

NATIONAL ADVISORY CHILD HEALTH AND HUMAN DEVELOPMENT COUNCIL

MEETING SUMMARY

June 6–7, 2023 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 June 6–7, 2023

The <u>NACHHD Council</u> convened its 182nd meeting at 12:00 p.m. ET on Tuesday, June 6, 2023. The hybrid meeting was held on the NIH Bethesda Campus in Building 31 and virtually. The meeting was open to the public from 12:00 p.m. to 1:00 p.m. 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, the session for the review, discussion, and evaluation of grant applications and related information was closed to the public from 1:15 p.m. to 5:00 p.m. The Council reconvened on Wednesday, June 7, 2023, at 9:00 a.m. ET, for a session that was open to the public. NICHD Director Diana W. Bianchi, M.D., presided.

Council Members Present¹

Diana W. Bianchi, M.D. (Chair) Shari L. Barkin, M.D. Christina M. Bucci-Rechtweg, M.D. (virtual) John P. Coughlin, M.D. (virtual) Kathleen B. Egan, Ph.D. Damien Fair, Ph.D. (virtual) Lucky Jain, M.D. Catherine E. Lang, Ph.D. Missy D. Lavender, M.B.A. Yvonne Maldonado, M.D. Genevieve S. Neal-Perry, M.D., Ph.D. (virtual) Adam C. Resnick, Ph.D. David H. Rowitch, M.D., Ph.D.

Council Members Absent None

Ex Officio Members

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

National Advisory Board on Medical Rehabilitation Research Council Liaison José L. Contreras-Vidal, Ph.D. **Department of Defense** Melissa R. Miller, Ph.D.

Executive Secretary Rebekah Rasooly, Ph.D.

In each section below, the number in parentheses following each heading refers to the time stamp on the <u>NIH VideoCast</u>; go to that point in the recording to listen to the full presentation.

¹Council 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 (0:03)

Dr. Bianchi opened the hybrid meeting and welcomed the members of the NACHHD Council to their first in-person meeting since the start of the COVID-19 pandemic. She reviewed the agenda for the two-day meeting.

Review of Confidentiality and Conflicts of Interest (1:06)

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 received and signed the required conflict-of-interest certification forms. Dr. Rasooly also reminded Council members that they were required to recuse themselves and leave the 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. Furthermore, during closed sessions, Council members must turn off cloud-based voice services (e.g., Alexa, Siri) that are capable of capturing confidential information.

Council Minutes (2:54)

Dr. Egan made a motion to approve the January 24–25, 2023, NACHHD Council meeting minutes as written. Dr. Resnick seconded the motion. The minutes were approved by a unanimous vote of the Council members.

Future Meeting Dates (3:57)

Dr. Rasooly announced that the future Council meeting dates and formats were September 6–7, 2023 (6710B Rockledge Drive, Bethesda, Maryland 20892); January 22–23, 2024 (virtual); June 3–4, 2024 (NIH Bethesda Campus, Building 31); September 4–5, 2024 (6710B Rockledge Drive, Bethesda, Maryland 20892); January 13–14, 2025 (virtual); June 9–10, 2025 (NIH Bethesda Campus, Building 31); and September 8–9, 2025 (6710B Rockledge Drive, Bethesda, Maryland 20892).

II. CONCEPT CLEARANCE (4:30)

Dr. Rasooly led the Council through a review of the following six concepts.

Academic Research Enhancement Award (AREA) for Undergraduate-Focused Institutions (5:04)

Mahua Mukhopadhyay, Ph.D., presented this concept from the Developmental Biology and Congenital Anomalies Branch (DBCAB). DBCAB was seeking approval to re-issue this R15 clinical trial funding opportunity. Council members had no comments or questions. **Decision: Approve.**

National Centers for Translational Research in Reproduction and Infertility (NCTRI) (7:40)

Travis Kent, Ph.D., presented this concept from the Fertility and Infertility Branch (FIB). FIB was seeking approval to continue to provide funding opportunities for NCTRI. Council members had no comments or questions. **Decision: Approve.**

<u>The Helping to End Addiction Long-term® (HEAL) Initiative: KIDS (Knowledge,</u> <u>Innovation and Discovery Studies) Acute Pain Clinical Trials Program (9:46)</u>

With the support of Tammara Jenkins, M.S.N., RN, PCNS-BC, FCCM, Perdita Taylor-Zapata, M.D., presented this concept from the Pediatric Trauma and Critical Illness Branch (PTCIB) and the Obstetric and Pediatric Pharmacology and Therapeutics Branch (OPPTB). PTCIB and OPPTB were seeking approval to provide funding opportunities and a coordinating center for the HEAL KIDS acute pain clinical trials program. A Council member expressed support for this large-scale, multidisciplinary, and trans-institutional concept. **Decision: Approve.**

NIH HEAL Initiative[®]: Outcomes of Babies with Opioid Exposure (12:32)

Caroline C. Signore, M.D., M.P.H., deputy director of the Division of Extramural Research (DER), presented this concept from the Pregnancy and Perinatology Branch (PPB). PPB was seeking approval to continue to provide funding opportunities to complete enrollment for this HEAL-initiated project. Council members had no comments or questions. **Decision: Approve.**

Implementing a Maternal health and PRegnancy Outcomes Vision for Everyone (IMPROVE) Initiative (14:49)

