

NATIONAL INSTITUTES OF HEALTH
NATIONAL INSTITUTE ON AGING

Summary Minutes

The 150th Meeting
NATIONAL ADVISORY COUNCIL ON AGING
September 19-20, 2023

National Institutes of Health
Hybrid Meeting
Bethesda, MD 20892

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Department of Health and Human Services
Public Health Service
National Institutes of Health
National Institute on Aging
NATIONAL ADVISORY COUNCIL ON AGING
SUMMARY MINUTES
September 20, 2023

The 150th meeting of the National Advisory Council on Aging (NACA) was convened on Wednesday, September 20, 2023, at 9 a.m. in person and by videoconference. Dr. Richard Hodes, Director, National Institute on Aging (NIA), presided.

In accordance with the provisions of Public Law 92–463, the meeting was closed to the public on Tuesday, September 19, from 3:00 p.m. to 5 p.m. for the review, discussion, and evaluation of grant applications in accordance with the provisions set forth in Sections 552(b)(c)(4) and 552(b)(c)(6), Title 5, U.S. Code and Section 10(d) of Public Law 92–463.¹ The meeting was open to the public on Wednesday, September 20, from 9:00 a.m. to 1:30 p.m.

Council Participants:

Dr. Sanjay Asthana
Dr. Darren Baker
Dr. Anne Case
Dr. Maritza Ciliberto
Dr. Yanira Cruz
Dr. Susan L. Greenspan
Dr. Yadong Huang
Dr. Rev. Cynthia Huling Hummel
Dr. Sharon K. Inouye
Dr. Sohail Khan
Dr. Frank Longo
Ms. Nancy E. Lundeborg (attended virtually)
Dr. Jennifer Jaie Manly
Dr. Charlotte Peterson
Dr. David B. Reuben
Dr. Julie A. Schneider
Dr. Linda J. Van Eldik
Dr. David R. Weir

Executive Secretary:

Dr. Kenneth Santora, NIA

Ex Officio Participants:

Dr. Radha Holavanahalli, Administration for Community Living (ACL)
Dr. Anne Ordway, National Institute on Disability, Independent Living, and Rehabilitation, ACL

¹ For the record, it is noted that members absented themselves from the meeting when the Council discussed applications (a) from their respective institutions or (b) in which a conflict of interest may have occurred. This procedure only applied to applications that were discussed individually, not to “en bloc” actions.

Members of the Public Present:

Dr. Stacey Drury, Psychiatrist-in-Chief, Boston Children's Hospital

Dr. Rebecca Harston, Executive Account Director, Business Development. PPD, part of Thermo Fisher Scientific

Celeste Crouse, Director, Project Management, PPD, part of Thermo Fisher Scientific

Dr. Eline Appelmans, Data Science Specialist, Digital Infuzion

In Addition to NIA Staff, Other Federal Employees Present:

Dr. Matthew W. Gillman, Director, Environmental Influences on Child Health Outcomes (ECHO)

592 live views via NIH videocast.

I. REVIEW OF APPLICATIONS

This portion of the meeting was closed to the public, in accordance with the determination that it concerned matters exempt from mandatory disclosure under Sections 552(b)(c)(4) and 552(b)(c)(6), Title 5, U.S. Code and Section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix).²

A total of 2,077 applications requesting \$5,687,178,508 for all years underwent initial review. The Council recommended 1,121 awards for a total of \$3,304,668,769 for all years. The actual funding of the awards recommended is determined by the availability of funds, percentile ranks, priority scores, and program relevance.

II. CALL TO ORDER

Dr. Kenneth Santora welcomed members to the open session of the 150th NACA meeting. Dr. Richard Hodes called the meeting to order at 9:00 a.m. on Wednesday, September 20, 2023.

Director's Status Report

Appropriations Status for the National Institute on Aging

The current fiscal year (FY) 2023 will end on September 30, and the National Institutes of Health (NIH) and NIA are awaiting the next congressional appropriation for FY2024. On June 14, 2023, the House Labor-Department of Health and Human Services spending bill advanced out of the subcommittee and is awaiting consideration by the full committee, followed by the House. If the House spending bill is enacted, NIH would receive \$43 billion, a \$3.8 billion decrease from FY2023, and NIA would receive \$4.41 billion as flat funding relative to FY2023. On July 27, 2023, the Senate Labor, Health and Human Services, Education, and Related Agencies appropriations bill advanced out of the full Committee on Appropriations and now awaits a Senate vote. If the Senate spending bill is enacted, NIH would receive \$47.8 billion, a \$943 million increase from FY2023, and NIA would receive \$4.51 billion, an increase of more than \$100 million from FY2023. The proposed Senate bill would also result in a \$100 million increase for Alzheimer's disease and Alzheimer's disease-related dementias (AD/ADRD) (\$90

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million increase to NIA and \$10 million increase to the National Institute on Neurological Disorders and Stroke) and an additional \$12 million for palliative care research. These appropriations depend on the avoidance of a government shutdown as well as signature from the President.

2025 Professional Judgment Budget for Alzheimer's Disease and Alzheimer's Disease-Related Dementias

Each year through 2025, the NIH Director submits a professional judgment budget directly to the President for the NIH initiatives pursuant to the National Alzheimer's Plan.³ This professional judgment budget reflects input from NIH, academia, industry, other federal agencies, nongovernmental organizations, and advocates. The budget outlines priorities, gaps, and opportunities that are then translated into specific milestones to address the initiatives' goals as well as funding allocation requests to accomplish each milestone. The [FY2025 Professional Judgment Budget Proposal](#) requests a total of \$4.07 billion for AD/ADRD research with a \$3.75 billion baseline based on FY2023 and an additional \$318.07 million for additional research (based on total new research cost of \$504.06 million minus \$186 million of funding from completed projects available to new research). The additional funding requested will support research in the following areas: epidemiology and population studies (\$82 million); disease mechanisms (\$35 million); diagnosis, assessment, and disease monitoring (\$72 million); translational research and clinical interventions (\$131 million); dementia care and impact of disease (\$28.05 million); research resources (\$101 million); ADRD (\$45 million); and staffing needs and administrative support (\$10.01 million).

2023 National Institutes of Health Report: Alzheimer's Disease and Related Dementias Research

The [2023 NIH Report on ADRD](#) summarizes significant NIH-funded dementia research advances over the past 10 years. These accomplishments include (1) advancing understanding of the risk factors, genetics, and mechanisms of dementia; (2) diversifying and de-risking the therapeutic pipeline for disease-modifying drugs; (3) accelerating drug repurposing and combination therapy development; (4) developing tools to detect, diagnose, and monitor dementia; (5) advancing clinical research on lifestyle interventions; (6) increasing our understanding of how social and environmental factors affect dementia risk and disparities; and (7) expanding research on dementia care and care partner supports.

National Institute on Aging Updates

Dr. Hodes summarized NIA updates. In September 2023, NIA launched the [EUREKA challenge prize competition](#) to discover the best data, methods, and strategies for the early prediction of AD/ADRD. This challenge includes an emphasis on building diverse teams and solutions to include groups historically excluded from participation in AD/ADRD research and will offer cash awards totaling \$650,000.

