Eunice Kennedy Shriver National Institute of Child Health and Human Development

NATIONAL ADVISORY CHILD HEALTH AND HUMAN DEVELOPMENT COUNCIL

MEETING MINUTES

January 18, 2018

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE

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

NATIONAL ADVISORY CHILD HEALTH AND HUMAN DEVELOPMENT COUNCIL SUMMARY MINUTES

January 18, 2018[1]

The National Advisory Child Health and Human Development (NACHHD) Council convened its 166th meeting at 8:00 a.m., Thursday, January 18, 2018, in Building 31, Conference Room 6, of the National Institutes of Health (NIH) in Bethesda, Maryland. The meeting was open to the public from 8:00 a.m. to 12:05 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, for the review, discussion, and evaluation of grant applications and related information, the meeting was closed to the public from 1:10 p.m. until 3:00 p.m.

Diana W. Bianchi, M.D., Director, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), presided.

Council members present:
Michael Boninger, M.D.
Barbara L. Collura
Patricia Flynn, M.D.
Melissa L. Gilliam, M.D., M.P.H.
Catherine Gordon, M.D., M.Sc.
Gregory S. Kopf, Ph.D. (remote)
Richard D. Krugman, M.D.
Stephen A. Petrill, Ph.D.
DeWayne M. Pursley, M.D., M.P.H.
Frederick P. Rivara, M.D., M.P.H.
George R. Saade, M.D.
Timothy P. Shriver, Ph.D.
Clifford Tabin, Ph.D.
Alyce Thomas, R.D.
Sheila C. Zimmet, J.D.

Council members absent:
Anne C. Case, Ph.D., M.P.A.
Lesli Rotenberg

Department of Defense
Col. Teresa L. Brininger, Ph.D.

National Advisory Board on Medical Rehabilitation Research Council Liaison
Richard K. Shields, Ph.D.

Ex officio members present:
Patricia Dorn, Ph.D.
Aaron M. Lopata, M.D., M.P.P.

Observers (pending members) present:
Atul J. Butte, M.D., Ph.D. (remote)

Others present:
Catherine Y. Spong, M.D., Deputy Director, NICHD
Della M. Hann, Ph.D., Director, Division of Extramural Research and Associate Director for

[1] 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.

Extramural Research, NICHD
Constantine Stratakis, M.D., D.Sc., Director, Division of Intramural Research, NICHD
Members of NICHD Staff
Members of NIH Staff

Invited Guests:
Joseph Laakso, Ph.D., Endocrine Society
Matthew Mariani, American Academy of Pediatrics

I. CALL TO ORDER AND INTRODUCTORY REMARKS

Dr. Bianchi began the meeting at 8 a.m. by welcoming Council members, guests, and staff. She announced that the morning portion of the meeting would be open to the public and would be broadcast on the NIH videocast network.

Dr. Bianchi recognized the Friends of NICHD for their work promoting the Institute's research efforts. The Friends of NICHD has a new chair, Mary Jo Hoeksema, of the Population Association of America.

A. Review of Confidentiality and Conflict of Interest

Dr. Della Hann reminded the Council that all members 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. Council members at the meeting also received a conflict-of-interest certification form, which they were required to sign prior to the closed session of the review of applications. Dr. Hann also reminded Council members that if there was a specific discussion involving any organizations or universities for which they were in conflict, in addition to those listed on the Council Action document, they were required to recuse themselves from the discussion and leave the room. Council members are not allowed to serve on the NIH peer review panel while serving as Council members. It is NIH policy that individuals may not serve on both the first and second levels of peer review.

B. Council Minutes

Dr. Hann moved to approve the September 2017 meeting minutes. The minutes were approved unanimously, as written.

C. Future Meeting Dates

Dr. Hann reviewed the future meeting dates:

June 7, 2018 (Thursday)
September 13–14, 2018 (Thursday–Friday)
January 24, 2019 (Thursday)
June 11, 2019 (Tuesday)
September 19, 2019 (Thursday)

II. NICHD DIRECTOR'S REPORT AND DISCUSSION

Dr. Bianchi said that she gave her first report to the Council one year ago, and much had changed in that year.

Inclusion

Dr. Catherine Spong and Dr. Bianchi published a commentary in *JAMA*: "Improving Public Health Requires Inclusion of Underrepresented Populations in Research." The commentary noted that pregnant women, older adults, people with physical disabilities, and people with intellectual and developmental disabilities (IDDs) have been excluded from research. These groups represent 58 percent of the U.S. population.

