

NATIONAL INSTITUTES OF HEALTH
NATIONAL INSTITUTE ON AGING

Summary Minutes

The 152nd Meeting
NATIONAL ADVISORY COUNCIL ON AGING
May 21-22, 2024

National Institutes of Health
Hybrid Meeting

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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
May 22, 2024

The 152nd meeting of the National Advisory Council on Aging (NACA) was convened on Wednesday, May 22, 2024, at 9:00 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, May 21, from 3:00 p.m. to 5:00 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, May 22, 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. Lundebjerg
Dr. Jennifer Jaie Manly
Dr. Charlotte A. Peterson
Dr. David B. Reuben
Dr. Julie A. Schneider
Dr. Linda J. Van Eldik
Dr. David R. Weir

Executive Secretary:

Dr. Kenneth Santora, NIA

Ad Hoc Participants:

Dr. Elissa Epel, Weill Institute for Neurosciences, University of California, San Francisco

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.

In Addition to NIA Staff, Other Federal Employees Present:
Dr. Tara Schwetz, Director, Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI), Office of the Director, National Institutes of Health (NIH)

Members of the Public Present:
Dr. Tuhina Neogi, Professor, Boston Medical Center

268 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 2,828 applications requesting \$8,036,835,796 for all years underwent initial review. The Council recommended 1,491 awards for a total of \$4,727,192,119 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 152nd NACA meeting. Dr. Hodes called the meeting to order at 9:00 a.m. on Wednesday, May 22, 2024.

A. Director's Status Report

In Memoriam: Norman B. Anderson, Ph.D.

Dr. Hodes recalled the significant contributions of Dr. Norman B. Anderson to NIA and the scientific community. Dr. Anderson was a leader in the fields of behavioral and social sciences research as well as a distinguished clinical psychologist. He was a dedicated and supportive mentor to colleagues. He held multiple leadership roles, including election to the Institute of Medicine (now part of the National Academies of Sciences, Engineering, and Medicine [NASEM]) and as the Inaugural Director of the NIH Office of Behavioral and Social Sciences Research. He served as a NACA member from 2011 to 2014 and coauthored the NIA Health Disparities Research Framework, critical for shaping NIA's research directions.

National Institute on Aging Appropriations

For fiscal year (FY) 2024, Congress appropriated \$48.6 billion to NIH, allocating \$4.51 billion to NIA. This allocation includes an increase of \$90 million for Alzheimer's disease and Alzheimer's disease-related dementias (AD/ADRD) research and \$12.5 million for palliative care research. In addition, the National Institute of Neurological Disorders and Stroke (NINDS) received an additional \$10 million for AD/ADRD research.

² 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 applied only to applications that were discussed individually, not to "en bloc" actions.

FY 2024 Allocations for Competing Research Grant Awards

Current NIH FY 2024 allocations for competing research grant awards still have potential for modification during the rest of the year. For applications under \$500,000 in direct costs reviewed by the NIH Center for Scientific Review (CSR), the NIA pay line is the 16th percentile (19th and 21st percentiles for new investigator [NI] and early-stage investigator [ESI] R01s, respectively). For applications over \$500,000 in direct costs reviewed by CSR, the payline is the 13th percentile (16th and 18th percentiles for NI and ESI R01s, respectively). For AD/ADRD applications under \$5 million in direct costs reviewed by CSR, the pay line is the 17th percentile (20th and 22nd percentiles for NI and ESI R01s, respectively). For AD/ADRD applications over \$5 million in direct costs reviewed by CSR, the pay line is the 14th percentile (17th and 19th percentiles for NI and ESI R01s, respectively). These pay lines for AD/ADRD research are lower compared to prior years because of an increase in number of applications, and although funding for AD/ADRD continues to increase, it has not increased enough to maintain pay lines from prior years. For NIA-reviewed applications, the general pay lines are associated with priority scores of 25 for program projects, 25 for other NIA-reviewed research, 22 for career development awards, and 30 for fellowship awards. NIA-reviewed AD/ADRD application pay lines are associated with priority scores of 25 for program projects, 25 for other NIA-reviewed research, 30 for career development awards, and 35 for fellowship awards.

National Institute of Aging Updates

Dr. Hodes summarized NIA updates. NIA is supporting 508 AD/ADRD clinical trials, classified as dementia care and caregiving trials (228); non-pharmacological (177); pharmacological (73); diagnostic tools, assessments, and imaging studies (23); and treatments for neuropsychiatric symptoms. The majority of the 228 dementia care and caregiving trials focus on formal care settings (47); improving caregiver health and well-being (45); and caregiver assessments, tools, training, and education (28). Most of the 177 non-pharmacological studies are testing exercise (44), neurostimulation (28), and cognitive training (21), as well as other modalities including sleep, diet/supplements, and social engagement. Current pharmacological clinical trials target a variety of disease processes, including inflammation, amyloid, metabolism/bioenergetics, receptors, vasculature, circadian rhythm, and tau. The neuropsychiatric trials consist of non-pharmacological (4) and pharmacological (3) interventions.