Beginning in 2022, NIA has offered several training awards designed to develop a wider range of professional skills and experiences (e.g., bio-entrepreneurship; intellectual property; science communications, policy, and education; regulatory affairs; drug discovery, approval, and production; consulting) both within and outside of academic research under the [Research and](#)

³ As required under section 2(d)(2) of Public Law 111-375.

[Entrepreneurial Development Immersion \(REDI\) Program](#). The next deadline for the REDI Mentored Entrepreneurial Career Development Award ([PAR-22-227](#)) is October 18, 2023. In addition, while a letter of intent is due 30 days prior, the deadline for the REDI Entrepreneurship Enhancement Award ([PAR-22-226](#)) is also October 18, 2023.

As required by the FY2023 Consolidated Appropriations Act, NIA and the National Institute on Neurological Disorders and Stroke have entered into an agreement with the National Academies of Sciences, Engineering, and Medicine (NASEM) to identify research priorities for preventing and treating AD/ADRD. The task order was established on March 27, 2023, and the NASEM committee is expected to be established in September 2023. The committee will (1) examine and assess the current state of biomedical research aimed at preventing and effectively treating AD/ADRD, along with the research and development pipeline from basic to translational to clinical research; (2) assess the evidence on nonpharmacological interventions aimed at preventing and treating AD/ADRD; (3) identify key barriers to advancing AD/ADRD prevention and treatment and opportunities to address these key barriers and catalyze advances across the field; and (4) explore the most promising areas of research into preventing and treating AD/ADRD. The final report is anticipated in the beginning of 2025.

NIA has launched [OutreachPro](#), an AD/ADRD clinical trial recruitment tool that helps researchers and grantees create outreach materials designed for and tested with specific audiences. These materials were systematically created through literature reviews, listening sessions with stakeholders, focus groups, surveys, and user feedback testing. Users can develop more than 200 unique, customized materials using combinations of designs, health statuses, demographics, and languages.

NIA, in collaboration with the Foundation for the National Institutes of Health and the McKnight Brain Research Foundation, will host the fourth Cognitive Aging Summit on March 20-21, 2024, at the Bethesda North Marriott Hotel and Conference Center. In addition, since May 2023, NIA has released 20 research highlights featuring NIA-supported publications, 16 blog posts, and 3 news announcements. Dr. Hodes and other senior NIA staff have participated in 15 stakeholder and advocacy group meetings as well as 4 congressional briefings and hearings.

National Institutes of Health Updates

Dr. Hodes also summarized NIH updates. On May 15, 2023, President Joseph R. Biden announced his intent to nominate Dr. Monica Bertagnolli as the NIH Director. She is the current Director of the National Cancer Institute and is a world-renowned surgical oncologist, cancer researcher, and educator. Her appointment as NIH Director requires confirmation by the U.S. Senate, and most recent conversations have suggested this hearing will occur in October 2023.

NIH posted a Request for Information (RFI) inviting comments and suggestions on updating the NIH mission statement ([NOT-OD-23-163](#)); the deadline for responses is November 24, 2023. The RFI is requesting feedback on the following proposed revised mission statement: “To seek fundamental knowledge about the nature and behavior of living systems and to apply that knowledge to optimize health and prevent or reduce illness for all people.” This new mission statement removes the intent to reduce disability, and NIH is especially seeking responses from those in the disability community.

NIH has established its Institutional Excellence in Diversity, Equity, Inclusion, and Accessibility (DEIA) in Biomedical and Behavioral Research Prize Competition, which is a new initiative that aims to recognize and reward effective strategies for enhancing DEIA in research environments across the United States. Entries are due September 26, 2023, and NIH will award up to 10 prizes of \$100,000 to academic institutions.

Discussion

Dr. Hodes clarified that the additional \$318.06 million in funding requested above the baseline from FY2023 is exclusively for new research projects. If approved, these additional funds will become part of the next FY baseline funds.

A. Staff Introductions

NIA leadership introduced new NIA staff members from the Divisions of Aging Biology (DAB), Behavioral and Social Research (BSR), Neuroscience (DN), Geriatrics and Clinical Gerontology (DGCG); the Division of Extramural Activities (DEA) Grants and Contracts Management Branch (GCMB), Office of Clinical Research (OCR), and Scientific Review Branch (SRB); the Office of Administrative Management (OAM) Contract, Acquisitions, and Procurement Branch (CAPB), Financial Management Branch (FMB), Workforce and Administrative Management Branch (WAMB), and Information Technology Branch (ITB); the Office of the Director (OD) and the OD Office of Special Population (OSP); the Office of the Associate Director (OAD) Office of Planning, Analysis, and Evaluation (OPAE) and Office of Legislation, Policy, and International Activities (OLPIA); and the Intramural Research Program (IRP). Dr. Hodes also thanked Dr. Ronald Kohanski, who will retire as Director of DAB.

B. Future Meeting Dates

January 23-24, 2024 (Tuesday and Wednesday), Virtual
May 21-22, 2024 (Tuesday and Wednesday), Building 45
September 18-19, 2024 (Wednesday and Thursday), Building 31

C. Consideration of Minutes of the Last Meeting

The minutes of the May 2023 Council meeting were considered. A motion was made, seconded, and passed unanimously to approve the minutes.

III. REPORT: TASK FORCE ON MINORITY AGING RESEARCH

Drs. Jennifer Manly and Yanira Cruz summarized presentations to the Task Force on Minority Aging Research by Dr. Karina Walters, Ms. Lisa Sockabasin, Dr. Natasha Bray, and Dr. Terry Cronan, which were centered on workforce development.

During her presentation, Dr. Walters acknowledged that NIH sits upon the ancestral homelands of the Piscataway Conoy Tribe and emphasized the sovereignty of 574 tribal nations in the United States, consisting of 9.7 million people who identify as American Indian/Alaska Native (AI/AN). AI/AN includes many diverse cultures and more than 200 languages. Approximately 70 percent of AI/AN people live in urban areas and 13.2 percent on tribal lands. Currently, AI/AN people have a life expectancy of 65 years, the lowest age since 1944 and 5.5 years less

than other racial and ethnic groups. Greater than 25 percent of AI/AN people die before the age of 45, compared to 15 percent for African American people and 7 percent for White people. In addition, the scientific workforce contains very few people who identify as AI/AN, with only 0.33 percent of Ph.D. holders identifying as AI/AN. Therefore, the NIH Tribal Health Office coordinates and collaborates with tribal partners to conduct research and build a workforce that is beneficial for AI/AN individuals. Dr. Walters provided specific strategies to increase the number of AI/AN researchers: changing institutional climates to be more welcoming and minimize distressful microaggressions and discrimination, increasing mentorship opportunities, and providing resources to help AI/AN researchers overcome challenges related to family and work-life balance, because one in four AI/AN undergraduates are parents. In addition, research funding specifically related to the AI/AN community is increasing, with \$180 million in FY2018, \$330 million in FY2022, and an expected \$347 million in FY2023.

Ms. Sockabasin spoke about the Center for Wabanaki Public Health and its current AD/ADRD study funded by the Native American Research Centers for Health in partnership with the University of Miami and Washington State University. This four-year project, which focuses on Wabanaki elders aged 55 years and older, uses a community-based participatory approach to study the health, lifestyle, risk factors, and AD/ADRD prevalence, and is building research capacity in the community.