Nahida Chakhtoura, M.D., presented this concept from PPB. PPB was seeking approval to continue to provide funding opportunities to advance the goals of the NIH-wide IMPROVE Initiative. Council members had no comments or questions. **Decision: Approve.**

The Road to Prevention of Stillbirth (16:57)

Monica Longo, M.D., Ph.D., presented this concept from PPB. PPB sought approval to provide funding opportunities to launch the stillbirth prevention initiative. Council members had no comments or questions. **Decision: Approve.**

Discussion (19:17)

A Council member asked how the concepts were developed and brought forward for the concept clearance process. NICHD Deputy Director Alison Cernich, Ph.D., and NICHD DER Director Rohan Hazra, M.D., explained that NICHD staff bring new initiatives forward for internal consideration. The initiatives are evaluated for alignment with NICHD's Strategic Plan and other NIH-wide initiatives. Dr. Bianchi added that initiatives developed within NICHD are associated with a financial commitment from the institute, so Council members are essentially approving the allocation of funds to each initiative.

Dr. Barkin asked whether all NICHD initiatives were tracked on an overall network diagram. Dr. Cernich said that all initiatives approved by NACHHD are listed on the Council website. There is currently no matrix to describe all the concepts approved over time, but each concept is outlined in the NICHD Strategic Plan.

Dr. Hazra described recent NICHD efforts to reduce the amount of time needed from concept clearance to funding opportunity announcement. He cited the example from the Council's Stillbirth Working Group. The working group finalized its report in March 2023, and the concept was presented and approved at this meeting in June 2023, because this is an area of science that needs to be addressed quickly. Dr. Jain thanked Dr. Bianchi and staff for moving forward so quickly on the Stillbirth Working Group's recommendations. Dr. Bianchi said that NICHD staff were to be credited for responding to events in real time.

Dr. Jain asked how the Road to Prevention of Stillbirth efforts would be coordinated with those of other government agencies (e.g., the Centers for Disease Control and Prevention [CDC]). Dr. Cernich said that the NIH Office of Research on Women's Health tracks and coordinates the <u>Maternal Morbidity & Mortality Web Portal</u> and that all NIH-wide efforts to study maternal health and other advisory committee meetings, including the Stillbirth Working Group of Council meetings, provide opportunities for staff to coordinate and collaborate efforts across federal agencies. Dr. Hazra added that all NICHD staff work to coordinate programs across NIH and other federal agencies.

III. COUNCIL STATEMENT OF UNDERSTANDING (26:41)

Dr. Rasooly said that the proposed updated <u>2023 Statement of Understanding</u> between NICHD and the NACHHD Council was posted on the Council website. This document describes the Council's membership and structure, grant application review procedures, concept review procedures, and emergency procedures. Council members voted to approve the 2023 Statement of Understanding.

IV. CLOSED SESSION (29:40)

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). NACHHD Council members provided second-level review of NICHD DER applications.

V. 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. The council considered and approved 733 HD-primary applications requesting \$302,612,525 in direct costs and \$423,988,992 in total costs.

VI. DAY 1 ADJOURNMENT

Dr. Bianchi adjourned Day 1 at 5:00 p.m. A total of 39 people viewed <u>the live VideoCast</u> of the open session.

VII. DAY 2 CALL TO ORDER AND INTRODUCTORY REMARKS (0:05)

Dr. Bianchi opened Day 2 of the virtual meeting and once again welcomed the members of the NACHHD Council and other participants.

In each section below, the number in parentheses following each heading refers to the time stamp on the <u>NIH Day 2 VideoCast</u>; go to that point in the recording to listen to the full presentation.

VIII. NICHD DIRECTOR'S REPORT (0:55)

In her report, Dr. Bianchi described the fiscal year (FY) 2024 budget, announced the NIH director nominee, and shared recent NICHD congressional interactions, research, staff updates, and the results from a recent NICHD career trajectory analysis.

NIH and NICHD FY 2024 Budget Requests (1:43)

The President's budget request for FY 2024 was released on March 13, 2023. The \$48.6 billion requested for NIH (an increase of \$0.9 billion from FY 2023) included \$1.75 billion for NICHD (no increase from FY 2023). The NIH Congressional Justification document highlighted several of NICHD's accomplishments, including how NICHD HEAL investigators demonstrated the benefits of a nonpharmacological treatment option for neonatal opioid withdrawal syndrome (NOWS). Set-asides for the <u>IMPROVE</u> initiative and the <u>Trans-NIH COVID Workgroup on</u> <u>Pregnant & Lactating Women and Children</u> remained level at \$30 million and \$3 million, respectively. The budget request also includes an increase of \$25 million for research on the health impacts of climate change.

Next NIH Director (4:09)

President Biden nominated Monica M. Bertagnolli, M.D., to be the next director of NIH. Dr. Bertagnolli has been serving as director of the National Cancer Institute (NCI) since October 3, 2022. Until her nomination is confirmed by the U.S. Senate, Lawrence A. Tabak, D.D.S., Ph.D., will continue to serve as Acting Director of NIH. The Senate confirmation process has begun, with Dr. Bertagnolli attending meetings with individual members of Congress. The Senate Committee on Health, Education, Labor, and Pensions will hold the confirmation hearing, which will be followed by the Senate vote. If confirmed, the nominee begins the new role immediately. NICHD staff have been preparing transition documents on a variety of topics, and Dr. Bertagnolli will use them to answer questions during the confirmation process.

