Eunice Kennedy Shriver National Institute of Child Health and Human Development

NATIONAL ADVISORY CHILD HEALTH AND HUMAN DEVELOPMENT COUNCIL

MEETING SUMMARY

September 12–13, 2022

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES (HHS)

NATIONAL INSTITUTES OF HEALTH (NIH)

***EUNICE KENNEDY SHRIVER* NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT (NICHD)**

NATIONAL ADVISORY CHILD HEALTH AND HUMAN DEVELOPMENT (NACHHD) COUNCIL MEETING SUMMARY
September 12–13, 2022

The NACHHD Council convened its 180th meeting at 12:00 p.m. ET on Monday, September 12, 2022, by NIH VideoCast. The meeting was open to the public from 12:00 p.m. to 5:15 p.m. The Council reconvened on September 13, 2022, at 12:00 p.m. to review intramural and extramural research applications. As provided in Sections 552b(c)(4) and 552b(c)(6), Title 5, U.S.C., and Section 10(d) of Public Law 92-463 for the review, discussion, and evaluation of grant applications and related information, the sessions on September 13 were closed to the public. Diana W. Bianchi, M.D., director, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, presided.

Council Members[1]: Those present are denoted with an asterisk (*):

*Diana W. Bianchi, M.D. (Chair)
Shari Barkin, M.D.
Christina Bucci-Rechtweg, M.D.
*Michele Caggana, Sc.D.
*John P. Coughlin, M.D.
*Kathleen B. Egan, Ph.D.
*Damien Fair, Ph.D.
Lucky Jain, M.D.
*Catherine E. Lang, Ph.D.
Missy Lavender, M.B.A.
*Yvonne Maldonado, M.D.
Martin Matzuk, M.D., Ph.D.
*Genevieve S. Neal-Perry, M.D., Ph.D.
*Carmen L. Neuberger, J.D.
*Adam C. Resnick, Ph.D.
*David H. Rowitch, M.D., Ph.D.
*Alan Thenevet N. Tita, M.D., Ph.D., M.P.H.
*Rebeca Wong, Ph.D.
*Anthony J. Wynshaw-Boris, M.D., Ph.D.

***Ex Officio* Members**

*Patricia Dorn, Ph.D.
*Aaron M. Lopata, M.D., M.P.P.

Department of Defense

Melissa R. Miller, Ph.D.

National Advisory Board on Medical Rehabilitation Research Council Liaison

*Jose L. Contreras-Vidal, Ph.D.

Executive Secretary

*Rebekah Rasooly, Ph.D.

The NIH VideoCast time stamp appears in parentheses for each section below.

[1] Council members absent themselves from the meeting when the Council discusses applications from their own institutions or when a conflict of interest might occur. The procedure applies only to individual applications discussed, not to en bloc actions.

I. CALL TO ORDER AND INTRODUCTORY REMARKS (0:05)

Dr. Bianchi opened the meeting and welcomed the members of the NACHHD Council and other virtual participants, especially those representing professional societies and research organizations. Dr. Bianchi introduced Dr. Fair and Dr. Maldonado as new members of the Council. Dr. Maldonado said that she is the senior associate dean for faculty development and diversity, the Taube Professor of Global Health and Infectious Diseases, and a professor of pediatrics (infectious diseases) and of epidemiology and population health at Stanford University School of Medicine. She is a pediatric infectious disease specialist who has studied a wide variety of populations and diseases. Dr. Fair was not present during introductory remarks but introduced himself after the director's report (1:01:20). He is a behavioral neuroscientist, the director of the Masonic Institute for the Developing Brain, and a professor in the Institute of Child Development and Department of Pediatrics at the University of Minnesota Medical School. Dr. Fair is working to break down research silos in maternal and child health by moving policy, psychology, and education researchers into the same building and creating a cooperative research community.

Review of Confidentiality and Conflicts of Interest (3:07)

Dr. Rasooly reminded NACHHD Council members that they were required to read, agree to, and sign the confidentiality and nondisclosure rules for special government employees on the Council member website before evaluating any NIH grant applications. Before the meeting, Council members had received a conflict-of-interest certification form, which they were required to sign. Dr. Rasooly also reminded Council members that they are required to recuse themselves and leave the virtual meeting before any discussion involving any organizations or universities for which they are in conflict, in addition to those listed in the Council action document. Council members are not allowed to serve on any NIH peer review panel while serving as Council members, because NIH policy indicates that individuals may not serve on both the first and second levels of peer review. Cloud-based voice services (e.g., Alexa, Siri) must be turned off during closed sessions.

Council Minutes (4:48)

A motion to approve the June 13–14, 2022, NACHHD Council meeting minutes carried.

Future Meeting Dates (6:32)

Dr. Rasooly reviewed future Council meeting dates: January 24–25, 2023 (virtual); June 6–7, 2023 (NIH Bethesda Campus Building 31); September 6–7, 2023 (to be determined); January 22–23, 2024 (virtual); June 3–4, 2024 (NIH Bethesda Campus Building 31); and September 4–5, 2024 (6710B Rockledge Drive, Bethesda, Maryland 20892).

