, New York, NY Dr. Richard E. Harris, Ann Arbor, MI Dr. Kendi Hensel, Fort Worth, TX Dr. Girardin Jean-Louis, Miami, FL Dr. Benjamin Kligler, Washington, DC** Prof. Rhonda Magee, San Francisco, CA* Dr. Helen Lavretsky, Los Angeles, CA Dr. Erica Sibinga, Baltimore, MD* Dr. Justin L. Sonnenburg, Stanford, CA Dr. Amala Soumyanath, Portland, OR

NACCIH Members Not Present

Dr. Anthony Delitto, Pittsburgh, PA Dr. Diana Fishbein, Chapel Hill, NC Dr. Tammy Born Huizenga, Grand Rapids, MI Ms. Lori Knutson, Bentonville, AR Dr. Wolf Mehling, San Francisco, CA Dr. Karen Sherman, Seattle, WA Dr. Lynne Shinto, Portland, OR

*Ad Hoc Member; Scheduled to participate as a regular Member in May 2023 **Ex Officio Member

I. Closed Session

The first portion of the eighty-third meeting of the National Advisory Council for Complementary and Integrative Health (NACCIH) was closed to the public, in accordance with the provisions set forth in Sections 552b(c)(4) and 552b(c)(6), Title 5, U.S.C., and Section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2). A total of 153 applications were assigned to the National Center for Complementary and Integrative Health (NCCIH). Applications that were noncompetitive, not discussed, or not recommended for further consideration by the scientific review groups were not considered by Council. Council agreed with staff recommendations on 76 scored applications, which requested \$32,147,676 in total costs.

II. Call to Order and Brief Review of Council Operating Procedures

Dr. Martina Schmidt, director of the NCCIH Division of Extramural Activities (DEA) and newly named NACCIH Executive Secretary, convened the open session at 11:40 a.m. ET. The minutes of the September 2022 meeting were approved unanimously. As required by the Council charter, Dr. Schmidt presented the annual review of Council operating procedures for secondary review of grant applications, NCCIH reports to Council, Council review of concepts for research initiatives, appeals and appeal criteria, and Council involvement in policy and research priorities. Council unanimously approved the operating procedures.

III. NCCIH Director's Welcome and NCCIH Report

Dr. Helene M. Langevin, director of NCCIH, welcomed new Council member Dr. Amala Soumyanath, professor in the Department of Neurology and director of the NCCIH-funded Botanicals Enhancing Neurological and Functional Resilience in Aging (BENFRA) Botanical Dietary Supplements Research Center at Oregon Health & Science University.

Dr. Langevin also welcomed five ad hoc Council members who are anticipated to become full members in May 2023: Dr. Helene D. Benveniste, professor, Department of Anesthesiology, Yale School of Medicine; Dr. Per Gunnar Brolinson, vice provost for research, Edward Via College of Osteopathic Medicine; Dr. Daniel Dickerson, associate research psychiatrist, Integrated Substance Abuse Program, University of California, Los Angeles; Rhonda Magee, professor of law, University of San Francisco School of Law; and Dr. Erica Sibinga, associate professor, Department of Pediatrics, The Johns Hopkins University School of Medicine.

NIH has issued the Data Management and Sharing policy, effective January 25, 2023, to promote the sharing of scientific data. Sharing data accelerates biomedical research discovery, in part by enabling validation of research results, providing accessibility to high-value data sets, and promoting data reuse for future research studies.

Dr. Alexander Chesler, Torri Wilson, Dr. Beda Jean-Francois, and Dr. David Shurtleff were recognized for receiving 2022 NIH Director's Awards. Dr. Langevin recognized Dr. Partap Khalsa,

who retired in December 2022 as director of DEA and NACCIH Executive Secretary. After an extensive search, Dr. Martina Schmidt has been appointed as the new director of DEA. Dr. Schmidt joined NCCIH in 2005 as a scientific review officer (SRO). She became director of the NCCIH Office of Scientific Review (OSR) in 2016, leading and coordinating activities related to NCCIH peer review. Dr. Jessica McKlveen, DEA, has been promoted from scientific review officer to acting director of OSR. New NCCIH staff include Dr. Kevin McBryde, medical officer in the Office of Clinical and Regulatory Affairs, and Dr. Jennifer Baumgartner, program director in DER. Staff who recently departed NCCIH include Dr. Sonia Nanescu and Sara Rue of DER and Dr. Melissa Treviño of DEA.