At the request of Congress in FY 2023 appropriations language, NIA and NINDS entered into an agreement with NASEM to identify research priorities for preventing and treating AD/ADRD. NASEM has formed an ad hoc committee to perform the study, with a final report expected by March 2025.

Launched in September 2023, the EUREKA Challenge for Early Prediction of AD/ADRD is a challenge prize competition to discover the best data, methods, and strategies for early prediction of AD/ADRD. Upon successful completion of research, competitors can receive cash awards totaling \$650,000 across three phases. For Phase 1, NIA received 40 submissions and will award prizes in fall 2024.

NIA also hosted a second iteration of the Healthy Aging Start-Up Challenge in 2023 to support efforts that foster diversity in aging research and innovation. The 2023 iteration focused on solutions that address health disparities in aging populations, and winners were selected from 20

finalists. Winners each received a \$60,000 prize and continued coaching and mentorship with NIA entrepreneurs-in-residence. The 2023 winners and their solutions are listed below:

- Gravitrex, LLC—mechanically-powered assisted walking device for accessible mobility rehabilitation
- POPCHECK Technologies—medical/digital device providing remote patient monitoring to predict surgical complications and improve post-operative care
- Lantern Laboratory—novel precision medicine device/platform using electroencephalography biomarkers to guide real-time dosing of pain relievers in the operating room and intensive care unit
- AgingSense—wearable technology to monitor for worsening heart failure symptoms and for responses to treatment
- Cardiost—implantable medical device to treat cardiovascular conditions, including advanced-stage heart failure
- Voice-it, Inc.—interactive conversational artificial intelligence that uses machine learning to assist with pain symptom management

Since January 2024, NIA has released 19 research highlights of NIA-supported publications, 16 blog posts, and 1 news announcement. In addition, senior NIA leadership has participated in 14 meetings with interest and advocacy groups as well as 8 Congressional briefings or hearings.

NIA is celebrating its 50th anniversary, and as part of this celebration, special articles were published in the *Journal of the American Geriatrics Society* that outline and reflect on NIA's accomplishments over the past 50 years.

NIA's Butler-Williams Scholars Program for junior faculty and researchers new to the field of aging will convene in person from August 21 to 23, 2024, on the NIH Main Campus.

The 2024 NIH Alzheimer's Disease Research Summit: Path to Precision Medicine for Treatment and Prevention will be held from September 23 to 25, 2024.

National Institutes of Health Updates

NIH established a new Common Fund program to support clinical research in primary care settings. Common Fund programs support research areas of interest across NIH institutes and centers (ICs). This NIH Common Fund program aims to address the declining health of the U.S. population, particularly among those who are medically underserved and underrepresented. The program goals are to (1) establish a primary care-focused clinical research network that is disease-agnostic, facilitating clinical research in mission areas across all ICs; (2) integrate innovative research with routine clinical care in real-world settings; and (3) create a foundation for sustained engagement with communities that are underrepresented in clinical research. The Office of the Director's anticipated budget for this program is \$5 million for FY 2024 and \$25 million for FY 2025, with an anticipated ramp-up in following years to \$50 million to \$100 million per year after assessing program feasibility and budget requirements. NIH will collect feedback through spring 2024 and will perform a quick launch later in FY 2024, with program expansion anticipated in FY 2025 and beyond.

Discussion

Dr. Hodes responded to questions by Council members about communications outreach, palliative care funding, and engagement with the U.S. Food and Drug Administration (FDA).

In response to a question about how the NIA monitors effectiveness of its communications, Cindy McConnell, Director of NIA's Office of Communications and Public Liaison, offered to share analytics data that indicate reach of blog posts and other public-facing material. Dr. Hodes will present these metrics in future NACA meetings, and NIA staff can send current data to Council members via email.

Dr. Khan emphasized that NIA should prioritize expanding its research dissemination efforts, particularly to Tribal communities via the Association of American Indian Physicians, National Indian Health Board, and Indian Health Service. Dr. Karina Walters, Director of the Tribal Health Research Office in DPCPSI may have additional important outreach contacts.