II. NICHD DIRECTOR'S REPORT (8:05)

60th Anniversary of NICHD (9:28)

NICHD will celebrate its 60th anniversary with a scientific symposium, "Healthy Pregnancies, Healthy Children, and Healthy and Optimal Lives," on October 17, 2022. Registration for this

virtual event is now open. More information on the symposium and other anniversary events is available on the 60th anniversary webpage.

NIH Leadership Updates (10:51)

Francis S. Collins, M.D., Ph.D., stepped down as NIH director in December 2021. Lawrence A. Tabak, D.D.S., Ph.D., who initially became NIH acting director but surpassed the acting position time limit, is now "performing the duties of the NIH director" while the White House continues to search for the next NIH director. The NIH director is a political appointee who requires U.S. Senate confirmation. No candidates are expected to be named until late 2022 at the earliest.

Monica Bertagnolli, M.D., has been named the director of the National Cancer Institute. This position is a political appointment that does not require U.S. Senate confirmation. Dr. Bertagnolli is a surgeon oncologist with pediatric research interests who previously served as a professor of surgery at Harvard Medical School, a surgeon at Brigham and Women's Hospital, and a member of the Gastrointestinal Cancer Treatment Center at Dana-Farber Cancer Institute. She will spearhead President Biden's Cancer Moonshot℠ Initiative.

NIH Appropriation Updates (15:22)

The fiscal year (FY) 2023 budget proposes $62.5 billion for NIH, of which NICHD would receive $1.68 billion. NICHD's congressional justification document includes a fact sheet and selected program highlights. It does not appear that the FY 2023 budget will be approved by September 30, so a continuing resolution is likely to be passed.

Because stillbirth affects 1 in 160 pregnancies in the United States and the rate of early stillbirth has remained unchanged over the course of 30 years, the FY 2022 Appropriations Report included language to require the HHS Secretary to establish a task force on stillbirth in the United States. This charge was delegated to NICHD, so the Stillbirth Task Force will be formed as a subcommittee of the NACHHD Council. Subcommittee members will include representatives from the Centers for Disease Control and Prevention, NIH, outside specialty organizations, and maternal and fetal medicine specialists. The subcommittee has been asked to focus on known risk factors for stillbirth, current barriers to collecting data on stillbirths in the United States, communities at higher risk of stillbirth, and the psychological impact and treatment for mothers following stillbirth. Subcommittee meetings will commence in 2022, recommendations will be presented to the NACHHD Council in January 2023, and a final report is due to Congress in March 2023.

NICHD Racial and Ethnic Equity Plan (REEP) (20:21)

As a major component of NIH's UNITE program, the "I" Committee is tasked with improving the culture and structure for equity, inclusion, and excellence at NIH. NICHD submitted its REEP in May 2022 and immediately began implementation. REEP activities have helped NICHD identify additional targets for projects and programs. The REEP plan was integrated into NICHD's existing STrategies to enRich Inclusion and achieVe Equity (STRIVE) Initiative.

Initial REEP activities included:

- Conducting a pulse survey of NICHD's climate and disseminating the survey results

- Examining workforce data related to demographics, equity, and inclusion across all positions and pay grades
- Examining recruitment, retention, and award data for NICHD employees based on demographics
- Establishing training curricula and opportunities for the development of NICHD personnel
- Providing opportunities for staff to demonstrate leadership in roles within and outside the institute in an open and transparent fashion

Researching COVID to Enhance Recovery (RECOVER) for Pediatric Patients (22:56)

RECOVER is an NIH-wide research initiative looking at the long-term health effects of COVID-19. To better prevent, test, and treat Long COVID, NICHD staff members are participating in Pediatric RECOVER, which aims to learn about the long-term health effects of COVID-19 in children. RECOVER is an observational study, so researchers collect information from participants but do not provide treatment or medicine for Long COVID. Pregnant people can participate in the adult study, and people with disabilities are also being recruited.

The pediatric RECOVER researchers want to answer the following questions: How many children are getting Long COVID? Why do some children get Long COVID and others not? What symptoms do children experience when they get Long COVID? How long do children feel sick when they get Long COVID? What causes Long COVID? How does having Long COVID affect later physical health, mental health, and development in children? How do clinical manifestations of congenital exposure to SARS-CoV-2 infection during pregnancy affect child physical health and child development?

The pediatric cohort study will have three tiers: baseline, acute follow-up, and post-acute longitudinal follow-up. The pediatric study opened for enrollment on April 20, 2022, and 19,500 children will be enrolled.

Maternal Health Research (26:51)

The Implementing a Maternal health and PRegnancy Outcomes Vision for Everyone (IMPROVE) Initiative is an NIH-wide effort that supports research focused on reducing preventable causes of maternal deaths and improving health for women before, during, and after delivery. The initiative, which was funded by a new $30 million appropriation in NICHD's FY 2022 base budget, places emphasis on health disparities and disproportionately affected populations.