The Consolidated Appropriations Act for Fiscal Year (FY) 2023 provides \$170 million for NCCIH—an increase of \$11 million (of which \$5 million has been specifically designated for pain research) or an overall increase of approximately 6.9 percent from the Center's FY 2022 enacted appropriation. This increase in budget is a recognition of NCCIH's leadership in pain research.

The NIH Common Fund's <u>Bridge to Artificial Intelligence (Bridge2AI)</u> program made its first awards, under <u>OTA-21-008</u>, Data Generation Projects for the NIH Bridge to Artificial Intelligence (Bridge2AI) Program (OT2). This is an especially important area for NCCIH as it deals with large datasets. NCCIH is one of five NIH Institutes/Centers (ICs) leading this program. Dr. Langevin recognized the work of Dr. Lanay Mudd, a program director in DER who is co-leading this program. There are four awards for data generation projects (including one on salutogenesis or return to health) and three center awards to build capacity.

Recent funding opportunities under the NIH Helping to End Addiction Long-term[®] Initiative, or NIH HEAL Initiative[®], include:

- Developing Quantitative Imaging and Other Relevant Biomarkers of Myofascial Tissues for Clinical Pain Management (R61/R33, Clinical Trial Required), <u>RFA-AT-22-003</u>. NCCIH is leading this program.
- HEAL Initiative: Restoring Joint Health and Function to Reduce Pain Consortium (RE-JOIN) (UC2 Clinical Trial Not Allowed), <u>RFA-AR-22-009</u>.

Dr. Langevin announced a new NCCIH webpage, "<u>NIH-Supported Research on Cannabis,</u> <u>Cannabinoids, and Related Compounds</u>" and described these music-related initiatives:

- The John F. Kennedy Center for the Performing Arts hosted "Sound Health: Renew/Remix" on October 2 and 3, 2022. At this event, Dr. Emmeline Edwards, director of DER, and Dr. Wen Chen, chief of the Basic and Mechanistic Research Branch, DER, participated in a panel on "Music-Based Health Interventions: The Path Ahead."
- Drs. Edwards and Chen co-chaired a symposium, "Music and Brain Circuitry: Strategies for Strengthening the Evidence-Based Research," at the 2022 Society of Neuroscience meeting.

 A new funding opportunity, Research Networks to Promote Multidisciplinary Mechanistic Studies on Music-Based Interventions for Pain or Alzheimer's Disease and Alzheimer's Disease Related Dementias (AD/ADRD) (U24 Clinical Trial Optional), <u>RFA-AT-23-009</u>, was released.

The inaugural progress report of NIH UNITE has been published. The UNITE initiative focuses on three domains—health disparities/minority health research, internal NIH workforce, and external biomedical and behavioral research workforce. An NIH-wide initiative pertaining to the current U.S. mental health crisis, Advancing Prevention Research for Health Equity Initiative (ADVANCE), is being led by the NIH Office of Disease Prevention (ODP). Recently, ADVANCE released a request for information (RFI), Innovative Approaches to Prevent Mental Health Problems and Promote Mental Wellness in Populations That Experience Health Disparities, NOT-OD-23-030. Complementary and integrative health clinical institutions are among the community sectors mentioned in this RFI. Dr. Beda Jean-Francois, a program director in DER, is among the NIH authors of a commentary/position paper published in *Translational Behavioral Medicine* in November 2022, Advancing digital health equity: directions for behavioral and social science research. The paper outlines five specific recommendations—with practice, policy, and research implications—to develop a multipronged and comprehensive research program toward promotion of digital equity and justice. Dr. Beda Jean-Francois, a program director in DER, is the NCCIH author.