Dr. Bray spoke about her work as Dean of the Oklahoma State University College of Osteopathic Medicine to recruit individuals who identify as AI/AN. The College uses alternative admissions strategies to increase the number of underrepresented students in its program. To date, 66 individuals who would have been rejected from the program based on traditional admission strategies have completed their education and are now practicing osteopathic medicine. She also spoke about branding and the removal of barriers that communicate bias to increase recruitment of faculty of color.

Dr. Cronan presented on her work as the Director of the Advancing Diversity in Aging Research Program at San Diego State University. This program enrolls rising junior-year students at San Diego State University, most of whom identify as Mexican American. This three-year program provides mentored research opportunities, including those outside of the university, intensive coursework seminars, and a special seminar dedicated to building resilience and fostering a sense of belonging among trainees who are often first-generation college students. Despite the effects of the COVID-19 pandemic, program scholars have experienced success, with students receiving honors and awards, authorship on published articles and abstracts, and admissions to graduate school.

Drs. Cruz and Manly emphasized the importance of inclusion in aging research as well as scientific research workforce diversity in improving health and aging in the United States. A common theme when discussing health inequalities is the need for community-based participatory research, which requires study teams to hire researchers from the community itself. Aging research on diverse populations requires early and intentional engagement with these communities to design more inclusive studies. The composition of research teams should also reflect that of the communities they study. A rate-limiting step in increasing diversity in the research community is organizational climate; as a major funder of aging research, NIA can require that funded institutions take concrete steps to improve their organizational climates. In

addition, NIA can add diversity and inclusivity efforts as a consideration in grant application reviews. Institutions need to engage with and provide mentorship to minority populations during high school and college to promote scientific workforce diversity.

Life course approaches to aging research must factor in structures and forces that are seemingly race neutral but can have disparate effects on minority populations. These disparate effects can result in a cascade of health consequences and disparities in aging. Research should not only focus on how to remove these negative factors but also begin to repair the historical damage done to these minority populations and commit to the healing of these populations and their future generations.

Discussion

Dr. Santora noted that the Clinical Research Office has hired Katasha Davis to specifically focus on ways to increase diversity and inclusion in aging research. She has expertise in community-based research and recruitment of underrepresented minorities.

Dr. Charlotte Peterson agreed that NIA should support efforts to increase institutional diversity and inclusivity but also discourage efforts that may impede the promotion of these values.

Dr. Frank Longo expressed concern about individuals from minority populations losing interest in science before they reach high school; this loss may contribute to the ongoing issue of too few faculty candidates from diverse backgrounds. He posited that institutions could perform outreach activities to students at a younger age to establish and maintain interest in research. Dr. Longo also noted that NIA could require grant applicants to describe activities promoting diversity and inclusion in the environment description portion of the application. Dr. Manly recalled Dr. Bray's efforts in promoting a sense of belonging to increase and maintain diversity of faculty at her institution through actions such as the promotion of inclusive cultural celebrations. Training programs that succeed at increasing diversity often include mentors who come from the very communities that these training programs are trying to include. By having mentors from similar cultural backgrounds with shared lived experiences, younger students and trainees can develop a sense of belonging from seeing those from their same communities—who were also likely first-generation college students—be successful in scientific research and health care.

Dr. Patricia Jones explained that institutions with knowledge of past and present relationships with local underrepresented communities are best positioned to develop outreach strategies that help promote diversity and inclusion. For example, the Clinical and Translational Science Institute at the Medical College of Wisconsin has a program called 500 Stars, which is a direct reflection of the College's understanding of historical racial tensions between the college and local community. This program promotes and enables conversations with middle school students about education, careers, and college choices. Dr. Jones also emphasized the importance of institutional and program leadership reflecting not only the demographic composition but also the lived experiences of underrepresented minorities.

Dr. Julie Schneider asked about how White researchers and institutional leaders can contribute to outreach efforts to underrepresented communities. Dr. Manly explained that White researchers who are sponsors and mentors to individuals from underrepresented communities should put these individuals forward for growth opportunities and career advancement. White mentors can also help these individuals gain leadership skills to prepare them for future roles. These actions

may also include stepping aside to make room for individuals from underrepresented communities in leadership. Dr. Jones emphasized that allyship can come in many forms, which can include White mentors, such as the Irish Catholic nun who played such a critical role in inspiring her to pursue basic science.

Dr. Sanjay Asthana acknowledged NIA's significant DEIA efforts that have made it possible to study diverse aspects of aging through multiple funding mechanisms. He further noted that building trust with underrepresented minority communities can take years of ongoing effort and asked whether NIA can further strategize to provide more funds to programs that aim to increase community-based research activities. Dr. Santora noted that NIA grant applications, particularly those that include larger clinical trials, propose plans for community-based activities. NIA can support community-based research activities by leveraging resources developed by NIA-funded studies to help develop best practices, resources, and tools that are culturally relevant for establishing community engagement activities.

IV. REPORT: WORKING GROUP ON PROGRAM

Dr. Greenspan, Chair of the Working Group on Program (WGOP), led the updates on all 23 concept clearances. The Council members unanimously and enthusiastically concurred with approval of all concepts, summarized below.

A. Notice of Funding Opportunity Concept Clearances: Division of Aging Biology

Dr. Greenspan invited Dr. Charlotte Peterson, the primary reviewer of the two proposed concepts for DAB, to present the concept to the Council. The Council members strongly supported renewing both the Nathan Shock Centers of Excellence in the Basic Biology of Aging and the Nathan Shock Centers of Excellence in the Basic Biology of Aging Coordinating Center concepts, summarized below.

Nathan Shock Centers of Excellence in the Basic Biology of Aging

The Nathan Shocks Centers of Excellence in the Basic Biology of Aging Program was initiated in 1995 and currently funds eight Centers of Excellence. These Centers provide expertise and core facilities for aging research and have been a cornerstone of basic aging biology research at NIA. These eight Centers cover the breadth of priority areas for DAB, and each offers diverse technologies and expertise to serve the aging research community in most areas supported by DAB. Centers also provide pilot funding for individuals to use core facilities. Although most of this pilot funding is awarded to young investigators at institutions with a Center of Excellence, the Centers are increasingly advertising these opportunities to encourage applications from investigators from any institution and country. Renewal of this concept would provide opportunities for new applications for Centers of Excellence. The Program underwent a review and evaluation between 2022 and 2023, and the evaluation team noted that the Centers were achieving their goals of leading and innovating aging research, attracting and training scholars, and promoting collaboration. The evaluation team identified some areas for improvement in promoting collaborations, and the NOFO addressed these prioritized improvements.

Nathan Shock Centers of Excellence in the Basic Biology of Aging Coordinating Center

The Nathan Shock Centers of Excellence in the Basic Biology of Aging Coordinating Center was established in 2017, well after the initiation of the initial Centers of Excellence. The goal of the

Coordinating Center is to provide outreach to the broader aging research community and to track the impact of each Center of Excellence. The Coordinating Center also underwent an evaluation in 2022, and the evaluation team noted significant progress in all goals, including outreach to researchers and enhancement of resource sharing across Centers. The Coordinating Center also provides logistical support to pilot grant recipients and has promoted interactions across Centers and with other aging organizations. When asked for feedback on the Coordinating Center, principal investigators (PIs) of each of the eight Centers expressed positive feedback on its contributions. The Coordinating Center has a broad social media presence where they advertise webinars and have increased the profile of these Centers of Excellence. The evaluation team provided some areas for improvement for the Coordinating Center, although most were strictly administrative.