A dissemination and implementation research notice of special interest (NOT-OD-22-125) was issued on May 5, 2022, to fund community implementation studies of evidence-based maternal health interventions. Additional FY 2022 IMPROVE programs are enabling the development of a longitudinal health record for a pregnant person and their child, including linkages for a woman across pregnancy, as well as encouraging maternal health challenge opportunities. Funding of the Maternal Health Centers of Excellence program will occur in FY 2023.

IMPROVE is using challenges and prize competitions to crowdsource and directly engage public innovators to find interesting ideas or solutions to important problems. NICHD can offer monetary and nonmonetary (e.g., meetings with key officials, networking opportunities, invitations to speak at a conference) benefits to competition participants. The benefits of challenge competitions include no obligation of award (because payment is made only for winning solutions), many possible solutions (which can encourage creative and unanticipated solutions), a broader pool of entrants (which increases the number and diversity of solvers), raising awareness of a particular public health need, encouraging application of NIH research data to address public health or medical issues, and stimulating private-sector investment.

- The first challenge, Connecting the Community for Maternal Health, encourages community-based and advocacy organizations in the United States to develop the infrastructure and capabilities necessary to conduct maternal health research. A total prize purse of $3 million will be distributed across multiple phases of the challenge. The challenge also includes nonmonetary incentives (e.g., mentoring, assistance to write research proposals, assistance to build infrastructure for research activities). The submission portal, which is hosted by HeroX, is accepting registrations through September 29, 2022.

- The second challenge, RADx® Tech for Maternal Health, prioritizes the use of home-based or point-of-care diagnostic devices, wearables, and other remote sensing technologies to extend postpartum care in regions lacking access to maternity care. This challenge is offering up to $8 million in prizes through several phases, and its submission portal will be open from September 15 through November 1, 2022.

The goal of the FY 2023 appropriation for the Maternal Health Research Centers of Excellence program is to reduce maternal morbidity and decrease preventable mortality. The designated funding will support partnering with the communities affected and incorporating their needs and perspectives in maternal health research. Studies will be performed by several research centers with a common data resource/coordinating hub and an implementation science resource hub. The following notices pertain to this program: RFA-HD-23-035, RFA-HD-23-036, and RFA-HD-23-037.

Data and Specimen Hub (DASH) (39:18)

DASH, designed to accelerate scientific findings that ultimately improve human health, is a centralized resource that allows researchers to share and access de-identified data and biospecimens from NICHD-funded studies. It has been enormously successful, especially for trainees. For example, the use of data from the Consortium on Safe Labor (CSL) has already led to the publication of at least 39 papers. Out of 494 requests for DASH data, 113 were for data from the CSL dataset. Much of this research has been conducted with machine learning and data modeling study designs.

NIH Clinical Center Pediatric Research Strategic Plan (43:11)

There are currently about 1,600 active research studies at the NIH Clinical Center, the largest research hospital in the world. Every patient in the clinical center is participating in a research

protocol, although none of the studies currently enroll pediatric patients under age 3 years. The Clinical Center's funding model provides opportunity for research equity, because all services are provided at no cost to the participant.

The Clinical Center has now formed a Pediatric Research Strategic Plan Working Group and charged it with identifying the most impactful scientific areas of pediatric research in which NIH can play a major role to substantially improve child health. The 15-member working group consists of clinical investigators who are scanning the horizon and performing long-term, strategic planning for intramural NIH-wide clinical pediatric research for the next decade and beyond.

NICHD Staff (46:59)

- Four excellent finalists are being considered for the position of scientific director of the Division of Intramural Research (DIR).
- Applications have been received for a new clinical director of the DIR. The search committee will soon be conducting interviews.
- NICHD is seeking to hire a chief diversity officer, personnel for the Office of Health Equity, three Division of Extramural Research (DER) branch chiefs, a scientific review officer, program officers, and program analysts. Many positions have the flexibility to work remotely.

Discussion (49:40)

As a neonatologist, Dr. Rowitch expressed his support for the task force on stillbirth in the United States, calling stillbirth "one of the great tragedies of society." Dr. Bianchi said that she hoped to include people with genomics expertise on the stillbirth task force.

Dr. Maldonado said that stillbirth is a topic of critical interest in the global health community and that the omics approach was a likely key to unlocking the answers to several questions. She added that she supported including pediatric patients in the RECOVER Initiative and that she is eager to see the DER branch chief positions filled, because fundamental genetic and epigenetic research is important for pediatric research.

Dr. Neal-Perry said that the women's and children's health projects that simultaneously evaluate maternal and fetal outcomes are critical. She thanked Dr. Bianchi for her leadership. Dr. Bianchi responded that NICHD and NIH staff have been working above and beyond to complete their assigned tasks plus additional COVID-19–related tasks on an accelerated schedule over the past 2 years. NIH leadership has been taking steps to recognize these efforts with awards, additional compensation, and mental health and wellness initiatives.