Dr. Langevin highlighted publications on studies funded or co-funded by NCCIH:

- 1. Hight SK, Clark TN, Kurita KL, et al. <u>High-throughput functional annotation of natural</u> <u>products by integrated activity profiling</u>. *Proceedings of the National Academy of Sciences*. 2022;119(49):e2208458119.
- Hays RD, Shannon ZK, Long CR, et al. <u>Health-related quality of life among United</u> <u>States service members with low back pain receiving usual care plus chiropractic care vs</u> <u>usual care alone: secondary outcomes of a pragmatic clinical trial</u>. *Pain Medicine*. 2022;23(9):1550-1559.
- 3. LeBoff MS, Chou SH, Ratliff KA, et al. <u>Supplemental vitamin D and incident fractures in</u> <u>midlife and older adults</u>. *New England Journal of Medicine*. 2022;387(4):299-309.
- 4. Orkaby AR, Dushkes R, Ward R, et al. Effect of vitamin D3 and omega-3 fatty acid supplementation on risk of frailty: an ancillary study of a randomized clinical trial. *JAMA Network Open.* 2022;5(9):e2231206.

Recent funding opportunities include:

- Notice of Special Interest (NOSI): BRAIN Initiative: Notice of Support for Research on Interoception Circuits, <u>NOT-AT-23-003</u>
- HEAL Initiative: Sleep Predictors of Opioid-Use Disorder Treatment Outcomes

Program (R01 Clinical Trial Optional), <u>RFA-DA-23-059</u>

- HEAL Initiative Integrated Basic and Clinical Team-based Research in Pain (RM1 Clinical Trial Optional), <u>RFA-NS-22-069</u>
- Enhancing the Use of the All of Us Research Program Data (R21 Clinical Trial Not Allowed), <u>RFA-PM-23-001</u>
- Small Grants to Enhance the Use of the All of Us Research Program Data (R03 Clinical Trial Not Allowed), <u>RFA-PM-23-002</u>

Recent events include:

- NCCIH Fellows and Trainees Virtual Workshop: Whole Person Health Research Careers (9/15–16/2022)
- Yet to Be Charted: The Lymphatic System in Health and Disease (9/19–20/2022) Archived videos are available for <u>Day 1</u> and <u>Day 2</u>.
- NIH Investigator Meeting on Functional Neurocircuits of Interoception (9/29/2022) <u>An</u> <u>archived video is available</u>.
- Repository and Database for Anatomical and Physiological Ontology of Acupoints Technical Assistance Webinar (10/6/2022) <u>A summary is available</u>.
- Stakeholder Meeting for Research on Whole Person Health (10/17–18/2022) The meeting agenda is available<u>https://www.nccih.nih.gov/news/events/stakeholder-meeting-for-research-on-whole-person-health</u>.
- 2022 Stephen E. Straus Distinguished Lecture in the Science of Complementary Therapies. "From the Mouths of Babes: What Can Research on Babies, Moms, Stress, and Substance Use Tell Us About Resilience?" by Dr. Laura Stroud, Warren Alpert Medical School and The Miriam Hospital. (12/13/2022)

Upcoming events include:

- 4th Annual NIH HEAL Initiative Investigator Meeting (2/21–22/2023)
- Emotional Well-Being 2nd Annual Investigator Meeting (3/27/2023)*
- NIH Pain Management Collaboratory Meeting (5/9–10/2023)*
- NIH Pragmatic Trials Collaboratory/Pragmatic and Implementation Studies to Improve the Management of Pain and Reduce Opioid Prescribing (PRISM) Investigator Meeting (5/16–17/2023)*
- Whole Joint Health Workshop (7/25–26/2023)
- NIH Consortium for Advancing Research on Botanical and Other Natural Products (CARBON) Program Investigator Meeting (7/27/2023)*

*Registration is open to investigators only.

Dr. Langevin noted that having investigator meetings are very important because it allows

investigators to build a community and inform each other about their findings, as well as exchange ideas and challenges.

Discussion. In response to a question from Dr. Haney, Dr. Langevin explained that the study by Hays et al., was pragmatic and did not control for additional attention from chiropractors. However, it is known from some studies that patients who see a chiropractor report better satisfaction with that care than with conventional care.