B. Notice of Funding Opportunity Concept Clearances: Division of Behavioral and Social Research

Dr. Greenspan invited primary reviewers to present their respective BSR concepts to the Council. Primary reviewers were Drs. Weir, Manley, Reuben, and Asthana.

Research Collaboration Network in Structural Racism Measurement and Modeling

This concept proposes the creation of a new R24 Cooperative Agreement Network to advance the study of health disparities in the context of structural racism. This concept follows recommendations from the 2019 NACA review of BSR and a previous NASEM meeting. Because researchers who study health disparities may not have expertise in measurement and modeling of structural racism, this type of research tends to be performed by social scientists who do not primarily focus on health research. By bringing together these two groups, health disparities researchers and social scientists can collaborate to better model and measure the effects of structural racism on health disparities. Dr. Manly had recommended the applicant improve the presentation and explanation about the specific agenda for this concept.

Centers on the Demography and Economics of Aging, Including Alzheimer's Disease and Alzheimer's Disease Related Dementias (AD/ADRD) and Coordinating Center

The renewal request for this concept would continue support for demography and economics of aging P30 programs that encourage new and innovative research in the field. Renewing this program would add a new emphasis on the inclusion of a more representative group of scholars and institutions. Currently, only 3 out of 15 demography and economics centers focus on AD/ADRD. These three centers support pilot projects, establish research networks, host conferences and workshops, develop and promote research resources and infrastructure, and share results and resources with the scientific community and general public. The new call for centers includes two optional cores—the pilot core and remote data enclave core—in addition to the administration and research support cores. The former would enhance research capacity building outside the boundaries of the respective institution, while the latter would enhance and streamline data access across multiple sources. Dr. Inouye recommended making all three cores required in the Request for Applications (RFA), and WGOP members accepted this recommendation.

Deriving Common Data Elements from Real-World Data for Alzheimer's Disease and Alzheimer's Disease Related Dementias

Real-world data have the potential to unlock actionable health care insights not typically obtained from traditional randomized clinical trials or surveys. Implementation of common data elements (CDEs) across data systems can help enable data harmonization and subsequent large-scale data analysis. NIA assembled a technical expert panel that recommended the creation of CDEs that would be acceptable in cross-sectional and longitudinal studies from seven domains using electronic health records (EHRs). Under this concept, researchers will standardize vocabulary and develop and test longitudinal CDEs using EHRs and Centers for Medicare & Medicaid Services data. This effort will complement the Real-World Data Platform RFA that focuses on data transformation and harmonization. In addition, researchers will manage a research study program to encourage researchers to use CDEs.

Open Measurement Coordinating Network for Non-Pharmacological AD/ADRD Primary Prevention Trials

Although midlife is the optimal age group to target for primary prevention of AD/ADRD, many trials do not target this age group. Therefore, NIA formed a working group to discuss the current needs for developing primary prevention trials for AD/ADRD. The working group recommended establishing outcome measurements (e.g., biomarkers, functional outcomes) as the first step toward successful primary prevention trials. The goal of this concept is to establish a measurement coordinating network for non-pharmacological primary prevention trials for AD/ADRD. Specifically, this network will develop a framework of innovation to support, develop, validate, and disseminate measures and methods for AD/ADRD prediction and underlying disease mechanism identification. These measures can then be used to effectively measure trial outcomes. The network will create a platform to enable development of these outcome measures and support trials targeting a broad range of outcomes including cognition, social determinants of health, biomarkers, psychosocial outcomes, and functional outcomes. The platform will also help identify new study designs and factors that may affect measure validation. The network will also evaluate the platform to ensure that it adapts to the changing research environment. In addition, the network will interact with other NIA programs, including the Health and Retirement Study, NIA Toolbox, and Roybal Centers.

C. Notice of Funding Opportunity Concept Clearances: Division of Geriatrics and Clinical Gerontology

Dr. Greenspan invited primary reviewers, Drs. Asthana and Inouye, to present their respective DGCG concepts to the Council.

Consortium for Palliative Care Research Across the Lifespan

The core elements of this proposed consortium are to treat symptoms (e.g., pain, spiritual, psychological), identify goals of care, and facilitate care coordination at the end of life. The goals of this consortium are to (1) generate new scientific information in geriatric palliative care, (2) foster development of new early- and mid-stage researchers in the field, (3) serve as a national resource center to facilitate high-quality research on palliative care, and (4) engage health care systems and communities. This concept clearly aligns with NIA's mission. Program development activities for this initiative include workshops involving the National Palliative Care Research Center and other working groups. The concept proposed several essential cores

that were appropriate, but there was some discussion about whether AD/ADRD itself should be a core. The Council decided that AD/ADRD would instead be integrated at all the program's cores rather than comprise a standalone core.

Safety and Early Efficacy Studies of Psychedelic-Assisted Therapy for Chronic Pain in Older Adults

Recent studies have demonstrated the efficacy of psychedelic-assisted treatment (PAT) in major and refractory depression; however, these studies did not include older adults. Therefore, the overarching goal of this concept is to develop a strong evidence base for the safety and preliminary efficacy of PAT for chronic pain in older adults. This concept will use a two-phased approach: (1) safety studies in healthy older adults and (2) expanded safety and preliminary efficacy studies in older adults with chronic pain conditions. Testing of PAT requires careful patient screening and preparatory psychotherapeutic sessions to avoid any counter-indications. PAT uses agents such as psilocybin and 3,4-Methylenedioxymethamphetamine (MDMA) in one to three dosing sessions in combination with psychotherapeutic approaches (e.g., cognitive behavioral therapy) across a week-long intervention period. The concept will include a multi-center consortium to support this two-phased approach to test PAT across a broad older adult age range, including people aged 80 and over and eventually people with mild cognitive impairment and dementia. The Council emphasized the importance of specifically outlining pain sources and developing stratification plans by specific age ranges and people with dementia to detect any differences in safety in those of advanced age. It also recommended developing a more in-depth assessment of PAT acceptability and strategies to reduce or address stigma associated with psychedelic drug use.

D. Notice of Funding Opportunity Concept Clearances: Division of Neuroscience

Dr. Greenspan invited primary reviewers to present their respective DN concepts to the Council: Primary reviewers were Drs. Huang, Longo, Van Eldik, Weir, Manly, and Longo.

Multi-Scale Models Bridging Levels of Analysis in Aging and AD/ADRD

The rapid evolution of computational science, including artificial intelligence and machine learning, is generating new strategies for studying AD/ADRD. These approaches enable multifunctional modeling that can provide useful new insights into aging and AD/ADRD. The concept aims to develop a multi-scale computational framework to model changes associated with aging and AD/ADRD to address a specific research question, and this framework should bridge at least two levels of analysis on the spatial (e.g., cells, behavioral, etc.) or temporal scales (e.g., short snapshots of time, generations, etc.). This integrative approach will help bridge investigators using computational approaches with those using experimental approaches.