Congressional Briefings (6:53)

Over the past few months, NICHD staff participated in congressional briefings on NICHD research. Presentations have covered implementing research specific to pregnant and lactating women; including women in clinical trials; conducting the HEAL Initiative's Advancing Clinical

Trials in Neonatal Opioid Withdrawal Syndrome (ACT NOW) Program's Eat, Sleep, Console (ESC) study; and launching studies on climate change and health.

Working Group Updates (8:16)

The Task Force for Research Specific to Pregnant Women and Lactating Women (PRGLAC) Implementation Working Group of Council has been formed to monitor and report on PRGLAC implementation (i.e., the inclusion of pregnant and lactating people in clinical trials). The working group will be co-chaired by Dr. Bucci-Rechtweg and Susan Abdel-Rahman, Pharm.D., chair of the Missouri Medicaid (MO HealthNet) Drug Utilization Review Board. The first meeting will be held later in 2023.

The Stillbirth Working Group of Council is co-chaired by Dr. Jain and Uma Reddy, M.D., M.P.H., Professor and Vice Chair of research in the Department of Obstetrics and Gynecology at Columbia University. The group presented its findings to the NACHHD Council in January 2023 and issued its final report in March 2023. Now extended, the working group will focus on implementing recommendations and continuing to identify current knowledge on stillbirth and prevention, areas of improvement for data collection, current resources for families, and next steps to gather data and reduce the rate of stillbirth in the United States.

NIH and NICHD Research Updates (11:49)

HHS Deputy Secretary Andrea Palm, M.S.W., met with Dr. Tabak, Dr. Bianchi, and other NIH staff on May 16, 2023, to learn more about ongoing initiatives. She expressed particular interest in learning more about research on children's health and then virtually attended an NIH-wide <u>Pediatric Research Consortium (N-PeRC)</u> subgroup meeting.

The N-PeRC subgroup on pediatric pain recently developed a new concept for the HEAL Initiative and released two Notices of Intent to Publish funding opportunity announcements:

- The <u>HEAL KIDS Acute Pain Clinical Trials Program</u> (U01 clinical trial required) will fund research to improve assessment, management, and treatment of acute pain in pediatric patients in various health care settings through innovative, multisite clinical trials across the continuum of care (e.g., pre-hospital settings, outpatient clinics, urgent care, dental clinics, emergency departments, neonatal intensive care units, pediatric intensive care units, acute care/hospital facilities).
- The <u>HEAL KIDS Pain Program Resource and Data Center</u> will fund data curation and harmonization, leverage relevant data standards, provide administrative and logistical support, and coordinate shared research-related resources. The Notice of Funding Opportunities will be published in July 2023, and applications will be due in November 2023.

Late talking (also known as late language emergence) is diagnosed when a child, usually more than 18 months old, is not meeting expressive language milestones. In a trans-NIH effort, NICHD joined with the National Institute on Deafness and Other Communication Disorders (NIDCD), the National Center for Advancing Translational Sciences (NCATS), the National Institute of Mental Health (NIMH), and the National Institute of Neurological Disorders and Stroke (NINDS) to use a \$10 million FY 2023 appropriation to create the Tackling Acquisition of Language in Kids (TALK) initiative to fund research to better understand early language learning. The program is <u>currently funding supplements to existing awards</u> to encourage research that leads to the understanding of developmental precursors and outcomes for late talking.

A \$15 million set-aside in the FY 2023 budget will be used to investigate the effects of technology use and digital media consumption on infant, child, and adolescent development. Three new awards focus on using novel technology to objectively monitor preschool-age children's digital media use (parent reports tend to underestimate screen time) and measure the effect on executive functioning, sleep patterns, and weight; characterizing the context, content, and use of digital media among children 1 to 8 years old and examining associations with the development of emotional regulation and social competence; and characterizing the complex relationships between social media content, behaviors, brain activity, health, and well-being during adolescence.

The NIH-wide <u>IMPROVE initiative</u>, which supports research focused on reducing preventable causes of maternal deaths and improving health for women before, during, and after delivery, received a \$30 million appropriation in NICHD's FY 2022 and FY 2023 base budgets. IMPROVE research emphasizes health disparities and disproportionately affected populations. To advance the initiative, funding awards have been announced for research dissemination and implementation, the Connecting the Community for Maternal Health Challenge, RADx[®] Tech for maternal health, and the <u>Maternal Health Research Centers of Excellence initiative</u>. Recently completed CDC research revealed that 65% of maternal deaths occur 1 to 365 days after a pregnancy ends. The Rapid Acceleration of Diagnostics (RADx[®]) Tech for Maternal Health Challenge prioritizes 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 (i.e., "<u>maternity care deserts</u>"). Up to \$8 million in prizes will be awarded through several phases; the top 10 RADx[®] Tech "deep dive" winners <u>were recently announced</u>.

NICHD-funded research led to many scientific advances published in 2022. In <u>a recent press</u> release, the NICHD Office of Communications highlighted several of these advances.

The Azithromycin-Prevention in Labor Use Study (A-PLUS), supported by NICHD's Global Network for Women's and Children's Health Research in partnership with the Bill & Melinda Gates Foundation, tested whether a single 2-gram oral dose of the inexpensive antibiotic azithromycin could reduce postpartum sepsis and death. After enrolling more than 29,000 women in seven low- and middle-income countries, the study was stopped early due to clear maternal benefit. Researchers found that a single dose of azithromycin could reduce the risk of postpartum sepsis and death by one-third; however, the intervention did not reduce the risk of stillbirth, newborn sepsis, or newborn death.