Dr. Resnick asked where pediatrics might fit into the Advanced Research Projects Agency for Health (ARPA-H), now that President Biden had announced his intention to name Renee Wegrzyn, Ph.D., its inaugural director. Dr. Bianchi said that she was encouraged about including the pediatric research agenda in both ARPA-H and the Cancer Moonshot. Dr. Bertagnolli (the new director of NCI) has approached Dr. Bianchi about the Pediatric Cancer Moonshot program.

III. ANNUAL DIR REPORT (1:04:44)

Chris McBain, Ph.D., the acting scientific director of NICHD's DIR, provided an overview of the intramural program, along with updates on its budget and personnel. He then described the work of the DIR's Office of Education and shared highlights from the NIH Intramural Research Program (IRP) collaboration with Howard University.

IRP Overview (1:06:18)

NICHD's IRP has eight divisions that create a large portfolio of science:

- Intramural Population Health Research (DiPHR)
- Developmental Biology
- Translational Medicine
- Molecular and Cellular Biology
- Neurosciences and Cellular and Structural Biology
- Basic and Translational Biophysics
- Translational Imaging and Genomic Integrity
- Obstetrics and Maternal-Fetal Medicine

DIR employs more than 750 people, including 75 principal investigators (PIs), 57 staff scientists, and 271 trainees. The basic and clinical programs are divided into 12 scientifically based affinity groups. The three branches and one program within DiPHR include epidemiology, biostatistics and bioinformatics, social and behavioral sciences, and contraceptive development. There are currently 69 clinical protocols and six accredited medical training programs within DIR.

DIR has a two-tiered structure, with investigators self-assembled into the 12 scientific affinity groups (which foster communication around a scientific area or theme) and an administrative organization of functional groups that is loosely based around geographic buildings. Associate scientific directors (ASDs) oversee the scientific management and shared resources of their building but do not oversee individual laboratory budgets. Affinity groups and ASDs both play a role in mentoring tenure-track investigators. The scientific director works directly with each PI on their budget and resource needs. There are ASDs who manage administrative portfolios (e.g., budget and administration, recruitment and retention.) Two new ASD positions were created in 2022: one for translational research and one for, diversity, equity, inclusion, and accessibility (DEIA).

Budget and Personnel Updates (1:14:39)

DIR and DiPHR currently receive 14% of the NICHD budget, or $215 million. Most of NICHD's total budget (81%) goes to extramural research, and the remaining 5% goes toward research management support.

The 300 to 350 DIR trainees include postdoctoral, postbaccalaureate, and graduate students, clinical fellows, and summer interns. More than half of these are postdoctoral researchers.

The following staff changes were announced in the past year:

- Una Grewal, Ph.D., M.P.H., was named director of DiPHR in December 2021.

- Laverne Mensah, M.D., FACOG, FACS, FASCO, was named acting clinical director on May 31, 2022.
- Forbes Porter, M.D., Ph.D., was named ASD for translational research.
- Stephen Gilman, Sc.D., was named ASD for DEIA.
- Harry Burgess, Ph.D., was named ASD for recruitment and retention.
- Mary Dasso, Ph.D., was named deputy ASD for recruitment and retention.
- Robin Kastenmayer, D.V.M., Ph.D., stepped down as animal program director and senior veterinarian.
- Rachael Labitt, D.V.M., M.S., was named acting animal program director and senior veterinarian on May 1, 2022.

New initiatives to improve staff retention, especially the retention of staff scientists (through training, mentoring, and a new awards system) have been launched. An NICHD awards committee has also been established to showcase and highlight the work that is being done from within the institute.

Office of Education Updates (1:23:57)

The NICHD Office of Education develops activities, programs, and professional development opportunities for career advancement (e.g., public speaking, teaching, grantsmanship, publishing, interviewing, networking). One of the office's 10 key activities is to meet annually with all 360 NICHD postdoctoral researchers to provide individualized training and career counseling.

Howard University Partnership (1:29:49)

In 2019, NIH signed a master affiliation agreement with Howard University for programs within the NIH Clinical Center and the IRP. The intent of the agreement was to facilitate a model network for research collaborations and training. The University of Maryland and Virginia Commonwealth University are also involved. The agreement includes four areas of collaboration:

- Providing secondary mentors to biology honors students in the College of Arts and Sciences
- Providing OB/GYN clerkship research mentors to third- and fourth-year students in the College of Medicine
- Providing OB/GYN research mentors to residents in the Howard University Hospital
- Providing a 6-week career path and professional development seminar series for biology undergraduates who are exploring M.D.-Ph.D. paths

Students from the professional development seminar series recently made presentations on their planned career trajectories, and most had adjusted their plans based on learnings from the series.

Discussion (1:33:45)

Dr. Wynshaw-Boris asked whether any future educational programs would be developed for the pediatric interest group. Dr. McBain said that the Office of Education was working with Howard University to expand its offerings.

IV. INVITED DIRECTOR: NATIONAL INSTITUTE OF ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES (NIAMS) (1:35:48)

Lindsey Criswell, M.D., M.P.H, D.Sc., director of NIAMS, presented "Examples of NIAMS Commitment to Enhancing Child Health and Human Development." She described the mission of NIAMS, its new strategic planning effort, and its intersections with NICHD.