Prof. Magee asked Dr. Langevin if there were any highlights in UNITE's first report that she would like Council to think about with regard to NCCIH. Dr. Langevin said NCCIH and the Council have been talking about and building on UNITE extensively in the past year. The two UNITE components she highlighted in her response were: (1) UNITE addresses the extramural research that NIH funds, to ensure grant dollars are distributed in a way that maximizes equity and with specific attention to underserved groups, communities, and institutions; and (2) UNITE is looking at the internal NIH environment to ensure principles of equity, diversity, inclusion, and accessibility are applied to hiring practices, promotion, etc. While there is more to the initiative, considerable progress has already been made in these two areas at NIH and internally at NCCIH. The Center's plan to implement UNITE's principles includes not just ideas and plans but also actions and accountability. Prof. Magee asked whether Dr. Langevin might have one or two areas of concern to offer. Dr. Langevin said there are areas in which there has been healthy debate. One is whether efforts to promote diversity and equity are distributed across the many areas in which attention needs to be paid to equity, such as gender, race, and disability. It is necessary to be very thoughtful to ensure that attention is paid to all areas and that inequity is not inadvertently created.

Dr. Lavretsky asked what the lessons and consequences are from the stakeholder meeting for research on WPH. Dr. Langevin said that the motivation for the meeting was that, unlike many ICs, NCCIH never had "a coalition or friends' group" of interest around a common goal. Rather, there has been fragmentation among disciplines, professions, and topics. This meeting was a first step, built around interest in the theme of whole person health (WPH). NCCIH was pleased in the response received and the group's interest in coalescing further around WPH. What happens next is up to the stakeholder group. NCCIH will be meeting with them to learn more and Dr. Langevin will report back to Council. Dr. Lavretsky asked about the state of affairs with regard to long COVID funding and said complementary and integrative WPH could lead in this area. Dr. Langevin said all interested parties have been waiting for the NIH Researching COVID to Enhance Recovery (RECOVER) Initiative to issue funding opportunities for testing of complementary and integrative interventions, which is part of the plan. The work of RECOVER has been complicated by the nature of the pandemic, which has been a moving target (i.e., evolution of new variants and vaccination status of the population since the start). Dr. Soumyanath asked how natural products fit into the WPH initiative with regard to multiintervention approaches. Dr. Langevin said that in a 2020 portfolio analysis, analysts found that more of NCCIH's natural product studies than expected involved multisystem approaches. The

natural products portfolio can be incorporated into multisystem research.

IV. NCCIH and the NIH All of Us Research Program

Dr. Joshua Denny, chief executive officer of NIH's <u>All of Us Research Program</u> (AoU), discussed the program's historic effort to collect and study data from 1 million or more people living in the United States for the purpose of building a critical resource. The AoU mission is to accelerate health research and medical breakthroughs, enabling individualized prevention, treatment, and care. The program launched in 2018 and has enrolled 582,000 participants.

Registered researchers (access is most often granted under a master institutional agreement) are using AoU datasets—a registered tier and a controlled tier—to study many topics. AoU approaches health not just from the point of view of personalized or precision medicine but with a holistic approach as well. Dissecting individual health is a bigger endeavor than the use of genomics, surveys, electronic health records (EHRs), mobile health, metabolomics, geospatial data, environmental and demographic data, and imaging, although all these are important pieces of the health picture.

The goals of the program are to nurture partnerships for decades with at least 1 million participants who reflect the diversity of the United States; deliver one of the largest, richest biomedical datasets that is broadly available and secure; and catalyze an ecosystem of communities, researchers, and funders who are working to make *AoU* an indispensable part of health research. Participation is open to people in all states and territories. Trust in *AoU* is earned through transparency, and participants have access to their information. Data will be accessed broadly for research purposes, and the program is committed to building trust among participants about how their data are being used. The program is designed to be a catalyst for positive change in research. Security and privacy are priorities. The COVID-19 pandemic caused a pause in enrollment but brought growth in ways to reach people.

Participants' diversity in many sociodemographic factors was discussed. Overall, more than 80 percent of participants are from groups underrepresented in biomedical research. An important factor in achieving this diversity has been partnerships (e.g., participant centers, community and engagement partners, medical schools, and health care provider organizations), which also provide valuable advice to *AoU*. Data are collected from participants through surveys, physical measurements, bio samples, mobile/wearable technologies, consent, and electronic health records (EHRs). Information from various sources can often be linked and digitalized.

AoU has various approaches for return of value to its participants, including provision of genetic information, survey data (comparative), EHR and claims data, ongoing study updates, aggregate results/counts, and scientific findings. Dr. Denny also discussed the *AoU* genetics return strategy; researcher data access; the public data browser containing summary statistics; and the Researcher Workbench, a cloud-based central resource offering access to low-level data that is often diverse

and longitudinal.