Translational Bioinformatics and Experimental Approaches to Advance Drug Repositioning and Combination Therapy Development for Alzheimer's Disease and Related Dementias

NIA previously established this [cross-disciplinary program](#) in 2017 to utilize translational bioinformatics to repurpose drugs and combination therapies for AD/ADRD. By repurposing existing drugs, researchers can shorten drug development times and reduce costs while improving drug development success rates. This program has brought together data science investigators and AD/ADRD investigators to apply computational methods for drug repurposing, identifying hundreds of candidate drugs for AD/ADRD. However, further development of these

candidates requires experimental and functional data validating the efficacy of drug and combination therapy for AD/ADRD. With the renewal of this concept, the program will (1) expand NIA's investment in data-driven approaches to AD/ADRD drug repurposing and combination therapy development and (2) conduct preclinical proof-of-concept efficacy and mechanistic studies in in vitro and in vivo disease models. To support both efforts simultaneously, the program will only support computational approaches when proposed in conjunction with experimental efficacy studies. This program will also facilitate full transparency of methods and data reporting.

Exploring Proteogenomic Approaches to Unravel the Mechanisms of Misfolded Protein Accumulation in Tauopathies

Although misprocessed and misfolded proteins are defining characteristics of AD and many ADRDs, traditional omics approaches cannot detect these protein states. Therefore, this concept aims to use a proteogenomics (i.e., a novel strategy combining proteomics, transcriptomics, and genomics data to identify novel proteins) approach to identify atypical proteins in tauopathies as a proof-of-concept to study the underlying mechanisms of protein processing in early pathogenesis of AD tauopathies. For example, single nucleotide variants, frameshift variants, and alternatively spliced isoforms may be associated with misfolded protein products. The concept will (1) identify and confirm changes in protein processing and folding and (2) use robust biological inference to improve understanding of proteomic data. This concept may require other approaches (e.g., RNA sequencing, mass spectrometry-based deep proteomic analysis, transgenic mice) for functional studies of altered protein homeostasis in response to the accumulation of misprocessed and misfolded proteins in AD.

Small Research Grant Program for the Next Generation of Researchers in Low- and Middle-Income Countries (LMICs) for Aging and Alzheimer's Disease and AD-Related Dementias Research

Diversity in global AD/ADRD research is critical for ensuring the generalizability of results. However, junior investigators in LMICs often lack sufficient financial support and face challenges in applying for and utilizing NIH K awards, the main mechanism for junior investigator development. Therefore, this concept proposes the use of Small Research Grants (R03) to support junior investigators in LMICs involved in AD/ADRD and aging research. By supporting these investigators, the concept will also advance AD/ADRD and aging research in LMICs, build local capacity for this research in LMICs, and support career development for researchers in the aging and AD/ADRD fields. The concept will also require applicants to include a professional development plan and identify a mentor. This Small Research Grant mechanism will provide LMIC junior investigators with greater flexibility and opportunities for data generation in preparation for later-stage independent funding proposals.

Consortium for Neuroscience AD/ADRD in Low- and Middle-Income Countries

This concept, along with others that will support LMICs, are crucial for future AD/ADRD research because two-thirds of the global population with AD/ADRD live in LMICs. This concept aims to provide five years of funding support to experienced LMIC scientists performing innovative and sustainable AD/ADRD research within their respective LMICs. With this funding, LMIC scientists can enhance their ability to compete for additional, future funding opportunities. This concept proposes using cooperative agreements to facilitate collaboration between LMIC and U.S. investigators. Proposed research should be investigator-initiated, and

applicants will need to explain how the proposed research can inform AD/ADRD prevention and treatment strategies across the globe. NIA will dispense awards directly to LMIC institutions.

Coordinating Center to Support the Consortium for Neuroscience AD/ADRD in Low- and Middle-Income Countries

This coordinating center will facilitate outreach, communication, and coordination for the Consortium for Neuroscience AD/ADRD in LMICs, which includes NIA LMIC junior investigator and established investigator awardees. This concept also proposes developing a portal to facilitate data sharing using existing databases in accordance with Findable, Accessible, Interoperable, and Reusable (FAIR) principles. The recipient of this coordinating center award will reside in the United States and have demonstrated expertise in coordination of research projects in LMICs.

Early- and Late-Stage Clinical Trials for the Spectrum of Alzheimer's Disease/Alzheimer's Related Dementias and Age-Related Cognitive Decline

Previously, this concept was successful in supporting a range of innovative treatment approaches beyond those targeting amyloid. This concept would support clinical testing (Phases I through III) of pharmacological and non-pharmacological interventions for cognitive and psychiatric symptoms in people with age-related cognitive decline and people across AD/ADRD stages. The concept may also support studies aimed at enhancing the design and methodology of AD/ADRD and age-related decline clinical trials, given the high cost of these clinical trials. This concept will require funding recipients to ensure diversity of study participants and make results and biospecimens available to the scientific community in a timely manner.

Alzheimer's Clinical Trials Consortium (ACTC) Clinical Trials

ACTC consists of NIA-supported clinical trials infrastructure and a network of 38 sites with the mission to provide optimal infrastructure to accelerate development of AD/ADRD interventions. This concept aims to increase the Consortium's number of pipeline interventions by funding clinical testing of promising interventions that target cognitive and psychiatric changes associated with age-related decline and AD/ADRD across disease stages (i.e., from pre-symptomatic to severe stages). Importantly, the Consortium does not duplicate efforts of pharmaceutical companies. ACTC's selection process involves a rigorous evaluation by a steering committee, and ACTC provides trial coordination and recruitment infrastructure to selected trials. One trial being launched is a small molecule clinical trial of a sigma-2 receptor antagonist, which may impact synaptic function. Another innovative trial under the ACTC involves testing the safety and efficacy of a combination of cannabinoids in hospice-eligible dementia patients.

Quantitative Systems Pharmacology Approach to Develop Predictive Models of Differential Responsiveness to Treatment

This concept addresses the challenge in AD/ADRD therapeutic development of identifying the patients most likely to respond to a particular treatment due to various patient and disease heterogeneities. This Quantitative Systems Pharmacology (QSP) approach combines computational and translational approaches at a systems level to determine mechanisms of action of drugs in preclinical models and patients. This concept will support the integration of multi-omics data generated from biosamples collected during previous and current AD/ADRD clinical trials. Multi-omics data paired with respective clinical and phenotypic data will enable the

construction of AD/ADRD predictive models and the discovery of determinants of treatment responsiveness, such as biomarkers. Importantly, this concept will also include support for QSP modeling of previously failed AD/ADRD therapeutics to understand why they failed. The concept will also encourage collaborations between academia and industry and require adherence to open-science principles.