Introduction to NIAMS (1:39:22)

NIAMS was established in 1986 to support and conduct research on the causes, treatment, and prevention of arthritis and musculoskeletal and skin diseases. It also aims to train the next generation of scientists and disseminate information about its discoveries and how they can be applied to improve health. The institute funds intramural and extramural research. Its FY 2022 budget is $656 million, with 84.1% of those allocations going toward its extramural research programs across the country.

Strategic Plan (1:40:54)

The NIAMS 2020–2024 Strategic Plan includes five core areas (systemic and rheumatic autoimmune diseases and skin, bone, muscle, and joint diseases), all of which intersect with pediatric medicine. There are several cross-cutting themes in the NIAMS strategic plan, including:

- Shared mechanisms in health and among diseases
- Patient-centric approaches to health and disease
- Precision medicine for arthritis and musculoskeletal and skin diseases
- Health and disease in diverse populations

NIAMS is soliciting public input on its 2025–2029 Strategic Plan through November 30, 2022.

Intersections with NICHD (1:43:23)

Because it seeks community engagement and input from patient voices, NIAMS has created the NIAMS Coalition, an independent consortium of professional voluntary organizations with shared interests in the institute's mission. This partnership can help leverage pediatric research in the NIAMS portfolio.

The Pediatric Dermatology Research Alliance (PeDRA) is holding its annual conference in November; Dr. Criswell will be presenting and participating in a plenary session on the community of resources at NIH.

The Childhood Arthritis and Rheumatology Research Alliance (CARRA) collaborated with NIAMS to conduct the Atherosclerosis Prevention in Pediatric Lupus Erythematosus (APPLE) study.

NIAMS is an active member of the Pediatric Patient Reported Outcomes in Chronic Diseases (PEPR) Consortium, the Environmental influences on Child Health Outcomes (ECHO) Program, and the Patient-Reported Outcomes Measurement Information System (PROMIS) program. Furthermore, several investigators in NIAMS' DIR have a pediatric focus to their research,

particularly for rheumatic diseases. A collaborative effort between the NIAMS and NICHD intramural programs is studying melorheostosis, a rare and progressive disease that affects the growth and development of bones. Extramural researchers are studying the impact of lupus on pregnancy.

NIAMS is collaborating with NICHD on the Maternal Health Research Centers of Excellence initiative, the Wellstone Muscular Dystrophy Research Network (where each institute supports two Centers of Excellence), the Brittle Bone Disorders Consortium, IMPACCT: Infrastructure for Musculoskeletal Pediatric Acute Care Clinical Trials, and the HEAL (Helping to End Addiction Long-term®) Initiative's Back Pain Consortium (BACPAC) Research Program, which also intersects with NICHD's rehabilitation research efforts.

Discussion (1:58:44)

Dr. Bianchi said that Michael Ombrello, M.D., is representing NIAMS on the NIH Clinical Center's Pediatric Research Strategic Plan Working Group.

Dr. Criswell said that she learned quite a lot about the shared projects between NIAMS and NICHD while preparing this talk and looked forward to many future collaborations.

Dr. Rowitch said that Dr. Criswell's points about the genetic burden of disease in certain presentations were being seen across pediatrics, so the work being done is this area is exciting. He added that there will also be room for synergies for pregnancy management in people with autoimmune conditions. Dr. Criswell agreed that genetic analyses in certain populations are likely to be quite informative.

Dr. Resnick asked whether NIAMS had created a strategy for sharing its data assets. Dr. Criswell said that this was an important topic and that NIAMS had begun a data science initiative and pilot study with intramural and extramural components. She added that it is important to consider data sharing strategies at the outset of every study, to accelerate progress across related conditions and NIH institutes and centers (ICs).

Dr. Maldonado asked whether training grants or other mechanisms were available to encourage and fund partnerships between pediatric scholars and internal medicine rheumatologists. Dr. Criswell said that the University of California, San Francisco has both pediatric and adult rheumatology training programs that successfully collaborate, creating a win-win relationship. She understands the importance of providing infrastructure, training opportunities, and funding in this area because of the relevance of pediatric presentations of diseases to adult practice. NIAMS is interested in new ideas for helping to create more beneficial programs. Dr. Bianchi added that the NICHD strategic plan includes the development of programs that transition pediatric and adolescent patients to adult care (e.g., arthritis).

V. SCIENTIFIC PRESENTATION: PRECISION MOUSE MODELS OF CHILDHOOD AMYOTROPHIC LATERAL SCLEROSIS (ALS) CAUSED BY EXCESS SPHINGOLIPID SYNTHESIS (2:11:02)

Claire Le Pichon, Ph.D., an investigator in NICHD's DIR unit on neurodegeneration, provided a technical presentation on her unpublished basic research developing mouse models that carry recently discovered, childhood-linked ALS mutations.

Neurodegeneration can be caused by genetic predisposition as well as environmental factors experienced during development and life. The Le Pichon laboratory studies downstream pathways common to neurodegeneration and models genetically caused syndromes. The group makes precision mouse models to learn about all aspects of a disease, especially the development of the disease process, and provide a preclinical model in which to test potential therapies.