Results from the ACT NOW ESC randomized controlled trial to study NOWS were recently published in <u>the *New England Journal of Medicine*</u>. When compared with usual care, the ESC approach reduced the time until infants became medically ready for discharge from the hospital and significantly reduced the need for pharmacologic treatment without negatively affecting safety outcomes through 3 months of age. The data provide strong support for establishing a universal, evidence-based standard of care for treating opioid-exposed infants with NOWS. The study also supported practice change by training more than 5,000 care providers in ESC techniques. ACT NOW is funded by the Helping to End Addiction Long-term (HEAL) initiative.

NICHD Career Trajectory Analysis (28:47)

NICHD recently conducted a career trajectory analysis of researchers receiving any NIH support (individual or institutional). NICHD staff were interested in determining at what career stage researchers received their first dollar of direct NIH funding (e.g., principal investigator [PI], trainee), but data identifying support received on grants in which the individual was neither an institutional trainee nor a PI (e.g., postdoctoral researchers contributing to a mentor's R01) are not currently available.

Research Questions

The project examined the following research questions:

- At each career stage, how many individuals who received support also received support at the next career stage?
- What pathways of NIH funding support were most common?
- How do each of these results or patterns differ among racial and ethnic groups?

Cohort Development

From FY 1989 to FY 2010, a total of 31,857 individuals submitted at least one individual grant application to NICHD or received afunded grant from any NIH institute. The cohort was stopped at 2010 to allow the analysis to include longitudinal career data (future cohorts may show different results). All types of NIH funding, including individual awards, institutional training, and career development support (e.g., T32, K12) were analyzed. Multi-year support on a single grant was counted once. Study limitations included the definition of racial groups as only White, Black, Asian, and American Indian/Alaska Native, and race or ethnicity data were missing for about 26% of the grantees.

Results

For White researchers, only about 1% receive support at all career stages, and 30% of predoctoral researchers re-enter at the research stage. About 40% of White researchers who enter at the postdoctoral stage receive only postdoctoral funding, but the highest percentage of researchers entering at the postdoctoral level are White. A minority of those who enter at an early-career stage go on to the research stage. Early-career plus pre- or postdoctoral awardees are more likely to go on to the research stage. The most common pathway for White researchers is to enter at the research stage.

For Black researchers, less than 1% receive support at all stages. Compared with White researchers, a lower percentage of Black researchers receive support at any subsequent stage. A lower percentage of Black researchers than White researchers enter at the postdoctoral stage. The most common pathway for Black researchers is to enter at the research stage. A higher percentage of Black researchers (42%) than White researchers (33%) enter at the research stage.

For Asian researchers, less than 1% receive support at all stages, and the lowest percentage enter at the predoctoral stage. A lower percentage of Asian researchers than White researchers enter at the postdoctoral stage. Asian researchers entering at the early-career stage are likely to receive research grants, even without previous career support. The most common pathway for Asian researchers is to enter at the research stage. Asian researchers had the highest percentage (55%) for entering at the research stage.

Conclusions

Many pathways through the NIH funding ecosystem are nonlinear. Across racial ethnic groups, very few funded individuals receive funding at multiple stages, and this is especially true for minority groups. About half of researchers who receive any NIH support receive their first direct NIH dollar at the research stage of their career. There is no single key point in the career trajectory that can be prioritized for NICHD efforts to improve workforce diversity. The takehome message is that the "pipeline" metaphor may be better revised to be a "braided river" metaphor.

Future Questions

What can we learn from the success of applicants receiving their first award at a later career stage? What is the best way to support a diverse array of applicants, given the varied entrance points and array of career trajectories? How has the picture changed for the applicant cohort from 2010 to 2020?

NICHD Staff Updates (37:18)

Amanda Alise Price, Ph.D., has been hired as NICHD's chief diversity officer and the director of its Office of Health Equity (OHE). She previously directed the preventative medicine portfolio and led the Division of Extramural Science Programs at the National Institute of Nursing Research.

Catherine Gordon, M.D., was selected as NICHD clinical director. She will come to NICHD from the Baylor College of Medicine, where she served as professor and chair of pediatrics and conducted research on adolescent medicine and pediatric endocrinology. She also previously served on the NACHHD Council.

This year, Council member Dr. Maldonado was honored with the American Pediatric Society's highest honor, the John Howland Award. The award recognized her significant contributions to advancing child health and the profession of pediatrics.

NICHD currently has several job openings for intramural and extramural staff.

Discussion (41:21)

A-PLUS Study

Dr. Maldonado asked whether the researchers had any concerns about the overuse of antibiotics or any downstream impacts in the current setting of antimicrobial resistance (AMR) issues, especially for typhoid fever. Dr. Bianchi said that this point was well taken, because AMR is a concern. Dr. Hazra said that the Gates Foundation staff also shared concerns about AMR, so next steps for A-PLUS include looking at downstream impacts, including the risk of AMR. Dr. Bianchi and Dr. Hazra said that NICHD would be collaborating with the National Institute of Allergy and Infectious Diseases to investigate the AMR issue for this population.

Career Trajectory Study

Dr. Maldonado said that she supported the "multiple pathways" terminology and preferred it over the word "pipeline." She added that she would like to see future work in this area include data from other ethnic groups, such as Hispanic/Latino researchers, and thanked Dr. Bianchi for

conducting this illuminating study. Dr. Bianchi said that although she did not present them at this meeting, the data on Hispanic/Latino researchers were available. Dr. Bianchi will send those data to Dr. Maldonado.