Dr. Hodes clarified that on May 23, 2024, at 10:00 a.m., Dr. Monica Bertagnolli, NIH Director, as well as directors of select ICs, including Dr. Hodes, will attend a [hearing on Capitol Hill to discuss the FY 2025 budget](#). This hearing is open to the public, and NIA will send details to Council members who are interested to observe.

Establishment of a Palliative Care Consortium

NIH will use appropriations for palliative care research to build a consortium and infrastructure with at least three sites to coordinate palliative care research efforts across NIH. Led by Dr. Amy Kelly, Deputy Director of NIA, this consortium will enable palliative care research specific to diseases of interest for NIH ICs.

Engagement with the U.S. Food and Drug Administration

FDA recently presented on real-world evidence-based research at the Spring 2024 Alzheimer's Disease Research Center (ADRC) Meeting. Notably, real-world data research is critical to NIA's current and future research efforts, and NIA has already supported other real-world data initiatives including the IMbedded Pragmatic AD/ADRD Clinical Trials (IMPACT) Collaboratory. NIA will also continue work with other ICs in close consultation with the Office of Data Science and Dr. Bertagnolli to expand real-world data efforts.

Dr. Longo asked about NIA's engagement with FDA in discussions about what aspects of aging are amenable to therapeutics. Dr. Hodes explained that NIA has met with FDA staff multiple times about this topic, and FDA has been receptive to interventions with clinically meaningful outcomes that are not necessarily disease specific. FDA has published [guidance](#) on the use of broad, clinically meaningful outcomes in the context of aging therapeutics. Notably, FDA has cited difficulty in determining where to house FDA regulatory activities related to non-disease-specific therapeutics.

Ms. Lundebjerg asked whether FDA intends to adopt any of the across-the-lifespan approaches that NIA and NIH have adopted in its regulatory activities. She expressed concern about the continued exclusion of older adults from clinical trials and clinicians subsequently prescribing these therapeutics to older adults when they have not been rigorously tested in that age range. Dr. Hodes explained that any requirements for inclusion of older adults in clinical trials would not be under the sole purview of FDA. He also cited nuances for age cutoffs in certain clinical studies,

particularly longitudinal studies across the lifespan and studies of approaches to prevent disease onset. However, many clinical studies have unjustified age exclusions, and Dr. Hodes explained that NIH has a responsibility to fund clinical studies with wider age ranges.

B. Staff Introductions

NIA leadership introduced new NIA staff members from the Divisions of Behavioral and Social Research (BSR), Aging Biology (DAB), Geriatrics and Clinical Gerontology (DGCG), and Neuroscience (DN); the Division of Extramural Activities (DEA) Scientific Review Branch (SRB), Office of Clinical Research (OCR), and Office of Strategic Extramural Programs (OSEP); the Office of Administrative Management (OAM); the Office of Communications and Public Liaison (OCPL); the Office of Legislation, Policy, and International Activities (OLPIA); the Office of Planning, Analysis and Evaluation (OPAE); and the Intramural Research Program (IRP) Center for Alzheimer's and Related Dementias (CARD), Clinical Research Core (CRC), Laboratory of Epidemiology and Population Science, Laboratory of Genetics and Genomics (LGG), Laboratory of Neurogenetics, Networks and Computing Technology Section (NCTS), and Translational Gerontology Branch (TGB).

C. Future Meeting Dates

September 18-19, 2024 (Wednesday and Thursday), Building 31
January 28-29, 2025 (Tuesday and Wednesday), Virtual
May 13-14, 2025 (Tuesday and Wednesday), Building 45 - Natcher
September 17-18, 2025 (Wednesday and Thursday), Building 45 - Natcher

D. Consideration of Minutes of the Last Meeting

The minutes of the January 2024 Council meeting were considered. A motion to approve the minutes was made, seconded, and passed unanimously.

E. Certificate of Recognition to 2023 Retired Members

NIA presented certificates of recognition to 2023 retired NACA members, Drs. Manly, Weir, and Peterson. Recipients all expressed appreciation and gratitude for the opportunity to serve on NACA.

III. REPORT: TASK FORCE ON MINORITY AGING RESEARCH

Drs. Cruz and Schneider summarized presentations to the Task Force on Minority Aging Research by Drs. Robert Turner, Jaime Perales Puchalt, and Bonnie Duran.

In her opening remarks, Dr. Cruz highlighted the three domains driving the Task Force as presented by Dr. Patricia Jones, Director of the NIA Office of Special Populations: (1) science of inclusion, (2) science of eliminating health disparities, and (3) methods used to examine the health of minorities. She also reiterated that the Butler-Williams Scholars Program will convene in August 2024, and registration will open soon for the Structural Racism Workshop in July 2024.