An analysis of Phase III and Phase IV trials on ClinicalTrials.gov showed that 68 percent of the trials excluded pregnant women, 47 percent of the trials excluded lactating women, and 75 percent of the trials excluded children. There were fewer stated exclusions of people with IDDs, but they were not often included. Excluding these groups means that these clinical trials do not represent the U.S. population.

The Inclusion Across the Lifespan Workshop, convened in the spring of 2017, contributed to the revision of the NIH policy to require grant applicants and grantees to include individuals of all ages in clinical research, unless there is a strong justification for exclusion. The policy change affects proposals submitted as of January 25, 2019.

Dr. Bianchi asked attendees to submit proposals for studies involving populations of interest to NICHD to the *All of Us* Research Program. The program's website explains this in more detail. The deadline to submit an idea is in February. The studies will launch in the spring.

Congressional Updates

At the time of the meeting, the government was operating on a continuing resolution.

NICHD continues to be involved in implementing the 21st Century Cures Act through the Inclusion Across the Lifespan initiative, the Task Force on Research Specific to Pregnant Women and Lactating Women, medical rehabilitation research, and the Next Generation Researchers Initiative. NICHD funded 29 early-stage investigators (ESIs) in fiscal year (FY) 2017. ESIs include those who have completed their terminal research degree or post-graduate clinical training within the past 10 years but who have not competed successfully for a substantial NIH independent award.

NICHD will continue to organize an annual Young Investigators Conference, but with some changes. The annual meeting facilitates the training of physician scientists and is open to fellows and junior faculty in neonatology, maternal-fetal medicine, and reproductive endocrinology. The conference will be held in Potomac, Maryland, so that NICHD staff can act as faculty. There will be more emphasis on skills building, including presentations on grant and career opportunities. The chairs of pediatric, obstetrician/gynecology, and rehabilitative medicine departments will nominate attendees. Dr. Rosemary Higgins will lead the effort.

Vision Update

NICHD is working with the National Institute on Drug Abuse (NIDA) and the NIH Environmental Influences on Child Health Outcomes program on neonatal opioid withdrawal. There is no consistent approach to caring for these babies and their mothers. The Advancing Clinical Trials in Neonatal Opioid Withdrawal Syndrome (ACT NOW) partnership will evaluate

treatment options for newborns with opioid withdrawal syndrome. The study involves the Neonatal Research Network and the Institutional Development Award (IDeA) States Pediatric Clinical Trials Network. The IDeA network includes areas heavily affected by the opioid crisis.

NICHD is partnering with the National Institute on Aging (NIA) and private foundations to identify additional resources for research on Down syndrome. NIH currently spends $27 million on Down syndrome research.

NICHD recently launched and is continuing to revise its new website to make finding information easier.

The NICHD Biosamples Task Force is examining all of its stored biosamples with the goal of making them available to researchers. The Task Force is assessing historical samples dating back more than 50 years and is working on policies to facilitate sharing. The Task Force has identified 831,000 samples that can be uploaded to the NICHD Data and Specimen Hub (DASH).

NICHD's scientific priorities strategic planning has begun. NICHD has developed a set of focus questions and will appoint a planning committee and a larger working group to develop the work plan. The working group will include some Council members. There will also be a facilitator.

III. DIVISION OF EXTRAMURAL RESEARCH REPORT

Dr. Hann reported on extramural research activities.

Staff Updates

- Dr. Tyl Hewitt of the Developmental Biology and Structural Variation Branch (DBSVB) retired after 31 years of government service. He is a former chief of the Branch.
- Dr. Lorette Javois of the DBSVB retired after 17 years of service. Among other duties, she led the Gabriella Miller Kids First initiative.
- Dr. David Siegel of the Obstetric and Pediatric Pharmacology and Therapeutics Branch retired after 10 years. His duties included leadership in advancing NICHD efforts on the Best Pharmaceuticals for Children Act.
- Ms. Kimm Witherspoon, director of the Office of Committee Management, has moved to a new position with the Food and Drug Administration (FDA).