AoU is working on a new release of the workbench's controlled tier that will contain more than 230,000 genomes. The diversity of genomic data from the AoU sample is noteworthy, and Dr. Denny hopes it will impact research globally. A hypothetical example was given of a genome-wide association study using some types of data in AoU. An actual AoU study was also presented, cosponsored with RECOVER, in people who possibly have long COVID. A demonstration workspace on this is available to researchers. The process for researchers to move from learning about the data available to them in AoU through the subsequent steps in access and use was presented. Dr. Denny then detailed the many kinds of studies and modalities of research AoU can support. He cautioned, however, that its sample is not representative of the United States and there is not uniform follow-up of all variables. He then provided results from several published papers.

Upcoming plans for *AoU* include more research in the COVID-19 space; a survey on mental health and well-being to be launched in collaboration with the National Institute of Mental Health (NIMH); and further development of an ancillary study, Exploring the Mind, also in partnership with NIMH. Major goals for *AoU* over the next 5 years include reaching enrollment of 1 million participants, expanding the data available to researchers, launching more ancillary studies; reaching a diverse global community of 10,000 researchers (up from 4,000 now) who use the data, and evaluating and expanding return of value to participants. He hopes the program will promote precision medicine across the United States. Dr. Denny gave examples of ancillary studies, including a detailed overview of the Common Fund's Nutrition for Precision Health study and some NIH research funding opportunities that are partnerships with *AoU*.

Discussion. Dr. Haney asked whether *AoU* includes substance use. Dr. Denny said that it does. *AoU* might get more involved in substance use research over the next year and would be interested in partnerships. In response to a second question from Dr. Haney, he said that the only data AoU is generating right now on its biospecimens is genomics. The program is seeking partnerships in ancillary studies that might build out additional types of analyses. Dr. Soumyanath asked whether AoU biospecimens are available for study and whether it has data on use of botanical dietary supplements. Dr. Denny said currently the biospecimens would not be available to researchers, but ancillary studies will take a stepped approach and probably eventually will open up availability. AoU encourages researchers to talk to NIH ICs in the dietary supplements space. Information AoU may have on participants' use of dietary supplements would be from EHRs and is usually minimal. This topic area is under-researched, and AoU might explore it in the future. To a question from Dr. Jean-Louis, Dr. Denny said that more than 100,000 whole genomes are available in the dataset, and the next release will be more than 230,000 whole genomes (AoU aims at 1 million). Prof. Magee asked whether AoU is obtaining information on contemplative practices. Dr. Denny detailed the types of information that might be pertinent and noted that researchers can query such data through the browser.

Dr. Langevin inquired about dietary supplements in the Precision Nutrition Study and noted that it might be an opportunity to look at how supplements act in relation to what a person eats. Dr. Denny said this very large nutrition study (and other studies) will examine this topic in greater depth. All the data will be coming back to the researcher workbench. Dr. Brolinson asked whether, if his medical school were an institutional member, students could participate in a mentored research project. Dr. Denny said yes, and AoU is very enthusiastic about trainees' use of these resources. Dr. Langevin brought up the WPH framework and asked about integration of a disease-focused approach with a more health-focused approach. Dr. Denny said this is one of the "million-dollar questions," and NCCIH and its Council would be experts for this topic. There has been more breadth in AoU's interests over time. He could foresee ancillary studies and elements that could be adopted. Dr. Langevin saw a shift in terms of a way to look at health that is complementary to the precision medicine targeted view. She looks forward to determining how NCCIH and AoU can interact and work together.

V. Environmental Influences on Child Health Outcomes (ECHO) and Shared Interests With NCCIH

Dr. Matthew Gillman presented information on the Environmental Influences on Child Health Outcomes (ECHO) program, for which he serves as the program director within the NIH Office of the Director. Following the closure of the National Children's Study in December 2014, Dr. Francis Collins, then-director of NIH, emphasized the importance of and need for research addressing the links between the environment and child health and development. In 2016, NIH launched the ECHO Program, a 7-year initiative, whose mission is to enhance the health of children for generations to come. The guiding concept is that a good start to life can last a lifetime and over generations. To ensure that good start, more knowledge and understanding are needed of potential risks and resiliencies and when and to whom they apply so as to undertake "precision prevention." This approach can inform programs, policies, and practices in an approach he called "solutions-oriented research."