During his presentation, Dr. Turner spoke about his experiences at George Washington University conducting AD/ADRD research in self-identified Black men. His research strategy uses a life course perspective to understand how sports participation can influence brain health in Black men. Black men are underrepresented in AD/ADRD research despite their overall willingness to participate, and Black male athletes reported that they had never been asked to participate in AD/ADRD research studies. To successfully recruit and retain Black men in these studies, researchers should create an inclusive and welcoming environment for both Black researchers and participants. Researchers should have and express a genuine interest in and respect for the Black male population. Creation of this inclusive environment requires community engagement and the use of community perspectives to inform research studies. Researchers should connect with individuals living in these local communities to understand their needs and culture.

Dr. Perales Puchalt discussed his experiences at the University of Kansas conducting AD/ADRD research in Latino communities. High rates of uninsurance, lower access to education, lower household income, misconceptions about the prevalence of memory loss and dementia among Latinos relative to Whites, and language barriers all impede Latino communities from seeking medical attention for detection and care of AD/ADRD. Many Latinos are also reluctant to participate in AD/ADRD clinical studies because of language barriers, previous discrimination experiences, and fear of deportation. Dr. Perales Puchalt outlined models for community engagement in research studies in Latino communities, including engagement models centered on warm and bidirectional participant-researcher relationships and the Cultural Accommodation Model. This model involves adjusting research designs and requirements to meet communities where they are; for example, research studies can opt to not require Social Security Numbers for participation to reduce fear of deportation in potential study participants. Dr. Perales Puchalt also shared overall lessons learned from his experiences. He recommended that researchers co-create research questions with communities by asking about their interests. Research funding programs should integrate support for engagement activities even after the study ends. Researchers should also engage community advisory boards and encourage community members to share their opinions on how to retain study participants, disseminate research findings, interpret research findings, and create research program sustainability via community partnerships.

During her presentation, Dr. Duran from the University of Washington provided a baseline definition of community-based participatory research: a partnership approach that equitably involves community partners, organization representatives, and researchers in all aspects of the research process. This approach has seen significant success for research on marginalized communities. Interventional research designs under the community-based participatory research framework should honor cultural knowledge and community voices by using both academic and community language, which can result in strength-based culturally-centered intervention settings and research. She also emphasized the importance of sharing research resources and paying people to participate in research studies.

Dr. Manly expanded on Dr. Duran's presentation by explaining the concept of health equity tourism, that is, researchers without expertise in health equity research conduct research in communities that experience health disparities. Avoiding health equity tourism requires building strong, sustainable, and inclusive community relationships.

She cited a [2022 publication by Lett et al.](#) in the *Journal of Medical Systems* as a source of additional information on health equity tourism.

Discussion

Dr. Schneider noted that researchers will naturally gravitate toward research projects that are most likely to receive funding. Because NIA has emphasized health equity in AD/ADRD, researchers from outside the health equity field have gravitated toward the field. Therefore, researchers with expertise in health equity need to develop ways to educate newcomers on the principles of health equity and how to avoid health equity tourism. Dr. Manly added that NIA can help ensure health equity expertise for research projects by requiring grant applicants to cite prior experience with health equity or equal partnerships with health equity research experts.

To further improve community engagement, Dr. Cruz suggested that training programs, such as those funded by the K22 mechanism, should engage the nonprofit sector to help build community relationships, because these organizations often already have the trust of their local communities. Dr. Khan added that researchers should disseminate research findings to the communities they research to build and sustain trust; NIH should prioritize presentation of findings to minority communities alongside academic publications and presentations.

Dr. Asthana noted that ADRC core facilities dedicated to recruiting participants from underrepresented groups have shown success, especially at the University of Wisconsin, and NIA should consider whether this type of core should be mandatory for ADRCs. However, ADRCs may struggle to establish another mandatory core facility with existing funding.

IV. REPORT: WORKING GROUP ON PROGRAM

Dr. Greenspan, Chair of the Working Group on Program, led the updates on one Small Business Innovation Research (SBIR) contract concept clearance. The Council members unanimously and enthusiastically concurred with approval of the NIA Small Business Committee's contract concept clearance, as summarized below, to add these NIA topics to the NIH SBIR Research Contracts Request for Proposals for FY 2025.