Impact of the Flexible Funding Model

NICHD has adopted a more flexible payline for the R01, R03, and R21 awards as a way to move towards more scientifically driven funding decisions. Data from funding in 2017 indicated that program was "reaching" for grants that had high program priority more so than the previous year, i.e., 9 percent of the R01 grants awarded in FY 2017 were reaches in priority areas, compared with 5 percent in FY 2016. The R03 and R21 reaches in priority areas increased from 4 percent to 9 percent. Overall, the first year of the flexible funding model was deemed successful.

Impact Analysis of Large Programs

NICHD is developing metrics to assess the scientific impact of NICHD-funded large programs. The plan is to develop metrics that could be applied to all funded programs. The assessment takes into account publications produced by the programs and the publications' impact on the

field. The program will also use the relative citation ratio, which considers the average number of citations typical in the field. Other metrics include whether a study led to new medical, practice, or insurance guidelines; public engagement through news stories, new policies, or legislation; or new products, devices, patents, biologics, or training.

NICHD is currently evaluating five programs using these and other metrics: The Maternal-Fetal Medicine Network, the Learning Disabilities Research Centers, the Pediatric HIV/AIDS Cohort Study, the National Centers for Translational Research in Reproduction and Infertility, and the Population Dynamics Centers Research Infrastructure Program.

Dr. Hann said that the analysis should be completed within six weeks. NICHD will choose more programs in the future to continue assessment of programmatic impact.

Progress in Clinical Trial Reforms

NIH is implementing several reforms for research involving clinical trials. Of note, all applications for clinical trial funding must be submitted on a funding opportunity announcement (FOA) that supports clinical trials. In addition, all multi-site domestic clinical research is now expected use a single IRB, with the exception of studies involving tribal nations. Finally, investigators must register all clinical trials in ClinicalTrials.gov and must report their results there.

NICHD has written four new FOAs for investigator-initiated clinical trials using the R01, R21, R03, and R15 mechanisms. NICHD will join NIH-issued Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs clinical trial FOAs and will continue to issue topic-specific FOAs to meet portfolio needs.

Council Discussion

Dr. George Saade said that the impact analysis could become a model for other research programs. He suggested that the analysis also measure a program's impact on disease outcomes. For example, the AZT/maternal transmission trial produced a sharp drop in maternal-infant transmission of HIV. This metric will vary for different fields, where some would require 10 years to see an outcome while another could produce results more quickly. Dr. Hann said that NICHD is looking to include a public health impact measure.

Dr. Saade suggested that the analysis include the impact of trials with negative findings. Those trials may prevent a harmful or unnecessarily costly intervention.

Dr. Melissa Gilliam asked whether the analysis framework is public. Dr. Hann said that the framework is still in development, but it will be published and made available on the NICHD website when completed.

IV. REHABILITATION RESEARCH AT NIH: TRENDS AND FUTURE DIRECTIONS

Dr. Alison Cernich, Director of the National Center for Medical Rehabilitation Research (NCMRR), said that the NCMRR collaborates with Institutes and Centers (ICs) across NIH. Since 2012, NIH funding for rehabilitation has grown by $100 million. NCMRR evaluates where those dollars are invested and whether there are research gaps that must be filled.

The 21st Century Cures Act requires that NCMRR update the rehabilitation research plan every five years; requires the trans-NIH Medical Rehabilitation Coordinating Committee (MRCC) to host scientific workshops and recommend research priorities; and reauthorizes the National Advisory Board on Medical Rehabilitation Research and specifies its membership. Those requirements have been accomplished. NCMRR will also develop a new definition of medical rehabilitation research and include it in the research plan, as required by the Act.

As a way to evaluate progress on the research plan, NCMRR analyzed the NIH research portfolio for FY 2015. These data will be used as a baseline to gauge progress on the research plan goals. The analysis found that NIH had funded 1,370 extramural rehabilitation projects. The portfolio most frequently included projects in clinical research, neuroscience, behavioral and social science, bioengineering, and brain disorders.

NCMRR funds workshops that include NIH ICs and other government agencies. In May 2017, NCMRR and the National Institute of Neurological Disorders and Stroke (NINDS) co-hosted a workshop to optimize investment in medical devices for rehabilitation. That workshop brought together federal agencies including the Department of Veterans Affairs (VA), the National Science Foundation, the Department of Defense (DoD), the FDA, and the Centers for Medicare & Medicaid Services. The meeting was videotaped and is available in the NIH videocast library.