Limited Competition: Renewal of, and Revisions to, the Alzheimer's Disease Genetics Consortium (ADGC)

This concept would renew ADGC, the coordinating center for the Alzheimer's Disease Sequencing Project (ADSP) Consortium. ADSP aims to sequence and analyze human genomes to identify genetic variants associated with increased or reduced risk of AD/ADRD. These results can also extend previous discoveries to result in new therapeutic directions for AD/ADRD. ADSP has more recently launched two initiatives: (1) diversity and phenotype harmonization and (2) functional genomics and AI/ML. Identification of risk variants in globally diverse populations can help identify personalized AD/ADRD interventions as well as more broadly generalizable disease mechanisms. In support of ADSP, ADGC will facilitate collaboration and communications across ADSP-funded projects and other NIA-funded efforts. ADGC will oversee and coordinate the following activities: generation of consortium methodologies, protocols, and tools; development and maintenance of a consortium resources online portal; data use for AI/ML initiatives; data sharing and access; pilot studies; and dissemination of ADSP resources to the research community.

E. Notice of Funding Opportunity Concept Clearances: Division of Extramural Activities

Dr. Greenspan invited primary reviewers to present their respective DEA concepts to the Council. Primary reviewers were Drs. Cruz, Schneider, Asthana, Van Eldik, and Schneider.

Renewal of Aging Research Dissertation Awards to Increase Diversity

This R36 award was established in 2005 to promote diversity of doctoral-level trainees engaged in aging and aging-related research. Applicants are Ph.D. students from underrepresented groups committed to a career as an aging researcher who require an additional one to two years of funding to complete their dissertation. This financial support provides recipients with a salary and may also cover travel to scientific meetings and other dissertation-related costs. Since its inception, the program has funded 78 awards, with 11 currently active awards. These awards have supported recipient authorship of more than 100 peer-reviewed publications. In the next phase of the program, NIA will set aside funding to support 10 awards per year and continue to identify additional strategies to best support those from groups underrepresented in aging research. Notably, increases in this R36 salary have not kept up with cost-of-living increases; this concept renewal proposes a salary of \$42,500 (an increase of \$15,356) and additional expenses support of \$28,656 (an increase of \$8,656).

Small Business Transition Grant for New Entrepreneurs

This concept aims to use lessons learned from the NIA REDI initiative and the National Cancer Institute Small Business Transition Grant to develop a diverse set of trainees with skillsets important for entrepreneurship and research and development. Under this concept, the SBIR/STTR mechanism will facilitate the development and transition of scientists to entrepreneurial roles. This funding would support small businesses in the hiring, salaries,

mentorship, and training of scientist-entrepreneurs to become Program Directors and Principal Investigators overseeing research projects. Small business recipients will provide robust training and mentorship to support career growth. This concept will strengthen the interface between small businesses and early career scientists to create new technologies and therapeutics.

Renewal of Institutional Training Programs to Advance Translational Research on Alzheimer's Disease (AD) and AD-Related Dementias

This concept aims to support the use of data science in AD/ADRD drug discovery by promoting the development of a diverse and interdisciplinary workforce. This concept uses the T32 mechanism to support institutional training programs for predoctoral and postdoctoral trainees with diverse educational backgrounds, emphasizing data science, drug discovery, and AD/ADRD clinical research skills. Trainees under these T32 awards will develop a strong foundational knowledge in AD/ADRD research and establish their scientific independence by conceptualizing their own research projects.

Renewal of NIA MSTEM: Advancing Diversity in Aging Research (ADAR) Through Undergraduate Education

Established in 2011, this R25 program actively supports 30 programs spanning all four NIA scientific divisions. Since its inception, more than 700 undergraduates have participated in these 30 programs, with 71 from underrepresented racial and ethnic groups, one-third from disadvantaged backgrounds, and 6 percent from the disability community. Nearly 400 undergraduates participated in programs funded between 2013 and 2018, with 75 percent from underrepresented racial and ethnic groups. Of these students, 54 percent were accepted to graduate school, and 83 percent of those students were admitted into aging-related programs. To attract and train a diverse workforce in aging and AD/ADRD research, this concept renewal will support creative research education programs with research experiences for undergraduates. Programs should allow for sustained, multi-year undergraduate involvement in programs during the academic year or summer session with various activities, such as structured research experiences, tailored learning opportunities, activities that explain the relevance of aging to students' lives, and engagement activities to diversify the aging research workforce.

Renewal of Summer Research Training in Aging for Medical Students

The Summer Research Training in Aging for Medical Students is a Ruth L. Kirschstein National Research Service Award program supported by NIA as a short-term training program to encourage medical students to pursue either basic science, health services, or clinical research careers in aging. By extension, this program helps increase the pool of physician scientists in clinical and research areas important to NIA's mission. Students in this program participate in various classroom, workshop, and research experiences under the supervision of experienced researchers to provide a better understanding of potential clinical and research career directions related to NIA goals, as well as necessary steps for career transitions.

V. RETIRING COUNCIL MEMBER REMARKS

Two retiring members of the Council—Drs. Manly and Weir—expressed appreciation for the honor of serving on the Council and reflected on their Council experiences.

VI. PROGRAM HIGHLIGHTS (BSR)

The Telomere Research Network: Current Accomplishments and Next Steps in Advancing Telomeres as a Sentinel of Psychosocial and Environmental Exposure and Predictor of Health

Dr. Stacey Drury, Psychiatrist-in-Chief, Boston Children's Hospital

Dr. Lis Nielsen introduced Dr. Stacey Drury and provided a historical background on the Telomere Research Network (TRN). Launched in 2019, TRN is a partnership between NIA and the National Institute of Environmental Health Sciences. TRN was created to establish standards for the measurement of telomere length as well as to make recommendations for conducting telomere assessments in different research contexts, including lab-based and population-based approaches. TRN also establishes and continues transdisciplinary dialogue among experts across basic research fields to help inform epidemiological and clinical investigations of telomeres.

Dr. Drury explained that the overall goal of TRN is to provide guidance to researchers on appropriate populations, study design, sample types, and methodologic assays for which telomere length analysis is expected to provide insight into the role of telomere biology in understanding the relationship between environmental and psychosocial stress and human health and disease. Challenges to this goal include (1) a lack of a gold standard method for measuring telomere length, (2) the balance of precision and scalability, (3) a multitude of different telomere length metrics (e.g., average, shortest, distribution, etc.) and methods with different variabilities and precisions, and (4) lower precision in large studies. To achieve this goal and address these challenges, TRN conducted two large-scale multi-laboratory methodologic precision studies. TRN also created a [toolbox](#) including protocols for telomere length measurements, quantitative polymerase chain reaction (qPCR) reporting guidelines, R code for calculating the intra-class correlation coefficient (ICC) for discerning assay repeatability, power calculations for sample size based on ICC, a primer on telomeres in health and disease, key recommendations for telomere length study design, a sample collection and storage checklist, and a packet of resources for new investigators.

TRN's two large-scale multi-laboratory studies addressed the following aims: (1) compare telomere length measurement precision in different laboratories using different extraction protocols using qPCR and (2) compare telomere measurement precision between methods and laboratories using centrally extracted DNA. Notably, TRN found that DNA extraction methods exhibited a strong effect on measurement precision and there was a large inter-laboratory variation in telomere length results. To assess inter-laboratory variability using centrally extracted DNA, TRN extracted DNA from 107 PBMC samples from 41 subjects; including multiple samples from each subject provided an additional level of sample blinding that was unknown to participating laboratories. The following telomere length methods were assessed in this study: multiplexed qPCR (four laboratories), absolute telomere length (two laboratories), monochrome multiplexed qPCR (three laboratories), and Southern blot (three laboratories), as well as single telomere length analysis (STELA), Oxford Nanopore sequencing, Flow-fluorescent in-situ hybridization (Flow-FISH), and DNA methylation (1 laboratory each). Notably, even Southern blotting—considered to be the silver standard in telomere length measurement assays—resulted in a variability of 0.33 kilobases when the same protocol was

used on the same samples. Based on the results of this study, TRN developed the following [recommendations](#):

- [Recommendation 1](#): Investigators should carefully consider the influence of variability in ICCs of telomere length assays when calculating statistical power and determining sample size.
- [Recommendation 2](#): All DNA samples for a cohort or study should be extracted using the same protocol. If samples have already been extracted using different protocols, investigators need to account for this variability and acknowledge that variability in sample processing can affect the feasibility of telomere length studies in some cohorts.