Funding Opportunity Announcement: Small Business Innovation Research Program Contract Concept Clearance

Dr. Greenspan invited the primary reviewer, Dr. Huang, to present the NIA SBIR Program contract concept to the Council. The contract concept is composed of three NIA office and division collaborators: DAB, OSEP, and BSR, each with their own project titles—Modeling Aging Through Microphysiological Systems, Digital Technologies as Tools to Screen and Monitor AD/ADRD, and Leveraging Multimodal and Generative Artificial Intelligence (AI) to Advance the Application of Social Robotics in Caregiving, respectively. Special reviews are required for these contract proposals because these topics require specific areas of expertise for adequate review and support. All three projects were discussed and approved by the NIA Small Business Committee, and Council members unanimously concurred to move forward with this contract concept.

Modeling Aging Through Microphysiological Systems

The majority of research investigating the biological mechanisms underlying the normal aging process and aging-related diseases has been conducted using static cell cultures and animal models that only partially recapitulate aging in humans. Microphysiological systems (MPS), which are in vitro 3-dimensional human tissue constructs that mimic human tissue and organ functions, could provide more translationally-relevant and cost-effective models to supplement or replace cell cultures and animal models in basic aging research and drug development. The short-term goal of this contract is to establish the MPS as a standardized tool for discovery science or drug development in aging research. The long-term goal is the further implementation of the MPS as an FDA-qualified drug development tool.

Digital Technologies as Tools to Screen and Monitor AD/ADRD

AD/ADRD are largely managed symptomatically, and disease-modifying treatments have become available only recently. Significant gaps, including screening, early detection, and enrollment in clinical trials, have prevented effective management and treatment of AD/ADRD. There is unmet need to develop new tools that can fill these gaps.

Recently, the development of medical devices and digital technologies to evaluate cognitive impairment in older populations has received increased interest. Medical devices and digital technologies, such as software, have the advantage of consistency in administering the test and reproducibility of results compared to self-report measures. However, to be universally accepted, these tools should be standardized and validated in diverse populations. The goal of this contract topic is to stimulate the participation of small businesses in FDA's Medical Device Development Tools program.

Leveraging Multimodal and Generative Artificial Intelligence to Advance the Application of Social Robotics in Caregiving

The burden of caregiving for persons with dementia (PwD) arising from psychological and non-psychological stressors is overwhelming. Assistive technologies can attenuate caregiving burden. However, most assistive technology solutions are mobile or web-based and have many limitations, such as triggering cognitive overload in PwD and failing to replicate physical reality, that inhibit meaningful engagement with PwD. Multimodal and generative AI can address these limitations through social robotics. The broad objective of this contract topic is to comprehensively leverage multimodal and generative AI to provide a new impetus to revolutionize the application of social robotics in caregiving for PwD.

V. PROGRAM HIGHLIGHTS (DGCG)

Osteoarthritis and Chronic Pain in Older Adults: Insights from MOST and Framingham

Dr. Tuhina Neogi, Professor, Boston University

While acute pain protects people from harm, chronic pain that lingers after an injury heals is generally maladaptive and lacks any protective function. Chronic pain affects 100 million adults in the United States, more than the number of adults with cardiovascular disease, diabetes, and cancer combined. Of these adults with chronic pain, 30 million have pain due to osteoarthritis (OA); the most common site of OA is the knee. Patients with knee OA initially experience pain when weight bearing and during activity, but the pain eventually progresses to more persistent

and severe pain often with unpredictable flares. Few management options for knee pain are available except for joint replacement surgery.

To study knee OA and pain, Dr. Neogi uses data from the Multicenter OA Study (MOST), composed of approximately 3,000 older adults with or at risk for knee OA, as well as the Framingham Heart Study, for which Dr. Neogi has NIA funding to study pain in the offspring cohort. Notably, pain and joint changes seen in radiographic images are not well correlated. Dr. Neogi opted to study the correlation between pain and radiographic changes in individuals with OA in only one knee, using the participant's healthy knee as a control for pain perception. She found a significant correlation between OA radiography severity (measured by Kellgren-Lawrence [KL] grade) and the odds ratio of having knee pain.

Dr. Neogi's research is the first to show that calcium deposition was associated with an increased risk of knee pain development and worsening as well as cartilage damage. Two therapeutics, canakinumab and colchicine, are used to treat the formation of calcium crystals, but OA-specific trials with these therapeutics failed to show improvement of OA symptoms. However, these trials had small cohorts and were short in duration. In two large, longer-term clinical trials of both therapeutics for cardiovascular disease, people taking canakinumab or colchicine were 40 percent or 30 percent less likely to have a joint replacement, respectively, suggesting that both therapeutics may have utility in treating OA.