Dr. Bucci-Rechtweg suggested analyzing the data in 10-year increments (e.g., from 1989 to 1999 and 2000 to 2010) to gain a better understanding of any dynamic changes that may have occurred over each decade.

Dr. Bucci-Rechtweg asked what further funding researchers who received early development funding received if they did not receive R01 funding (i.e., where did they go?). Dr. Bianchi said that that was a good research question and wondered whether some of the researchers went into industry or clinical care instead of academic research.

Dr. Dorn suggested that the strength of mentoring might affect whether researchers received future funding. She said that if mentoring was a contributing factor in securing future funding, then awards to fund mentoring might be a good idea.

Dr. Lang said that receiving an R award may make some researchers ineligible for early-career awards (e.g., failing to receive an F or K award does not mean that a researcher will not later receive an R award). She added that young researchers may be receiving good mentoring even if they are not named on an R award.

Dr. Barkin said that the pathways model may provide opportunities for growth as researchers move through different phases of their careers. She asked whether data could be collected for all NIH institutes and centers (ICs) that conduct research on children and suggested defining a model of success for research funding throughout the career trajectory. Dr. Barkin also noted that the study would ideally identify areas of leverage, such as mentoring, training, or personal skills. She asked about the next steps for the study. Dr. Bianchi said that NICHD staff would be meeting with the institute's Office of Science Policy, Reporting, and Program Analysis team to share feedback from various audiences and encourage continued work on this topic across NIH.

Dr. Jain asked whether the data could be analyzed to compare the career trajectories for Ph.D. versus M.D. researchers, because he suspected that fellows in clinical training may not have the same access to NIH funding as postdoctoral researchers do. Dr. Bianchi said that because it was funding more institutional than individual K awards in 2017, NICHD conducted an analysis (published in *JAMA Pediatrics*) of individual versus institutional K awards for M.D.s only, Ph.D.s only, and M.D.-Ph.D. researchers. The analysis found that M.D.s were much more likely to apply for an NIH grant and be funded if they had an individual K award. NICHD did not change the amount of funding; it shifted the funding from the institutional level to the individual level. As a mentor of pediatric subspecialty trainees, Dr. Jain expressed concerns that fewer trainees are pursuing clinician scientist careers.

Dr. Resnick said that he had read a statistic that 30% to 50% of researchers who receive an NIH R01 award (or the equivalent) will never receive another one. He asked whether these types of data were also being analyzed in the career trajectory study. Dr. Bianchi said that that would be a good metric to evaluate.

IX. SPECIAL COUNCIL REVIEW (SCR) (57:00)

Dr. Rasooly provided an update on SCR, a mandated process that began in 2012 to review applications from program directors (PDs) or PIs who receive large amounts of NIH funding. SCR was implemented in 2012. All applications that meet SCR criteria must be considered and voted upon by the NACHHD Council. One of the rationales for SCR is that, according to an <u>NIH study</u>, 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.

In 2022, NIH raised the SCR threshold 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. No review is required for applications submitted in response to a Request for Applications (RFA). NICHD is exploring ways to further reduce the concentration of funding.

Previously proposed strategies included the following:

- Closing eligibility loopholes
- Tightening the award criteria (e.g., lowering the payline to 6% or better, requiring the application to represent an NICHD high-priority area and include plans for enhancing workforce diversity)
- Limiting the effort and duration of PIs/PDs with well-funded status by requiring a minimum 20% effort on the project, limiting the time with more than \$2 million in support to 12 months from the time of the award, or both

Analysis of Previously Proposed Strategies

Dr. Rasooly acknowledged assistance from NICHD Program Analyst Christopher Belter, M.L.I.S., and provided answers to the following NACHHD Council questions from September 2022:

<u>Q:</u> In the past, how many of the well-funded PI applications were actually brought to Council for SCR?

A: From 2018 to 2022, a total of 39 applications met SCR criteria. The NACHHD Council reviewed 31 of the 39 qualifying applications and approved 100% of the reviewed applications.

Q: What would the impact of the proposed SCR changes be (i.e., how many applications would be affected)?

A: The number of applications that would require SCR dropped from 30 to 60 with the threshold of \$1 million in direct costs from any PI to 15 to 20 with the threshold of \$2 million in total costs from any PI. Therefore, the NIH policy change that raised the cost threshold from \$1 million to \$2 million returned the SCR process to status quo. Further analyses showed that including the cost threshold for any PI, lowering the payline, and limiting the duration of well-funded status to 12 months after an award would affect fewer than five applications per Council review cycle, so the proposed policies to tighten the SCR criteria were irrelevant. Requiring 20% PI effort could not be analyzed with the available data.

Q: Can we assess the potential impact on workforce diversity? Has the SCR policy had any impact on workforce diversity?

A: These questions could not be analyzed with the data that are available to NICHD.

Newly Proposed Strategies

Because the previously proposed strategies did not lead to a meaningful reduction in the concentration of funding because so few applications were impacted, Dr. Rasooly suggested three new strategies to flag more applications for SCR and tighten the award criteria: lowering the threshold for SCR to \$1 million in total costs, closing eligibility loopholes (as previously proposed), and lowering the payline to applications that scored 6% or better.