The program's two major components are (1) the ECHO cohorts (for observational research in pediatric cohorts—this component was the focus of this presentation); and (2) the ECHO Institutional Development Award (IDeA) States Pediatric Clinical Trials Network (ISPCTN), for interventional research. The latter is relatively new. ECHO research is being conducted in 44 states, the District of Columbia, and Puerto Rico.

The goal of the ECHO cohorts is to answer solution-oriented questions about the effects of a broad range of early environmental exposures in six categories on health and development from conception to age 5. ECHO research focuses on five key pediatric outcomes with high public health impact: pre-, peri- and postnatal; upper and lower airway; obesity; neurodevelopment; and positive health. The diverse ECHO-wide cohort weaves together data from 69 preexisting and ongoing maternal-child cohort studies, and its related data platform has data from more than 103,000 participants from 69 cohort studies (including about 65,000 children and more than

90,000 specimens). The goals are to harmonize existing measures and standardize new measures for the common data collection protocol. In August 2022, ECHO announced the first release of <u>a</u> <u>controlled-access database</u>, which underpins a nationwide research resource: the Data and Specimen Hub (DASH) of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD). Researchers can apply for access. ECHO benefits from collaborations, not only with NCCIH but with other NIH Institutes, Centers, and Offices (ICO)—to date, almost 30 such collaborations. The next cycle for cofunding with the ECHO cohorts component is in September 2023 and is meant to last for another 7 years. Once underway, it will look at possibilities for co-funding with other NIH components.

Dr. Gillman explained that the usual approach in health research is a "negative" one that emphasizes suffering and disease, and studies what goes wrong. However, one can also study what goes right. For ECHO, positive health is more than the absence of disease; it encompasses physical, mental, and social well-being. It can be not only an outcome but an asset-based approach (i.e., focusing on strengths and assets that interact with each other). Assets can be personal assets, integrated functions, and environmental resources. Positive health is defined as well-being, measured as global health and/or life satisfaction and/or meaning and purpose. ECHO has measures for children aged 5 to 17, including the Patient-Reported Outcomes Measurement Information System (PROMIS) Meaning and Purpose Scale for Children. The approach to measurement allows specificity of outcome, facilitates communication, and fosters consistency over analyses.

Dr. Gillman said that ECHO's approach overlaps with the approach and framework of the NCCIH Strategic Plan (Objectives 1, 2, and 3). He detailed several high-impact collaborative ECHO analyses and their top-line results, along with potential implications for actions, strategies, tools, care, and development of interventions, including in complementary and integrative health, that appear consistent with NCCIH's whole person framework:

- Blackwell CK, Mansolf M, Sherlock P, et al. <u>Youth well-being during the COVID-19</u> <u>pandemic</u>. *Pediatrics*. 2022;149(4):e2021054754. **Key takeaways:** COVID-19-related family hardships contributed to caregiver and thus child stress, which, in turn, had an impact on child life satisfaction. Social connection and family engagement can promote children's life satisfaction, even amidst COVID-19 stress and hardships.
- Schuchard J, Blackwell CK, Ganiban JM, et al. <u>Influences of chronic physical and mental</u> <u>health conditions on child and adolescent positive health</u>. *Academic Pediatrics*. 2022;22:6,1024-1032.

Key takeaways: Many children with chronic conditions have similar levels of positive health as counterparts without chronic illness. Depression is associated with lower positive health and has a higher prevalence among children with chronic health conditions. More study is needed of the potential benefits of facilitating screening and/or treatment for depression among children with chronic conditions.

 Blackwell CK, Hartstein LE, Elliott AJ, et al. <u>Better sleep, better life? How sleep quality</u> <u>influences children's life satisfaction</u>. *Quality of Life Research*. 2020;29(9):2465-2474. Key takeaways: Children who sleep better have more satisfied lives. Poorer sleep quality was associated with poorer general health, which in turn was associated with lower life satisfaction via stress and global health. Sleep quality is important to children's health. This study was one of the first to examine sleep quality and positive health.

Dr. Gillman said ECHO is a major investment in understanding early environmental influences on child health. ECHO usually tries to identify gaps through engagement with stakeholders and seeks to inform practices, policies, and programs to the extent possible. The sample size is large, diverse, and generalizable, and the work is becoming a U.S. nationwide research resource. In closing, Dr. Gilman mentioned ECHO IDeA, which helps address disparities in pediatric research by including children from rural or underserved populations in clinical trials and building pediatric research capacity in states with historically low NIH funding.