Pain perception is also affected by alterations to nociceptors that impact neuronal signaling from the periphery to the spinal cord and brain. For example, central sensitization occurs when noxious stimuli trigger nociceptors that may fire at sub-threshold inputs, resulting in more action potentials and hyperalgesia. In addition, non-noxious stimuli can trigger low threshold mechanoreceptors and result in allodynia (i.e., pain in response to a stimulus that normally does not cause pain). These abnormalities in the ascending facilitation and descending pain modulation pathways can contribute to the overall pain experience.

In OA patients, ascending facilitation and temporal summation were associated with pain severity, but not with degree of radiographic severity or with time since OA diagnosis. Based on magnetic resonance imaging (MRI) data, synovitis and effusions but not bone marrow lesions were associated with central sensitization. Ultimately, these and other findings demonstrate that OA severity and duration do not contribute to increased risk of central sensitization, suggesting that central sensitization is an inherent trait, rather than something that is induced by a disease state.

To better understand risk factors that impact OA pain susceptibility, Dr. Neogi studied susceptibility phenotypes in individuals without knee pain. Across a research period of two years, those with high central sensitization based on pressure pain threshold (PPT) measures had a two-fold increased risk for developing persistent knee pain. Using latent class analysis of study participants, she identified four clusters of pain susceptibility based on central sensitization measured by PPT and facilitated temporal summation. These clusters remained stable across nine years, even in study participants who transitioned from being pain-free to having knee pain. In the future, Dr. Neogi will further investigate risk factors associated with pain sensitization, and consequences of pain sensitization, post-knee replacement pain, and disease-agnostic chronic pain.

Discussion

Prevalence of OA and lower back pain is lower in Japan and Europe compared to the United States. When asked about potential underlying causes for this difference, Dr. Neogi cited hypotheses that obesity and lack of physical activity result in higher rates of pain. Notably, data from Japan were taken from very physically active cohorts. Differences in pain prevalence remain an ongoing area of research.

Dr. Longo asked how exercise may affect pain thresholds and mechanisms. Dr. Neogi noted that exercise is generally beneficial for OA as long as it avoids injury to the affected joint. She observed that some people experience a “runner’s high” or exercise-induced hypoalgesia, but others experience no improvement or worsening of pain during exercise. Therefore, identifying factors associated with exercise-induced hypoalgesia can help clinicians recommend physical activity for pain management only for people who are likely to benefit.

Dr. Longo also asked about Dr. Neogi’s plans for conducting proteomics analysis on synovial fluid. Dr. Neogi’s research group is participating in a larger worldwide effort for identifying biomarkers for OA in synovial fluid.

Dr. Neogi also referenced current research with a group in Norway on hand OA. Many of the pain mechanism findings from hand OA are similar to those from knee OA. In addition, individuals with localized OA may have a disease mechanism distinct from those with generalized OA at multiple joints.

Dr. Manly cited research from Dr. Naomi Eisenberger using functional MRI to study the mind-body connection and asked whether Dr. Neogi’s research examines the mind-body connection in pain. Dr. Neogi agreed that evidence suggests that the mind-body connection is important for pain management, and noted that cognitive-behavioral therapy is often prescribed for pain management. Other research suggests that similar areas in the brain activate in response to both experiencing a noxious stimulus and seeing something painful, suggesting that individuals anticipate the feeling of pain.

Dr. Asthana noted recent research findings that suggest mammalian target of rapamycin (mTOR) inhibitors as a promising therapeutic for OA. Dr. Neogi acknowledged that many promising OA therapeutics that target specific intracellular signaling pathways are in development. However, preclinical findings for these drug candidates often fail to translate into humans. Dr. Neogi indicated that therapeutics may be more effective in earlier stages of OA and should be tested in these early contexts prior to extensive joint damage. However, enrollment of early-stage OA patients requires a more granular early OA staging approach than standard KL grading.

Dr. Khan asked about any differences across racial groups in OA and pain sensitization. Prior research has shown that pain processing in Native Americans is somewhat dampened. Dr. Neogi explained that to best frame and understand population differences in pain perception, she wants to better understand structural racism and other factors that can contribute to any observed differences. She also noted that her research group is currently studying OA in the Jackson Heart Study cohort of African Americans, which will provide a larger sample size for subsequent stratification by racial group.

Ideally, future OA interventional clinical trials will be designed to detect positive results in OA patient subgroups. Historically, OA trials have been small, limiting statistical power and the ability to perform stratified analyses across patient subgroups. In addition, OA therapeutics should be tested in early-stage OA before extensive joint damage occurs. Lastly, longer OA clinical trials will enable detection of long-term results. Dr. Neogi also explained that OA is not a monolithic, singular disease; multiple disease pathways contribute to OA phenotypes. Therefore, therapeutics should be methodically tested in OA patient subgroups who are expected to benefit based on disease mechanisms.