NCMRR and the National Center for Complementary and Integrative Health have joined a funding announcement with the VA and DoD on a non-opioid pain management initiative. NCMRR is participating in interagency committees and working groups, participates in reviews of other agencies' grant applications, has joined in a government-wide review and analysis of rehabilitation portfolios, and has entered an interagency agreement to establish a limb loss registry.

The World Health Organization invited NCMRR to help plan for the Rehabilitation 2030 initiative. NIH is involved with the research agenda for physical and sensory disability that is being developed.

NCMRR, the National Institute of Biomedical Imaging and Bioengineering, and NINDS cosponsor the Medical Rehabilitation Research Resource Network, which aims to develop the medical rehabilitation research infrastructure by providing expertise through six centers specializing in different areas of rehabilitation research.

Council Discussion

Dr. Timothy Shriver asked whether children with disabilities are included in the Center's research strategy. Dr. Cernich said that one of the problems has been that any individual who is 21 or younger is classified as a child. She said that her recent portfolio analysis suggested that a focus on children is lacking. Projects involving people with IDDs are included, but they are usually referred to as habilitation projects, not rehabilitation.

V. INTELLECTUAL AND DEVELOPMENTAL DISABILITY RESEARCH AT NICHD: TRENDS AND FUTURE DIRECTIONS

Melissa A. Parisi, M.D., Ph.D., Chief of the NICHD Intellectual and Developmental Disabilities (IDD) Branch, provided an overview of IDD research at NICHD.

Genomics Revolution

New methods of DNA sequencing have made sequencing much faster and less costly. The volume of data generated is significantly greater than with the old method of sequencing, leading to the problem of storing and interpreting very large data sets.

Some practical barriers to implementing the genomics revolution in the IDD field include knowing how to apply genomic testing in the clinic to diagnose IDDs and how to translate new gene discoveries into development of treatments.

Discovering the clinical significance of genetic variants will require an interdisciplinary and collaborative approach that will involve the clinic and the research laboratory. Dr. Parisi showed that the diagnostic yield of testing for IDD-related genetic causes has increased from about 5 percent in the 1980s to about 65 percent today. Between 600 and 700 genes have been identified that are related to intellectual disabilities. However, identifying a genetic cause still leaves the challenge of being able to use the information to improve the individual's outcomes.

Another challenge to genomics research includes limited knowledge about the biomarkers, target molecules, and pathways involved in human cognition. The few animal models that are available cannot replicate complex human IDD phenotypes. Also, comorbid conditions such as epilepsy make an individual's condition difficult to model. Other challenges are the lack of natural history studies of rare IDD conditions and a lack of understanding of the role of the environment and epigenetics in complex IDD phenotypes. Companies are hesitant to invest in pharmaceutical development because drugs to treat IDD conditions have not been very successful.

Progress in Intellectual and Developmental Disabilities Research Centers (IDDRCs)

The IDDRCs are working to address the challenges of translating basic science discoveries into development of therapies and interventions for IDDs through collaborative, multidisciplinary research. Each of the 14 Centers supports between 38 and 70 principal investigators and 50–100 projects. The IDDRCs play a key role in the translational research cycle from basic science to clinical trials, as well as in training new researchers in the field.

The Centers have formed five work groups, including a group that has inventoried all projects and resources across the Centers for collaborative projects. There is also a genomic variants work group, an animal cores work group, and a clinical/translational cores work group. To meet their goal of dissemination, the Centers are developing publications to engage lay and scientific audiences about the discoveries that are made and research opportunities that are available. In these ways, the IDDRCs are functioning as a network of collaborating sites that stimulate new research discoveries in IDDs.

Inclusion and Informed Consent for People with IDD

People with IDDs are often not included in research. Only 12.4 percent of 338 NIH-funded Phase III and Phase IV clinical trials excluded people with IDDs. But while most trials do not explicitly exclude these individuals, they are usually not actively included. Only about 2 percent of trials specifically included them.

Dr. Parisi said that people with IDDs must be included in research for a variety of reasons. Some people with IDDs may require alternative drug delivery methods than traditional oral administration, and this may impact the drug's availability. Others with IDDs may have a lower threshold for drug toxicity that may result in devastating side effects. More pharmacokinetic and pharmacodynamic studies are needed, because some IDDs are associated with biochemical

conditions that alter metabolism. Many people with IDDs take multiple psychotropic and other medications even though knowledge of their utility or adverse effects is limited. In addition, people with IDDs may have physiological differences that could advance knowledge about disorders that affect the general population. For example, people with IDDs are at higher risk of developing early Alzheimer's disease but are at lower risk of developing solid tumors.