ALS is a fatal neurodegenerative disease that causes a person's brain to lose connection with the muscles. Patients gradually lose the ability to walk, talk, eat, and, eventually, breathe. The onset of ALS is usually between the ages of 40 to 70, but it can strike at any time. NIH research teams discovered that novel mutations in the serine palmitoyltransferase 1 (*SPTLC1*) gene were associated with childhood onset of ALS.

After describing the biochemical pathway and introducing the molecules involved, Dr. Le Pichon shared data from her mouse models. The *SPTLC1* mutation results in elevated levels of sphingolipids throughout the body, which can be measured in the serum. It causes several types of nerve pathology, reduces the functional connectivity between the muscle and nerve, and produces elevated levels of a biomarker of neurodegeneration, neurofilament light. The gene-edited mice have neurodevelopmental issues and progressive degeneration that vary by phenotype.

This research has implications for patients with all types of ALS.

Discussion (2:44:47)

Dr. Rowitch asked for clarification on the types of pathology in the neurons and whether Dr. Le Pichon had evaluated the motor neurons in later stages. Dr. Le Pichon further explained the pathology and said that her group was still in the process of evaluating the motor neurons.

VI. VOICE OF THE PARTICIPANT: GENETIC CHILDHOOD ALS (2:48:29)

Payam Mohassel, M.D., associate professor of neurology at the Johns Hopkins University School of Medicine, introduced Rivka Herzfeld, a patient with genetic childhood ALS who has been interested in learning more about what is causing weakness in herself and her three siblings, all of whom carry the same genetic mutation (in one copy of the *SPTLC1* gene). The disease affects each of them in different ways.

Ms. Herzfeld shared her personal experiences, such as observing gait abnormalities in her sister ("moonwalking") and having difficulty maintaining her active lifestyle. She realized that her brain was not properly controlling her muscles when activities became more difficult over time. This was the start of her quest to figure out what was wrong with her and her siblings.

Over the past 10 years, Ms. Herzfeld and her siblings have been evaluated by neurologists, received incorrect diagnoses, and decided to undergo whole genome sequencing. When the mutation was found in the *SPTLC1* gene, she was referred to Dr. Mohassel.

Ms. Herzfeld hopes that genetic medicine can change the course of her disease and allow her to regain a quality of life that allows her to experience nature, work out, play sports, practice taekwondo, and participate fully in her synagogue (e.g., performing acts of service, standing for prayer). She would like to be part of the medical solution and ensure that she does not pass the gene on to her future children.

Discussion (3:02:18)

Dr. Bianchi thanked Ms. Herzfeld for openly and honestly sharing her lived experience. She asked whether Ms. Herzfeld's father carried the ALS mutation. Ms. Herzfeld said that her father has an idiopathic neuropathy that necessitates the use of assistive devices. When Dr. Bianchi asked whether all family members had been tested for the genetic mutation, Ms. Herzfeld said no. Dr. Mohassel clarified that Ms. Herzfeld's father carries the same autosomal dominant genetic mutation as all the affected siblings, but it presents with a slightly different phenotype and metabolic profile. Dr. Bianchi told Ms. Herzfeld that the technology was currently clinically available for her or her siblings to undergo *in vitro* fertilization and transfer only the embryos that did not carry the genetic mutation.

Dr. Contreras-Vidal asked whether Ms. Herzfeld was aware of exoskeleton technologies that could help her regain mobility. Ms. Herzfeld said yes, but she was afraid of falling due to her inadequate ankle control and weak thigh muscles. Dr. Contreras-Vidal encouraged Ms. Herzfeld to further explore this possibility. Dr. Bianchi told Ms. Herzfeld that NICHD houses the National Center for Medical Rehabilitation Research and offered to connect Ms. Herzfeld with experts on rehabilitative medicine.

Dr. Neal-Perry encouraged Ms. Herzfeld to consult with a reproductive endocrinologist to learn more about possible menstrual cycle challenges for patients with ALS and offered to connect her with a specialist.

VII. SPECIAL COUNCIL REVIEW (SCR) (3:12:56)

Dr. Rasooly led a discussion on SCR, which is a mandated process that began in 2012 to review applications from Program Directors (PDs) or Principal Investigators (PIs) who receive large amounts of funding. Applications that meet SCR criteria must be considered and voted upon by the NACHHD Council.

In 2022, the SCR threshold was raised from $1 million in direct costs to $2 million in total costs for research project grants. Resource awards (e.g., Centers, Cores) and training awards (e.g., T32s) are excluded from SCR.

SCR was implemented when an NIH study revealed that the top 10% of funded investigators were more likely to be male, White, and non-Hispanic and that the top 10% of PDs/PIs have traditionally received approximately 40% of all NIH funding.