VI. COUNCIL SPEAKER

Coordinating NIH Science Strategy: A Vision for DPCPSI

Dr. Tara Schwetz, Director, DPCPSI, NIH

Housed within the Office of the Director, the Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI) consists of 14 offices. In addition, NIH is currently moving the *All of Us* Research Program Office and the Environmental Influences on Child Health Outcomes (ECHO) Program Office under DPCPSI, and DPCPSI recently added the INvestigation of Co-occurring conditions across the Lifespan to Understand Down syndrome (INCLUDE) Project. Multiple DPCPSI offices are involved in programmatic coordination (e.g., Office of Data Science Strategy, Office of Research on Women's Health, Office of Behavioral and Social Sciences Research, Tribal Health Research Office [THRO]), while others focus on developing resources and tools for NIH (e.g., Office of Portfolio Analysis and the Office of Evaluation, Performance, and Reporting) and on pursuing specific research topic areas and support (e.g., Office of Research Infrastructure Programs and Office of Strategic Coordination's Common Fund). DPCPSI leads synergistic coordination of its offices and vital IC partnerships, identifies and catalyzes research to address scientific gaps and opportunities, fosters collaborations, develops methods to enable research goals, and serves as an experimental testbed for innovative NIH-wide activities to improve the health of the nation.

DPCPSI's vision is to advance biomedical and behavioral science through coordinating cross-cutting, innovative solutions that foster IC collaboration and improve the health of the nation. Its goals are to advance NIH research; align internal workforce, resources, and infrastructure; and engage with external parties. DPCPSI's proposed values are as follows:

- Respect—Fosters a respectful, inclusive, and professional environment that acknowledges and celebrates the diversity and contributions of everyone on the DPCPSI team.
- Coordination—Facilitates, convenes, and catalyzes cross-cutting research at NIH.
- Partnership—Leads through partnerships and builds collective buy-in.
- Excellence—Promotes excellence in all aspects of its work and inclusive of all populations to achieve its mission.

DPCPSI Program Updates

Dr. Schwetz provided some DPCPSI program updates. In response to the new Executive Order that established the Women's Health Research Initiative, NIH has initiated multiple aligned efforts. NIH released an NIH-wide Women's Health Research Notice of Special Interest with links to NIH parent funding opportunities across institutes, centers, and offices. DPCPSI, in collaboration with the Agency for Healthcare Research and Quality, will also launch its inaugural Pathways to Prevention series on menopause and management of related issues, which, after a 1.5-year process, will result in a report with recommendations and an action plan for menopause research and care. NIH's SBIR and Small Business Technology Transfer Programs have also committed to increase funding for women's health activities by 50 percent.

NIH has established a new Common Fund program within DPCPSI—Clinical Research in Primary Care Settings—to address declining health in the United States, especially among underserved and underrepresented populations. The program goals are to (1) establish a primary care-focused clinical research network that is disease-agnostic, facilitating clinical research in mission areas across all ICs; (2) integrate innovative research with routine clinical care in real-world settings; and (3) create a foundation for sustained engagement with communities underrepresented in clinical research. DPCPSI is now gathering feedback from the scientific community and requesting applications from organizations interested in becoming network research hubs for this Common Fund program ([OTA-24-016](#)).

NIH's Data Initiative aims to address an urgent need for high-quality comprehensive data from clinical care environments to generate evidence for U.S. Department of Health and Human Services agency decision-making. The initiative's goals are to (1) facilitate learning health system initiatives through better data to assess health outcomes that matter to individual people and to society overall; (2) eliminate costly data formatting and collection redundancies that create silos; (3) reduce clinical care site burden for data submission; (4) increase data quality and speed time to data access for use in agency decision-making; and (5) apply artificial intelligence methods to health data that are comprehensive and represent the diversity of the U.S. population. NIH is currently considering feasibility study options that demonstrate and develop standards and requirements with a limited group of data partners and data sources. Examples include a collaboration with the Centers for Disease Control and Prevention (CDC) to modernize data collection for the Surveillance, Epidemiology, and End Results (SEER) Program and a collaboration with FDA for post-market data collection.

Since 2018, NIH has funded 330 awards through the INCLUDE Project to investigate conditions that affect individuals with Down syndrome and the general population, such as AD, autism, cataracts, celiac disease, congenital heart disease, and diabetes. DPCPSI recently hosted a meeting for INCLUDE-funded investigators to discuss research updates, foster collaboration, and identify ways that NIH can help advance the next five years of Down syndrome research.