Discussion. Dr. Lavretsky asked whether ECHO ever works on intergenerational interventions. Dr. Gillman replied that he and many people on the staff are interested in this. In IDeA, the focus so far has been on pediatrics as a place to start in a new network, but now there is discussion of studying intergenerational interventions by starting before birth. The ECHO cohorts component studies all have intergenerational research, and the preconception and prenatal periods will be added in the next ECHO cycle. Dr. Sibinga asked how much work ECHO is doing on inter-rater reliability between caregiver and child reports. The information received directly from children is an important piece. Dr. Gillman said one question is: from which respondents are the right answers coming? Another question is: how can we take both perspectives (caregiver and child) into account? A person-reported outcomes core is doing some work on reliability. Dr. Harris asked whether pain and sleep are tightly linked to well-being in the ECHO study, as is the case for adults. Dr. Gillman said that this question has not been addressed yet, but he will take the question back to staff.

Dr. Coghill commented that ECHO's emphasis on healthy development and defining what is protective against developing a disease state are important. Dr. Gillman said some ECHO investigators are doing studies of positive outliers who are resilient in the face of stressors. A theme at ECHO is how to keep children healthy who were born healthy. Dr. Langevin said that NCCIH's WPH framework does appear to align with ECHO's well-being model, and she asked if NCCIH and ECHO could also align on its measurement. Dr. Gillman said he thinks the three domains from ECHO encompass components of what is meant by well-being. ECHO conceptualizes positive health as well-being and measures it by global health life satisfaction, meaning, and purpose. Especially for children, this is a child-centric outcome and disease agnostic. Dr. Langevin agreed and mentioned seeing this as similar to the Department of Veterans Administration's (VA) Whole Health program.

Dr. Lavretsky said she works in this area and has struggled with measurement. She thinks it would be important to understand what features represent resilience—beyond whether a person

has depression. There is no good PROMIS measure on resilience, especially for children. Dr. Gillman said people in the ECHO consortium have been thinking about resilience, not as a domain in itself but as one of the assets. He and Dr. Lavretsky are interested in talking further. Dr. Kligler mentioned work going on at the VA on how to define and measure whole health. Also, there is a Federal interagency workgroup that focuses on equitable long-term recovery and resilience (ELTRR). It is making progress toward a definition of well-being and assessing what measures agencies use. Dr. Langevin agreed that resilience is very complicated and layered, including to attempt to define the term. She suggested "pinning down well-being" could be a first step. Dr. Gillman said he does not think the field has all the needed measures yet, but he is happy to be in this conversation. Dr. Gillman confirmed the start of the next cycle for ECHO and the plans for funding announcements; the latter have been released, and all the applications are in. There will be ancillary study opportunities to which outside collaborators can respond if they will collaborate with an ECHO investigator.

VI. Concept Clearance: Research Resource for Systematic Review of Complementary and Integrative Health

Dr. Peter Murray, a program director in DER, presented this concept to establish a research resource for systematic reviews in complementary and integrative health. NCCIH funds clinical research to generate data that informs clinical practice, health policy, and research program decision making. Aggregating study results is challenging, especially when methods and outcomes differ across studies. Systematic reviews provide a methodological tool to summarize study results in an unbiased manner and to assess literature for publication bias. Systematic reviews may conclude that additional research is needed before a recommendation can be made regarding a given intervention, which may help guide health care practitioners, patients, health care policy, and research administration and can help inform NCCIH about research gaps and shape portfolio development.

NCCIH has funded several groups to conduct systematic reviews of complementary and integrative health approaches: (1) acupuncture systematic reviews, (2) evidence report summaries from the Agency for Health Research and Quality (AHRQ), and (3) Cochrane Complementary Medicine (formerly called the Cochrane CAM Field). These projects have resulted in high-impact publications of systematic reviews. NCCIH continually funded Cochrane Complementary Medicine starting in 2003. Its register includes over 101,000 published complementary and integrative health-related controlled trials and nearly 1,000 systematic reviews.