Dr. Drury outlined the suitability of different telomere length assays for longitudinal studies based on ICC. The effect of ICC on statistical power is large for longitudinal studies because telomere shortening is slow relative to individual variation in telomere length. If the ICC of an assay is less than 0.95, a very large sample size is required for an adequately powered longitudinal study. Although monoplex qPCR and absolute telomere length assays may be suitable for cross-sectional studies, based on their ICCs, they are inappropriate for detecting change in telomere length over time. However, monochrome multiplexed qPCR and Southern blotting methods are suitable for longitudinal studies, although these studies still require large sample sizes because of the variation in telomere length across individuals. In summary, both pre-analytic and post-analytic factors differentially influence telomere length based on both the factor and the telomere length assay. In addition, different biological samples are likely differentially susceptible to these factors, and precision needs to be established both by laboratory and protocol.

Current TRN efforts include using the [FinnBrain](#) cohort to evaluate predictors of newborn telomere length and telomere length trajectories as well as the study of DNA methylation telomere markers in jackdaws with very precise and established telomere length measurements. Because of data sharing restrictions, FinnBrain cohort data are only accessible within the European Union. Years four and five of TRN funding will support larger pilot studies to address current challenges in measuring telomere length, including the following topics: (1) developing a CRISPR-based telomere length assay to measure chromosome-specific telomere length, (2) understanding correlations between prenatal maternal behavior and factors, and postnatal baseline telomere length, (3) characterizing the role of telomere length in immune-aging, and (4) determining the utility of longitudinal DNA methylation telomere estimates and their relationship to other telomere-associated outcomes.

Discussion

Dr. Hodes acknowledged the TRN's work as a great example of the convergence of basic molecular science and population science, which demonstrates the need for further collaboration to develop and pursue useful telomere length measurement strategies.

Dr. Longo noted that as telomere length measurement assays improve in precision and sophistication, the telomere and neurodegeneration research communities will need to revisit any previously described associations between telomere length and neurodegeneration. Dr. Drury added that studies of telomere length in cerebrospinal fluid and peripheral blood samples will help researchers better understand the role of telomeres in neurocognitive aging and how to use peripheral blood sampling as a proxy for telomere length in the brain.

Dr. Schneider asked about how blood telomere length relates to brain and CSF telomere length. Dr. Drury explained that a trainee in her lab performed a complex cross-tissue correlational analysis and found that different tissue pairs have vastly different telomere levels or correlations, and consideration of biological mechanisms is required for meaningful interpretations of how telomere length in different tissues may relate to tissue-specific diseases (e.g., a specific type of cancer).

Dr. Longo also asked for more detail on the relationship between DNA methylation and other aging indicators. Dr. Drury explained that TRN analyzed an existing dataset containing information on DNA methylation biological clocks and found that each clock is associated with aging outcomes in a different way and is differentially related to telomere length. Therefore, composite markers are likely necessary to better understand biological aging.

Dr. Peterson asked for Dr. Drury's opinion on the existing mouse telomere literature. Dr. Drury explained that many inbred laboratory mouse strains have very long telomeres whose trajectories do not follow the same age-related decline and changes in structure and length seen in humans. However, wild rodent telomeres do still follow telomere trajectories associated with aging. This difference is likely because repeated inbreeding in a laboratory environment has eliminated many environmental perturbations that may be important determinants for telomere length and aging trajectories. Notably, rhesus macaques have telomeres with very similar characteristics to those of humans.

Dr. Darren Baker noted that based on Dr. Drury's findings on telomere length assay variability, these assays are likely poor methods to test interventional strategies for aging. Dr. Drury agreed and emphasized that current methods are not precise enough to detect any meaningful change in telomere length within an individual unless length is measured across a decade or longer. Telomeres also have dynamic roles via interactions with mitochondria that may be disrupted when telomeres are artificially lengthened. These dynamic roles, paired with oncogenic chromosomal fusions associated with abnormally long telomeres, indicate that telomeres require a balance of dynamics beyond simply lengthening to potentially improve aging and health outcomes.

Dr. Sohail Khan asked whether Dr. Drury stratified her telomere length analysis by race. Dr. Drury explained that the TRN study comparing telomere length ICCs only included samples from 41 individuals and was therefore not sufficiently powered to stratify by race. However, existing literature contains consistent evidence of racial differences in telomere length and changes in telomere length over time. Part of the accelerated aging seen in minority and marginalized populations is a function of multigenerational exposure to structural racism and inequity; additional data suggest that the effects of these exposures have been embedded across multiple generations. However, studies of racial differences in telomere length are limited to the United States, and further data from international populations are required to separate the effects of genetic ancestry from direct impacts of racism on telomere length. TRN does support some ongoing studies on intergenerational transmission of telomere length and how exposure to structural racism affects this transmission. Notably, a recent publication on accelerated aging in the placentas of women of color as compared to White women explored the implication that this accelerated aging may be related to increased rates of preterm birth in subsequent generations.

VII. COUNCIL SPEAKER

Environmental Influences on Child Health Outcomes (ECHO)

Dr. Matthew W. Gillman, Director, Environmental Influences on Child Health Outcomes (ECHO)

Dr. Nielsen introduced Dr. Matthew Gillman and the ECHO program. ECHO has catalyzed interest across NIH in research on the developmental origins of health and disease and has expanded from childhood development to include research questions relevant to aging. ECHO uses large existing study cohorts to conduct research on the effects of environmental exposures on child health and development.

Dr. Gillman outlined the ECHO mission, which is to enhance the health of children for generations to come. He acknowledged that a healthy start to life can impact a person's lifetime and future generations. The ECHO observational cohort data are being used to answer solution-oriented questions about the effects of a broad range of early environmental exposures—from societal to biological—on child health and development from conception until age 5. Exposures during this timeframe have lasting effects because development is highly integrated and sensitive to exposures. In this timeframe, human biological systems retain some plasticity, which suggests that early interventions can result in healthier downstream life and aging trajectories than later interventions during periods of lower plasticity. ECHO focuses on five key outcomes with high public health impact: pre-, peri-, and postnatal; upper and lower airway; obesity; neurodevelopment; and positive health.

The ECHO cohort is highly diverse in sex, age, socioeconomic status, race, and ethnicity. The ECHO cohort currently contains data from 42,000 mothers and fathers and 65,000 children, as well as more than 83,000 biospecimens; of the children, 34,000 are active in follow-up studies. These data have resulted in more than 1,200 publications, and more than 100 of those are collaborative multi-award papers. In addition, ECHO cohort de-identified data are now available to the entire scientific community.