Challenges and Initiatives for DPCPSI

DPCPSI is currently formulating an Indigenous Data Sovereignty Policy to create a consistent approach across NIH to data management and sharing grounded in Tribal sovereignty, research laws, codes, and ordinances. In addition, DPCPSI will coordinate a non-human primate evaluation and analysis study and strategic management planning for future NIH non-human primate usage. DPCPSI is also leading implementation efforts in accordance with the Advisory

Committee to the Director Working Group on Catalyzing the Development and Use of Novel Alternative Methods to Advance Biomedical Research recommendations.

DPCPSI continues to face challenges, including those related to budget cuts and leadership turnover. Funding for *All of Us* and the Common Fund declined by 34 percent and 7 percent, respectively, in FY 2024. DPCPSI recently filled five DPCPSI office director positions, but two office director vacancies remain.

Discussion

Indigenous Data Sovereignty

In response to a question from Dr. Khan, Dr. Schwetz provided more detail on Indigenous Data Sovereignty Policy progress. The THRO is leading this effort and is one of the newer offices at DPCPSI, with its director having been hired within the past year. DPCPSI is hosting listening sessions with NIH and Tribal communities to understand current challenges to data sovereignty, which include management of Tribal data. This effort plans to outline consistent sovereignty principles for urban Native Americans and for situations when Tribal data are collected from reservations. Dr. Khan recalled that people of the Cherokee Nation have been contributing cancer data to SEER since 1997, and their data reside on a separate data island at the National Cancer Institute. However, the Cherokee retain ownership of and control access to the data, and Dr. Khan noted that this model has worked well.

Real-World Data Collection

Multiple Council members expressed interest in collection of real-world data, especially in primary care settings. Notably, the Clinical Research in Primary Care Settings Common Fund program and NIH's Data Initiative are separate efforts that converge, with data collected from primary care networks being critical for the Data Initiative. NIH wants clinical sites to have a suite of options that enables them to participate in different real-world data research studies. Dr. Schwetz clarified that the Common Fund is cross-cutting across ICs, that is, each IC has its own diseases and conditions of interest for data collection. Eventually, NIH intends to create a national network of sites but will initially focus on sites that serve rural populations. NIH will centrally monitor data quality and leverage existing networks and infrastructure, including the National Institute of General Medical Sciences (NIGMS) Institutional Development Award (IDeA) Program, the National Center for Advancing Translational Sciences Clinical and Translational Science Award Program, and the Patient-Centered Outcomes Research Institute.

Ms. Lundebjerg noted that clinical sites experience difficulty structuring their electronic health records (EHRs) to report data into a central repository. Therefore, she asked whether NIH plans to set aside funding for Federally Qualified Health Centers (FQHCs) to support connecting clinical sites to larger data infrastructure. Dr. Schwetz acknowledged this common issue and noted that NIGMS IDeA launched an effort to build capacity at FQHCs a few years ago, and DPCPSI will use NIGMS IDeA experiences to inform EHR data collection strategies for FQHCs. DPCPSI has also been hosting public listening sessions on the topic of EHRs and data infrastructure.

Climate Change–Related Efforts

Dr. Schwetz acknowledged that older adults are especially vulnerable to climate change and noted that the Community Partnerships to Advance Science for Society (ComPASS) Common Fund program is studying structural approaches, such as transportation and housing access, to improving community health. She anticipates that these community health efforts will overlap with those aimed at mitigating the effects of climate change.

Actions in Response to Funding Cuts

DPCPSI anticipated the drastic cut in FY 2024 to *All of Us*, because much of these funds were from the 21st Century Cures Act, and was able to plan accordingly. *All of Us* currently has 800,000 participants, and its enrollment progress will slow as a result of this budget cut. *All of Us* had planned to launch an initiative focused on pediatrics, but this funding cut may delay or halt the launch altogether. Notably, *All of Us* continues to add ancillary studies in collaboration with ICs, which provides an alternate source for additional funding.

Given the number of offices within DPCPSI and its limited funding, DPCPSI identifies cross-cutting and synergistic efforts across NIH to maximize its overall impact. Most DPCPSI offices are congressionally mandated with individual line-item appropriations. With these appropriations comes varying degrees of flexibility for the different offices.

VII. ADJOURNMENT

The open session of the 152nd meeting of the National Advisory Council on Aging adjourned at 1:30 p.m. on May 22. The next meeting is scheduled for September 18-19, 2024.

VIII. CERTIFICATION

I hereby certify that, to the best of my knowledge, the foregoing minutes and attachments are accurate and complete.³



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.

³ These minutes will be approved formally by Council at the next meeting on September 18-19, 2024, and corrections or notations will be stated in the minutes of that meeting.