There are several proposed strategies to reduce the concentration of funding, including lowering the monetary threshold for SCR, or lowering the payline, requiring a higher effort level, and closing eligibility loopholes for well-funded investigators. Other ICs have moved to a broader, well-funded investigator policy that includes all NIH and non-NIH funding (as the National Institute of General Medical Sciences did); lowered the payline and threshold, included multi-PI applications, and required a higher minimum effort (as the National Institute of Neurological Disorders and Stroke did); or lowered the payline and required a higher minimum effort (as the National Institute of Mental Health did).

NICHD is proposing the following new SCR criteria:

- An application that has been received from a well-funded PI must meet one or more of the following criteria:
  - Received an outstanding score (less than the sixth percentile).
  - Represent an NICHD priority area.
  - Include plans to enhance workforce diversity.
- The application must require a minimum 20% effort or limit the time with greater than $2 million in support to 12 months from the time of the award (or both). This would limit the duration of the PI's well-funded status.
- Close a major application loophole that currently allows an application with multiple PIs to not be flagged for SCR unless all the PIs have more than $2 million in NIH funding. As many as 95% of applications from PIs with more than $2 million in NIH funding are missed because of this loophole.

Discussion (3:22:36)

Dr. Lang asked whether the $2 million in total costs meant direct plus indirect costs. Dr. Rasooly said yes. Dr. Lang said that in her 2 years on the Council, she had not seen an application not pass SCR. She asked whether any application had ever been rejected during SCR or whether applications were rejected without reaching SCR. Dr. Rasooly said yes to both cases and added that reviewing the additional 95% of applications from the loophole represented a significantly increased workload for staff and for Council.

Dr. Lang suggested implementing the changes incrementally in a time series and measuring their impacts instead of making all the changes at once.

Dr. Wong asked whether the $1 million or $2 million was an annual amount or the amount of the award. Dr. Rasooly said that the amount was created by an algorithm built into the system that calculates the current support of the investigator in a year.

Dr. Tita said that he understood the need for the changes and asked whether a review had been done to determine whether the SCR process was effective or led to more equitable distribution of funding.

Dr. Tita said that he would not be in favor of any changes that interfered with the completion of important scientific endeavors, especially for projects that are being done with large teams. Dr. Resnick agreed, adding that he would have concern about limiting the potential of projects with

multiple PIs and resources. Dr. Rasooly said that the funding algorithm proportions the funds when there are applications with multiple PIs.

Dr. Resnick said that there was a wide range of indirect costs across institutions, which could create an unintended disparity when PIs cannot control indirect rates.

Dr. Resnick said that the transition process may create a risk of premature termination for some programs if the completion timeline is limited to a single year.

Dr. Fair said that review section culture favors senior investigators who are helping younger investigators secure grants. He agreed with the suggestions to quantify the effects of SCR and said that senior investigators could also be effective changemakers if they were incentivized to create diverse research teams. Dr. Dorn agreed with the idea of creating a metric to improve researcher DEIA. Dr. Wong also agreed with assessing the impact of the proposed changes on the study sections.

Dr. Dorn asked for clarification on why the criteria included percent effort requirements. Dr. Rasooly said that the criteria for 20% effort or more on a new grant would prevent investigators from committing less than 20% of their time to a project.

Dr. Wong said that R01 funding for population health studies often covers costly longitudinal studies that provide data for public use. She added that publications tend to include senior authors as PI. This change might create a situation where the senior author is not PI, and would require a cultural shift in the study sections.

Dr. Contreras-Vidal said that SCR should consider the entire team for multi-PI applications, because optimizing the team can increase the work's impact and lead to greater career development and improved diversity. He added that creating a cap could prevent some important work from being done because increasing the percent effort would have a significant impact on the budget. Dr. Contreras-Vidal said that the study sections should also be considered. He would like to learn more about the number of applications that do not go to SCR.

Dr. Neal-Perry said that study section culture is a huge part of the problem. She added that PIs may lower their percent effort on an application to allow the project to include more staff. Dr. Neal-Perry said that she was in favor of adding diversity requirements to grant applications, because previous suggestions to diversify research teams have not been followed through.

Dr. Wynshaw-Boris said that the Council was not likely in a position to change study section culture. He suggested bringing additional applications to SCR, including those that are outside of the stated parameters. Dr. Wynshaw-Boris suggested adding these topics to future Council meeting discussions of SCR applications. Dr. Fair said that although it was not in the position to change study section culture, the Council could express opinions about the culture and its need for change.

Dr. Maldonado said that the time to first R01 for junior investigators was incredibly extended, with a mean age of 45 years and rising. She suggested creating a different funding mechanism so that junior faculty were not competing against senior faculty for the same awards.

Dr. Maldonado advocated for means testing of the proposed criteria to determine whether the proposed changes would create the intended effects. She agreed with the others who said that study section culture needed major change, because it worsened during the pandemic.

Dr. Bianchi suggested that Council members contact Noni Byrnes, Ph.D., in the Center for Scientific Review to learn more about the implicit bias training course that has been implemented. The course includes discussion of biases toward senior investigators who are White and male. NICHD will also be implementing this training into its study sections.

Dr. Bianchi said that Dr. Tabak is taking action to improve opportunities for young investigators and diverse investigators, including data modeling. The Office of the Director of NIH, along with individual ICs, is acting on this topic.