Common barriers to including people with IDDs in research include inability to provide informed consent, difficulty in complying with the protocol, and ethical concerns because people with IDDs are considered vulnerable subjects. These barriers can often be overcome with accommodations and some additional effort. Barriers that may be difficult to overcome include studies that require typical cognition or that have a risk that outweighs the knowledge to be gained.

NIH has resources to include people with IDDs in research, including registries such as DS-Connect®: The Down Syndrome Registry.

Among other efforts, NICHD is working with the *All of Us* Research Program to include people with intellectual and physical disabilities and children. The Trans-NIH Down Syndrome Working Group is working to engage the families of people with intellectual disabilities in this effort.

Council Discussion

Dr. Frederick Rivara asked what NIH and NICHD are doing to move whole exome sequencing into the clinic so that children with IDDs can be diagnosed sooner. Currently, children are waiting up to seven years for sequencing and diagnosis. Dr. Parisi said that the Undiagnosed Diseases Network is creating centers across the country to use genomic approaches to help with diagnosis. As more academic centers do this sequencing, it is expected to become the standard of care. Dr. Parisi also said that NICHD and the National Human Genome Research Institute will sponsor a workshop on genomics implementation in the health care setting from preconception through the neonatal period this April.

Dr. Shriver asked that the issue of including children with IDDs in research be discussed in more depth at a future meeting. The failure to include people with IDDs is unacceptable. He urged NICHD to advocate for this population within the scientific enterprise.

VI. TOWARD PRECISION MEDICINE FOR PEOPLE WITH INTELLECTUAL DISABILITIES

Stephanie Sherman, Ph.D., Emory University School of Medicine, co-director of the Down Syndrome Center at Emory University, said that her research covers intellectual disabilities including Down syndrome and Fragile X syndrome.

Dr. Sherman began with a short history of the scientific and medical efforts to understand Down syndrome beginning in the mid-1800s. One of the first discoveries was that the risk of Down syndrome increased with the mother's age at birth. Further work showed that having an extra chromosome 21 was the cause in 95 percent of Down syndrome cases. Later work showed that 4 percent of cases are caused by having two normal copies of chromosome 21 plus extra material from chromosome 21 attached to another chromosome. The remaining 1 percent are mosaic, having an extra copy of chromosome 21, but only in some of the body's cells. Over time,

research has drilled even deeper into when the genetic errors appear and how the timing might affect the individual's outcome.

Dr. Sherman also traced the discoveries related to Fragile X. Science has uncovered mechanisms of Down syndrome and Fragile X, but much more needs to be understood to effectively treat individuals with these genetic conditions.

Individuals with the same genetic mutation can vary widely in their levels of cognitive, behavioral, and physical disability. Differences in clinical outcomes are related to the environment, genetics, and random or unexplained effects. The tools to investigate these differences are already available. What is missing are large cohorts and funding.

Down Syndrome 360 (DS360) is a genotype/phenotype project to move toward precision medicine for people with Down syndrome. DS360 includes clinical and biological repositories of samples from 2,800 individuals with Down syndrome that were collected across three separate projects. DS360 is funded by NICHD, the National Heart, Lung, and Blood Institute, and the Down Syndrome Research Foundation.

The Down Syndrome Cognition Project draws on a subset of samples from DS360 to explore cognitive variation in people with Down syndrome. NIH and the LuMind Foundation are funding that project.

Among other projects, DS360 is working with the Trisomy 21 Research Society to create a core test battery for people with Down syndrome and to harmonize data that are collected. DS360 has provided genomic data to Down syndrome cancer studies, and cognitive data to assess possible adverse effects of cancer treatment.

DS360 is working to expand the available data and sample sizes for studies. Potential avenues include merging with existing large cohorts such as the Human Trisome Project, using existing infrastructure and services such as DS-Connect®, and working with the Trisomy 21 Research Society to create an international consortium.

Dr. Sherman highlighted DS-Connect® as a way to facilitate clinical research by connecting families with researchers. About 4,000 individuals with Down syndrome have contributed their data to the registry since it began in 2013. The registry's de-identified data can help better delineate the natural history of Down syndrome.