The present concept is for a research resource for the continuation of a database of controlled trials of complementary and integrative health interventions. The research team would need to describe how to establish a database or convert an existing database, as well as how it will be maintained and kept current. They would also need to increase outreach on, access to, and availability of the database to a broader scientific community, the public, and policymakers.

They would conduct and/or update a series of high-quality systematic reviews and meta-analyses each year that align with the NCCIH Strategic Plan; WPH would be of particular interest. Another objective is to further develop and enhance the methods of systematic reviews and metaanalyses for nonpharmacologic interventions.

Discussion. Dr. Kligler asked how this work would relate to the present field on this topic in Cochrane. Dr. Murray responded that NCCIH's longtime award for the Cochrane work is coming to an end, and NCCIH is thinking about how to continue to provide a similar resource. Per policy he could not give more specifics, but he returned to the overall goals. Dr. Haney asked for a little more clarification on the concept, and Dr. Murray said that in this kind of concept put forward to Council, strategies have not been worked out yet to accomplish the goals outlined. Dr. Lavretsky asked whether the project(s) would be similar to those from Cochrane or offer other features. Dr. Murray said that it appears the proposed objectives are quite aligned with what Cochrane is doing, but NCCIH thinks applicants could propose different strategies to meet the goals of the initiative. Dr. Langevin explained that a concept for clearance can provide a preview of a general idea that NCCIH is thinking about and receive feedback from Council. It does not go into specific funding opportunities.

Dr. Shurtleff said that following on the current NCCIH-supported Cochrane work, which is coming to an end, NCCIH would think not only about the past but aspects of whether to continue the work. "Is there value there?" is a question. Prof. Magee asked about goals or objectives to make this information more available to the non-researcher community. Dr. Shurtleff said this concept has a relation to NCCIH's Know the Science program, which helps people learn to evaluate scientific and medical information in a critical way. Dr. Murray gave more examples of NCCIH's information dissemination activities to reach the general public, not just the research community.

Dr. Soumyanath called this kind of work important and said it should continue. There is much nuance in complementary and integrative medicine, including in botanicals. She suggested exploring a means to provide funding (e.g., as administrative supplements) for experts to produce reviews as a way to support such an initiative. Many experts do this already for their own knowledge, but it is time consuming. Dr. Brolinson noted the complexity and importance of this topic, and that despite Cochrane's long existence, most of what health care providers do in practicing medicine may not be evidence-based or may be based on flawed or poorly designed studies. Dr. Dickerson said that adding some specifics (e.g., "to understand pain" or "to inform decisions about cannabis") might help the focus toward achieving the desired benefits. He also thought there might be more mention of implementation science and translation of findings, which are major elements in HEAL. Dr. Edwards said that NCCIH staff published a position paper 2 years ago detailing NCCIH's interest and progress in dissemination and implementation science and has offered funding opportunities in that space. She also noted that the Center has added a component on it to NCCIH's clinical trial framework. Dr. Langevin added that through the work of NCCIH staff who are part of the NIH HEAL Initiative, she sees that NCCIH has had

an impact on promoting pragmatic and implementation trials within that initiative.

Dr. Sibinga expressed support of the concept and the importance of systematic reviews and meta-analyses to clinicians. This seems appropriate for NCCIH to lead, in a thoughtful way, as otherwise this work often gets folded into other projects and the complexity of the analytic approach might not be served. Council voted on the concept and approved it unanimously.

VII. Public Comments

Oral public comments cannot be given during this virtual meeting, but written comments can be submitted to Dr. Schmidt by email (Martina.Schmidt@nih.gov) or postal mail (<u>address</u> on the NCCIH website) within 15 days after the meeting. Comments may be up to 750 words.

VIII. Final Comments and Adjournment

Dr. Langevin thanked Council for their time, attention, and engagement and thanked Dr. Schmidt for leading her first Council meeting. Dr. Schmidt thanked Council and the staff who made the meeting and teleconference possible, noting that NCCIH would not be able to pursue its mission without Council's expertise and feedback and the help of staff Center-wide. Dr. Langevin added her thanks to staff. The meeting adjourned at 3:50 p.m. ET.

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

Martina Schmidt, Ph.D. Executive Secretary National Advisory Council for Complementary and Integrative Health Helene M. Langevin, M.D.ChairpersonNational Advisory Council for Complementary and Integrative Health