Implementing these changes should raise the number of applications that qualify for SCR and encompass applications requesting 6% to 20% of all dollars in a Council round. A significant proportion of the applications would then be identified as coming from well-funded PIs and become ineligible for funding consideration.

Tightening the eligibility criteria would make more than half of the identified applications ineligible for funding consideration. Compared with the existing policy, identifying more applications from well-funded PIs and tightening eligibility criteria would exclude two to five times more grant applications from funding consideration. NICHD gives approximately \$350 million in new awards each fiscal year. The combination of these proposed policies would allow NICHD to reduce the proportion of funds going to well-funded investigators. There would be the potential to reallocate approximately \$20 million each fiscal year.

Discussion (1:10:55)

Dr. Resnick asked whether the proposed strategies would disincentivize a well-funded PI from collaborating with an early-career investigator on multi-PI projects. Dr. Rasooly said that such policies could also keep a junior investigator in the shadow of a senior investigator.

Dr. Resnick asked whether applications that landed above the payline would still undergo SCR. Dr. Rasooly said that this may not be the single best forum for deciding which applications merit funding.

Dr. Miller asked what NICHD was trying to achieve with the proposed SCR revisions. Were the changes proposed to reduce the amount of funding going to a small number of investigators or to increase workforce diversity? Dr. Rasooly said that the resources are limited, and that although a maximum of 20% are funded, more are highly meritorious. The goal is to slightly redistribute the resources to de facto increase the breadth and diversity of the pool. Dr. Miller said that the cut to 6% of the payline may not be enough. She suggested cutting the payline even further to create more diversity of investigators.

Dr. Egan suggested measuring the impact of the policy changes beyond the metrics. She proposed creating three categories for the applications: applications for mentoring new investigators, applications for investigators who are contributing scientific advances, and applications for diverse investigators.

Dr. Lang said that she supported the newly proposed strategies but cautioned NICHD staff to be careful about how the new policy changes were communicated to investigators.

Dr. Fair said that he supported the newly proposed strategies for diversifying the researcher pool and improving the science. He agreed with the idea of incentivizing well-funded investigators to support diverse investigators. Dr. Fair asked what would happen to applications from wellfunded investigators from underrepresented groups. Dr. Rasooly said that that had not been considered and that it would be unfortunate if the new policies had a negative effect on diversity. She added that further analysis could be done by NICHD staff with access to data on applicants from underrepresented groups.

Dr. Neal-Perry said that she supported the newly proposed strategies. She cautioned that funded investigators needed to go beyond supporting underrepresented investigators and allow diverse investigators to become independent. The trickle-down effect does not work.

Regarding what problems that the new policy should solve, Dr. Barkin said that the allocation of NICHD research funding should be equitable and develop sustained research from a diverse workforce. She suggested a pilot study to measure whether the new approach yields the intended results over time.

Dr. Bucci-Rechtweg said that she also favored a pilot project to measure results from the newly proposed strategies. She asked whether there was another way to evaluate how the funded applications allocated the funding. Dr. Bucci-Rechtweg added that the way the policy changes are communicated is important, including describing from where the funding originated.

Dr. Jain asked whether these NICHD decisions would be coordinated with other NIH ICs, because many PIs receive awards from several ICs. Dr. Rasooly said that each IC was working independently on this issue and experimenting with the paradigm.

Dr. Jain asked whether some RFAs were earmarked for early-career investigators and whether reviewers were included in the processes to improve SCR. Dr. Rasooly said that several programs were being implemented to fund early-stage investigator applications.

Dr. Cernich asked NACHHD Council members to submit additional comments or questions after the meeting.

X. COMMENTS FROM RETIRING MEMBERS (1:29:47)

Dr. Lopata has served on the NACHHD Council for 8 years. He shared his departing thoughts with messages of thanks and by emphasizing the importance of the ongoing collaboration between NICHD and the Maternal and Child Health Bureau of the Health Resources & Services Administration. Dr. Lopata said that he would miss the other members of the Council and wished that the general public could see the dedication, passion, and commitment that government employees have for the health of children and women.

XI. SCIENTIFIC PRESENTATION: RESEARCH SUPPORTED BY THE GABRIELLA MILLER KIDS FIRST PROGRAM ON STRUCTURAL BIRTH DEFECTS AND CHILDHOOD CANCER (1:33:50)

James Coulombe, Ph.D., M.S., chief of NICHD's Developmental Biology and Congenital Anomalies Branch, is also the NIH Working Group coordinator for the Gabriella Miller Kids First Pediatric Research Program (Kids First). Philip J. Lupo, Ph.D., M.P.H., director of the Epidemiology and Population Health Center, is a genetic epidemiologist and professor of pediatrics in the hematology-oncology section at Baylor College of Medicine. Dr. Coulombe described the Kids First program, and Dr. Lupo described his Kids First–funded research on the relationship between structural birth defects and childhood cancer.

The Gabriella Miller Kids First Program (1:35:24)

Dr. Coulombe said that in October 2013, Gabriella Miller, a childhood cancer advocate, died at age 10 from an aggressive brain cancer. In her short life, she was a powerful advocate for pediatric health research. In April 2014, the Gabriella Miller Kids First Research Act authorized the appropriation of \$12.6 million per year for 10 years for pediatric research at NIH. In September 2015, NIH received the first annual appropriation for the Kids First program, which is currently funded through FY 2024. Kids First is a trans-NIH Common Fund program. The Kids First Working Group is charged with building a cloud-based genomic data resource to share data and accelerate collaborative research. Because an association between structural birth defects and childhood cancer has been found it makes sense to focus on these conditions. Kids First believes that collaborative research and data sharing will accelerate pediatric research, leading to better prevention, diagnosis, and treatment and alleviate suffering for patients and families with pediatric cancer and structural birth defects.