ECHO cohort funding is entering its second seven-year funding cycle between September 2023 and May 2030. During this time, the cohort will be extended and expanded to further investigate the influences of a broad range of early exposures from society to biology, including the preconception period, on child health. This work will also include data from follow-up study visits of more than 30,000 children, as well as enrollment of an additional 30,000 new pregnancies. Notably, the postpartum period for these new pregnancies will serve as the preconception study period for a second pregnancy.

Dr. Gillman outlined some potential new and expanded scientific opportunities being pursued by ECHO investigators, including (1) identification of the early origins of health disparities; (2) characterization of social determinants of health, including stress biology; (3) studies of the effects of natural experiments (e.g., societal shifts) or health crises; (4) characterization of the effects of exposures to novel chemicals; (5) identification of early critical periods and their impacts on health trajectories; (6) characterization of resilience and reversibility of exposure effects; (7) identification and characterization of biological pathways involved in early exposures; (8) characterization of the impacts of media use on health trajectories; and (9)

characterization of the effects of preconception exposures such as social behaviors, weight changes, and chemicals, on health trajectories. Cross-cutting themes across research projects within ECHO include DEIA in participants and the scientific workforce, solution-oriented research, stakeholder engagement, team science, and the development of the next generation of researchers.

Dr. Gillman outlined multiple studies, previous and ongoing, using ECHO cohort data. One such study analyzed psychosocial determinants and how they relate to childhood obesity, which can impact aging via biological processes such as epigenetic changes, telomere dysfunction, DNA methylation changes, and oxidative stress. ECHO investigators developed the Child Opportunity Index (COI) consisting of 29 indicators of neighborhood conditions important for children's health across educational, health and environment, and social and economic domains. Higher COI scores indicate more favorable neighborhood opportunities. They also developed the Social Vulnerability Index (SVI) consisting of 15 U.S. census variables that identify high-risk populations during public health emergencies across socioeconomic, household composition and disability, racial/ethnic minority and language status, and housing and transportation domains. Lower SVI scores indicate less social vulnerability. Based on ECHO cohort data, investigators concluded that residence in higher opportunity neighborhoods, especially at younger ages, promotes lower body-mass index (BMI) patterns in children. This finding indicates a broader need for community-level interventions to prevent obesity starting early in the life course.

Other ECHO studies are assessing the determinants and outcomes of epigenetic age at birth. One such study analyzed cord blood and newborn blood spots to assess the association between epigenetic age and birth outcomes. Notably, gestational diabetes and pre-eclampsia were associated with decelerated epigenetic age at birth, even though these conditions are associated with worse health outcomes. Therefore, the importance of epigenetic age at birth, maternal epigenetic age, and placental epigenetic age in determining subsequent health outcomes remains unclear.

Additional work using ECHO data studied whether oxidative stress is a mechanism by which social determinants can affect rates of preterm birth and other adverse health outcomes. Through analysis of urinary biomarkers of oxidative stress from pregnant individuals, investigators found that lower education, nonmarried status, non-White race, smoking, and high pre-pregnancy BMI are all associated with increased oxidative stress, which in turn is associated with a higher risk of preterm birth. Dr. Gillman also noted that, similar to TRN, the ECHO program is interested in studying the relationship of telomere lengths between mothers and their babies.

Overall, ECHO is a major investment in understanding early environmental influences on childhood health. The ECHO cohort enables studies to fill evidence gaps on the long-term influences of prenatal and early childhood factors on health outcomes.

Discussion

Dr. Peterson asked what factors were driving the neighborhood effects on birth outcomes. Dr. Gillman explained that maternal obesity, gestational diabetes, and pre-eclampsia had independent effects from neighborhood characteristics on birth outcomes. However, the mediators of neighborhood factors remain unclear. Community norms are very important for changes in behaviors that reduce obesity rates in later childhood and adulthood. In addition, determinants transduced biologically should also be considered. Dr. Peterson further asked whether the study involved data collection on prenatal care. Dr. Gillman explained that investigators were unable to identify the causes of the neighborhood effects on birth outcomes but noted that other studies later in childhood and adulthood suggest that behaviors outside of the medical care system may mediate these neighborhood effects on birth outcomes.

Dr. Hodes noted that years of education is one of the most reliable predictors of dementia risk. He asked whether Dr. Gillman expected that these early life variables will prove to be similarly reliable predictors of dementia risk. Dr. Gillman explained that overlapping determinants identified in future ECHO studies of the prenatal/preconception through adolescence timeframe and the adolescence to early and mid-adulthood timeframe may provide insights into additional factors in early life that affect dementia risk.

Dr. Hodes asked Dr. Gillman whether he anticipates that a panel of biologic measures could help prioritize interventions at different years of development to improve aging outcomes. Dr. Hodes further noted that because some factors that negatively affect health outcomes occur so early in life, interventions to reverse these effects are needed beyond conventional prevention strategies. Dr. Gillman acknowledged the need for interventions that can reverse these effects and noted that better understanding of the biological underpinnings can provide further information about potential interventions and opportunities to reverse negative impacts on health outcomes.

Dr. Asthana explained that another measure of neighborhood disadvantage is the Area Deprivation Index, which consists of 17 variables, and asked how moving during childhood from one neighborhood to another can affect health outcomes. Dr. Gillman explained that the ECHO investigators who developed the COI and SVI are now looking at changes in these indices over time, especially when people move to other neighborhoods. However, results from this study may be confounded by the overall ability and willingness of families to move to other neighborhoods.

Dr. Peterson asked whether ECHO studies have ever analyzed the relationship between epigenetic markers in parents and their offspring. Dr. Gillman explained that several current studies are looking at maternal DNA methylation and DNA methylation of paternal sperm to measure epigenetics prior to conception. Based on rodent studies, certain behaviors that affect sperm epigenetics may impact birth outcomes.

Dr. Longo asked whether ECHO studies have assessed oxidative stress levels and epigenetics in children living in wealthy neighborhoods. Dr. Gillman indicated that ECHO investigators have not proposed studies in this area.

Dr. Nielsen asked about ECHO's data harmonization efforts across cohorts for cognitive function and educational exposures. Dr. Gillman explained that initial ECHO studies used existing cohorts with different study designs and collection approaches. However, in the second funding cycle of ECHO, the program will use a single standardized protocol, including standardized approaches to collection of cognitive and neurodevelopmental outcomes as well as educational exposures in children and adolescents. He further noted that current ECHO funding only supports following study participants through age 21.

VIII. ADJOURNMENT

The open session of the 150th meeting of the National Advisory Council on Aging adjourned at 1:30 p.m. on September 20. The next meeting is scheduled for January 23-24, 2024.

IX. CERTIFICATION

I hereby certify that, to the best of my knowledge, the foregoing minutes and attachments are accurate and complete.⁴

Richard J. Hodes, M.D.
Chairman, National Advisory Council on Aging
Director, National Institute on Aging

Prepared by Kenneth Santora, Ph.D.
With assistance by Rose Li and Associates, Inc.

⁴ These minutes will be approved formally by Council at the next meeting on January 23-24, 2024, and corrections or notations will be stated in the minutes of that meeting.