VIII. COMMENTS FROM RETIRING MEMBERS (3:54:46)

Each of the retiring members expressed gratitude to their fellow Council members, Dr. Bianchi, NICHD staff, and Council buddies. Most expressed disappointment about being unable to meet in person over the past 2 years and gratitude for the diverse perspectives gained and connections made through their participation on the Council. Beyond the messages of thanks, the retiring members spoke about the topics listed below.

Dr. Caggana (3:55:15)

- Learning about important NICHD initiatives and its response to the pandemic
- Listening to the voices of the participants

Dr. Matzuk (3:58:55)

- Enjoying a myriad of personal interactions with NICHD staff, program officers, scientific review officers, and branch chiefs
- Praising Dr. Bianchi's leadership

Dr. Wong (4:04:09)

- Describing her background as a Mexican immigrant bringing a social scientist perspective to the Council
- Participating in a Council of Councils working group on health disparities
- Witnessing NIH's rapid and impressive response to the pandemic from the inside

Dr. Wynshaw-Boris (4:09:56)

- Developing and implementing NICHD's strategic plan
- Advancing the mission of child health
- Working on diverse issues

- Including children in the *All of Us* Research Program to allow them to benefit from genomic sequencing
- Including children in trials at the NIH Clinical Center
- Understanding which diseases and conditions in adults have their onset in childhood or fetal life
- Conducting embryonic stem cell research
- Combatting challenges that have arisen in maternal-fetal medicine

Ms. Neuberger (4:17:33)

- Describing her background as a nurse turned attorney working for a pediatric health system
- Learning about and then providing feedback on critical research
- Listening to the voices of the patients
- Advancing the reproductive health and well-being of the pediatric population

Dr. Tita (4:20:27)

- Serving as a PI and investigator in several networks while making new contacts and networking
- Learning about NICHD's research portfolio, transformative programs (e.g., maternal centers of excellence, social determinants of health, community engagement, global health), and ability to brave COVID-19 while catalyzing cutting-edge research
- Attending workshops, conferences, and review panels
- Advocating for a short and nimble review cycle for the new mechanism to conduct studies in the Clinical Trials Network
- Advocating for NICHD as a friend of the Institute

IX. CONCEPT CLEARANCE (4:26:26)

The Council reviewed seven concepts.

Using Archived Data and Specimen Collections to Advance Maternal and Pediatric HIV/AIDS Research (4:26:52)

Dr. Maldonado said that she supported this concept as an important way to conduct the next generation of HIV/AIDS research with existing and leveraged resources. Decision: Approve.

Development of Novel, Nonsteroidal Contraceptive Methods (4:30:49)

No comments or questions. Decision: Approve.

Centers for Research on Health Disparities in Uterine Fibroids (4:33:27)

No comments or questions. Decision: Approve.

Opportunities for Advancing Limb Regeneration Research (4:35:45)

Dr. Wynshaw-Boris said that he supported this concept because it was timely with regenerative medicine technologies and ongoing basic research. Decision: Approve.

Pediatric Critical Care and Trauma Scientist Development Program (4:39:00)

Dr. Rowitch said that he supported this program because of the field's need for a stronger research base. Decision: Approve.

Translational Research in Pediatric Pharmacology and Therapeutics (4:41:53)

No comments or questions. Decision: Approve.

INCLUDE Project Initiative (4:44:01)

Dr. Caggana said that she supported this initiative because it would provide a large benefit to the Down syndrome community and extrapolate to other conditions. Decision: Approve.

X. DAY 1 ADJOURNMENT

Dr. Bianchi adjourned Day 1 at 5:15 p.m. A total of 360 people viewed the live VideoCast.

XI. DAY 2 CLOSED SESSIONS

Day 2 of the meeting was closed to the public in accordance with the provisions set forth in Section 552b(c)(4) and 552b(c)(6), Title 5, U.S.C., and Section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2).

XII. REVIEW OF APPLICATIONS

The session included a discussion of procedures and policies regarding voting and confidentiality of application materials, committee discussions, and recommendations. Members absented themselves from the meeting during discussion of and voting on applications from their own institutions or other applications in which there was a potential conflict of interest, real or apparent. Members were asked to sign a statement to this effect. For the 202208 and 202210 Councils, the Council considered and approved 522 HD-primary applications requesting $188,814,896 in direct costs and $262,331,996 in total costs.

XIII. ADJOURNMENT

There being no further business, the meeting adjourned at 5:00 p.m. on Tuesday, September 13, 2022. The next meeting, scheduled for January 24–25, 2023, will take place virtually.

I hereby certify that, to the best of my knowledge, the foregoing minutes and attachments are accurate and complete.[2]

Diana W. Bianchi, M.D. NACHHD Chair NICHD Director	Date
Rebekah Rasooly, Ph.D. NACHHD Executive Secretary Associate Director, NICHD DER	Date

[2] These minutes will be formally considered by the Council at its next meeting, and any corrections or notations will be incorporated in the minutes of that meeting.