To date, Kids First has funded 63 X01 sequencing projects. The <u>Kids First Data Resource Portal</u> allows researchers to explore datasets, assemble synthetic cohorts of participants for analysis, find harmonized genomic data files for further research, and connect data from multiple Kids First studies. The portal currently contains data from more than 28,000 participants, 22 birth defects, and 15 cancer cohorts, and the amount of data and number of complex conditions are rapidly growing. Kids First data are part of a larger data ecosystem with many other data efforts, providing a large resource for genomic, phenotypic, and clinical data that is accessible through a researcher-friendly portal that has been used by more than 3,300 researchers from 50 countries.

Birth Defects and Childhood Cancer (1:42:30)

Dr. Lupo said that there are <u>hundreds of various birth defects</u> with a wide range of health consequences. The incidence of childhood cancer has been steadily increasing over the last five decades, at a rate of 1% per year. Conversely, mortality associated with childhood cancer has decreased over the past 50 years. The types of cancer that affect children are different from those that affect adults, with the most common in children being leukemias, cancers of the central nervous system, and lymphomas. Chromosomal anomalies (e.g., trisomy 21) and single-gene defects (e.g., Costello syndrome) are known to be associated with an increased risk of cancer (e.g., lymphoblastic leukemia and rhabdomyosarcoma, respectively). What is less known is the risk of cancer in children with nonsyndromic birth defects, so this is an area of focus for research.

Researchers are interested in studying the following questions:

- Which birth defects are associated with which cancers?
- Do specific birth defect-cancer associations represent undiscovered Mendelian syndromes?
- Why do some children with birth defects develop cancer while others do not?

To answer these questions, investigators linked birth defects registries with cancer registries (the Genetic Overlap Between Anomalies and Cancer in Kids [GOBACK] Study). The GOBACK Study created a retrospective cohort of more than 10 million people, and the data were used to determine that individuals with any chromosomal birth defect had an 11.6-fold increased risk of developing any childhood cancer and that individuals with a non-chromosomal birth defect had a 2.6-fold increased risk. Investigating specific birth defects has led to the discovery of several strong associations and informed how the medical community thinks about birth defects and how to address them. Importantly, the more birth defects someone has, the greater their risk of developing cancer.

Studying family genomics has also led to new discoveries and proved that researchers can leverage registry data to inform genomic studies. Dr. Lupo presented several technical examples of genomic-based discoveries funded by Kids First (e.g., how birth defects are associated with acute lymphoblastic leukemia and acute myeloid leukemia) and described how future studies will continue to expand and build on progress made thus far. His recent Kids First–funded study on Down syndrome and acute lymphoblastic leukemia was published in April in *Blood*. Molecular subtype classifications may affect the types of therapeutics that are chosen to treat these children. Future studies will include germline analyses and deep phenotyping of children with Down syndrome and cancer.

In conclusion, evaluating the overlap between birth defects and cancer provides novel insights into development and carcinogenesis. Insights into factors influencing cancer among children with birth defects may guide improved genetic counseling, surveillance, and treatment interventions. Kids First has accelerated the timeline of discoveries about the link between birth defects and childhood cancer, provided a springboard for new funding opportunities, and fostered collaborative research.

Discussion (2:07:20)

Dr. Maldonado asked whether future research (e.g., clinical trials) would include risk profiles and treatment failures to inform children's oncology therapies. Dr. Lupo said that there may be chemotherapies that are cardiotoxic, so these types of trials are needed, and the data can be used to compare treatment protocols with outcomes.

Dr. Barkin asked whether all children with genomic variants or congenital heart disease should be screened for cancer. Dr. Lupo said that cancer is rare in childhood, so the overall risk is low unless the sequencing identified a variant in a known cancer gene. Children with congenital heart disease are good candidates for sequencing to look for variants in cancer genes, but there is still a lot to learn about screening these children (e.g., some diagnostic procedures can also increase the risk of cancer). Dr. Jain asked whether whole genome sequencing could or should be done in every child born in the United States each year to identify treatable birth defects, predict cancer risk, and promote precision medicine for proper treatment when needed. Dr. Lupo said that he was a proponent of including sequencing as part of newborn screening, especially given sequencing's decreasing cost and its utility as a public health prevention measure.

Dr. Jain asked whether the Kids First registry was connected with any of CDC's birth defects registries. Dr. Lupo said that it is. Kids First is working to link CDC's <u>National Birth Defects</u> <u>Prevention Study</u> with NCI's <u>National Childhood Cancer Registry</u> (NCCR) and include the data in the Kids First data portal (along with population-based data).

Dr. Bianchi asked about the possible underlying mechanism behind the high hazard ratio for biliary atresia and Hodgkin's or non-Hodgkin's lymphoma. Dr. Lupo said that this was a great example of a non-genetic cause. Biliary atresia is the leading reason for solid organ transplantation; the treatment is a liver transplant, which drives the association. A variety of etiologies underlie the associations.

XII. VOICE OF THE PARTICIPANT (2:17:28)

Dr. Bianchi introduced Ellyn Miller, a patient advocate, founder of the <u>Smashing Walnuts</u> <u>Foundation</u>, and Gabriella Miller's mother. While speaking, Mrs. Miller shared images of children who died from cancer. The families of each child shown had donated their child's tissues for biomedical research. She asked the attendees to consider the voices of the children shown on the screen as the donors of their research specimens.

Although Gabriella died from a walnut-sized diffuse intrinsic pontine glioma (DIPG) brain tumor 50 years after astronaut Neil Armstrong's daughter, Karen, died from the same disease, the treatment of radiation and a Phase I clinical trial, along with the prognosis of living 6 to 9 months, had not changed. In the 10 years since Gabriella died, things have begun to change because of discoveries made through the Kids First program. For example, research that was not imagined as possible a decade ago is now underway, and the genomic and clinical data gathered in the Kids First database have led to the creation of more than 30 cohorts of patients that are now available in the public domain. The data have been used in more than 30 manuscripts, and the database is being accessed by more than 600 users around the world.

Mrs. Miller provided examples of the strength of the data in Kids First and said that many researchers still do not know about the vast resources available. She asked attendees to continue to help spread the word about the resources that have been developed through Kids First. Losing the progress made by Kids First would be devastating, so Mrs. Miller is working with Senator Tim Kaine's office to advocate for continuation of the program with increased funding.

The presentation ended with <u>the video of Gabriella</u> that inspired the addition of her name to the Kids First program. In the video, Gabriella expressed frustration with elected leaders. She died 2 weeks after the interview.

XIII. INVITED DIRECTOR: NCI (2:32:58)

Dr. Bertagnolli, director of NCI, was scheduled to present "Ending Cancer as We Know It: Everyone Has a Role." However, a last-minute change in her schedule prevented her from attending the meeting. Instead, Gregory Reaman, M.D., the scientific director of the Childhood Cancer Data Initiative (CCDI) at NCI, stood in to deliver the presentation, which highlighted NCI research progress and opportunities.

In his 2023 State of the Union address, President Biden <u>outlined his vision</u> to accelerate progress to end cancer as we know it today. NCI developed the <u>National Cancer Plan</u> to align broad societal engagement and focus on critical needs to end cancer as we know it. The plan's <u>eight specific goals</u> (each of which is fully defined and explained in the plan) are to prevent cancer, detect cancers early, develop effective treatments, eliminate inequities, deliver optimal care, engage every person, maximize data utility, and optimize the workforce.

The National Cancer Plan lists the goals, strategies, and actions needed to end cancer as we know it. It provides a long-term vision and a framework for collaboration that takes an all-of-government, all-of-society approach and is inclusive of everyone (organizations and individuals). It is not a medium-term strategic/action plan, and it is not confined to research. The plan includes care, advocacy, policy, and individual behaviors. Everyone <u>has a role</u> in the National Cancer Plan.

The goal of the Cancer Moonshot is to achieve a 50% reduction in cancer mortality by 2047. To achieve this goal, cancer death rates must decline faster than the current rate (from 2.3% to 2.7% per year). As a country, we need to accelerate progress for all cancers; increase the use of what is already known to prevent, detect, and treat common cancers; develop or implement new methods of preventing, diagnosing, treating, and surviving cancer; and address health disparities and inequities. Dr. Reaman will be working with Brigitte C. Widemann, M.D., at NCI to provide leadership on childhood cancer research.

NCI's CCDI is building a large community that is centered around childhood cancer care and research data. CCDI's three foundational goals are to gather data from every child, adolescent, and young adult diagnosed with a childhood cancer, regardless of where they receive their care; create a national strategy of appropriate clinical and molecular characterization to speed diagnosis and inform treatment for all types of childhood cancers; and develop a platform and tools to bring together the clinical care and research data that will improve preventive measures, treatment, quality of life, and survivorship for childhood cancers. CCDI's two main programs are the NCCR and a Molecular Characterization Initiative (MCI). MCI is pursuing whole genome sequencing for every child or young adult diagnosed with cancer. CCDI is planning a national rare childhood cancer initiative that will be synergized with other rare tumor efforts.

NCI is also planning the Childhood Cancer Data Integration for Research, Education, Care, and Clinical Trials (CC-DIRECT) program, which will standardize portable electronic health records and provide patient navigation services (e.g., where to go, what to do, who to see). Other Cancer Moonshot programs that address childhood cancer include the My Pediatric and Adult Rare Tumor Network (MyPART) network, the Fusion Oncoproteins in Childhood Cancers (FusOnC2) Consortium, and the Pediatric Immunotherapy Discovery and Development Network (PI-DDN).

In conclusion, Dr. Reaman encouraged attendees to read the National Cancer Plan, follow @theNCI and @NCIDirector on social media, use the #Every1HasARole and #NationalCancerPlan hashtags, and subscribe for email updates to learn about ways to engage with the plan.

XIV. CLOSING REMARKS (2:59:42)

Dr. Bianchi provided the final meeting logistics and thanked the attendees.

XV. ADJOURNMENT

There being no further business, Dr. Bianchi adjourned the meeting at 12:17 p.m. on Wednesday, June 7, 2023. The next Council meeting is scheduled for September 6–7, 2023, and it will take place at 6710B Rockledge Drive, Bethesda, Maryland 20892.

A total of 102 people viewed the Day 2 VideoCast live.

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 Director, NICHD Division of Extramural Activities Date

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