The Centers for Collaborative Research in Fragile X program, funded by NICHD, supports research to improve the diagnosis and treatment of Fragile X syndrome and related conditions. These centers are geared toward stimulating multidisciplinary, multi-institutional research, with the goal of facilitating the translation of basic research findings from bench to bedside and from bedside to community.

The National Fragile X Foundation, with the support of the Centers for Disease Control and Prevention (CDC), has established the Fragile X Online Registry with Accessible Research Database (FORWARD). The Foundation is also building a biobank and pulling together a collaborative biomarker research project. This is becoming an international effort.

Research on Down syndrome and Fragile X has come a long way, Dr. Sherman said. The efforts to understand the clinical variations within these conditions can bring precision medicine to people with these and other IDDs.

VII. VOICE OF THE PARTICIPANT

Dr. Kathleen Egan introduced her son David who is 40 years old and has Down syndrome. He is the oldest of four children. She recounted his early life, including the critical early interventions, involvement in research, and especially his inclusive education at the Waisman Center Early Childhood Program at the University of Wisconsin in Madison. "What started with 12 kids is now an accredited program with 100 children and two thirds of them have some intellectual and developmental disabilities."

She and her husband were graduate students at the university, and they provided their son with an inclusive and stimulating environment. They had expectations of him. David is a successful man and has been competitively employed for the past 20 years. His passion is to advocate on behalf of people with Down syndrome and other intellectual disabilities.

Dr. Egan expressed concerns with the accelerated aging process that some people with Down syndrome experience, including the risk of developing Alzheimer's disease at an earlier age. Families need more information to know how to navigate this phase of life. Well-designed clinical trials would help. Dr. Egan encourages families who have a member with Down syndrome to enroll in DS-Connect®. She also urged NICHD to continue its work in this area.

Her son, David Egan also addressed the Council.

Mr. Egan shared his life story and involvement with research. He is proud to have had an inclusive life. His first job was at Booz Allen Hamilton as a clerk in the Distribution Center. He currently works full time as a community relations specialist at Source America ensuring that people with disabilities have meaningful employment choices and opportunities.

He attributes his success to family support and people who believed in him. He recounted some of his special accomplishments, such as being a Special Olympics athlete, an international Global Messenger, and a Joseph P. Kennedy Jr. Public Policy Fellow, first ever to be selected with an intellectual disability. He served for one year as a fellow on Capitol Hill with the Congressional Ways and Means Social Security Sub Committee and with the National Down Syndrome Society in Washington DC.

This was his second visit to NIH as the previous time he was there for the renaming of NICHD in honor of Eunice Kennedy Shriver. Ms. Shriver has inspired him and many others with disabilities to pursue their dreams. "I think research is needed and my extra chromosome may unlock discoveries that benefit not only those with Down syndrome but the larger population." He spoke about his participation in research since he was very young, and later with his dad when they donated skin biopsies for the latest induced pluripotent stem cell research studies at the Waisman Center. He urged NICHD to continue its commitment to Down syndrome research, which can greatly improve the quality of life for those with and without the condition. He said, "Anything that can give us an edge to lead fulfilling lives is worth pursuing. It is an investment that will pay off, and you will not regret it, I am a living proof it works." For more info about David, visit **www.davideganadvocacy.com.**

VIII. UPDATE: NIH OFFICE OF DISEASE PREVENTION (ODP)

David M. Murray, Ph.D., Director of the ODP, said that the ODP's mission is to improve public health by increasing the scope, quality, dissemination, and impact of prevention research

supported by NIH and to provide leadership for the development, coordination, and implementation of prevention research in collaboration with the ICs and other partners.

ODP serves as the NIH liaison to other agencies within the Department of Health and Human Services (HHS). It manages the Tobacco Regulatory Science Program and offers training and education programs as well as Pathways to Prevention, an evidence-based assessment program.

One of the ODP's priorities is to monitor NIH investments in research. In 2013, the Office collaborated with the Office of Portfolio Analysis to help automate the portfolio analysis process. This project will help the Office more easily assess the progress and results of NIH investments in prevention research and identify areas that may deserve additional investment.

Another priority of the Office is to continue to identify gaps in prevention research.

The ODP also works with stakeholders such as other ICs and federal agencies. ODP works with the U.S. Preventive Services Task Force (USPSTF) on the Insufficient Evidence survey and has partnered with the HHS Office of Disease Prevention and Health Promotion and the ICs to support Healthy People 2020 and develop Healthy People 2030.

ODP promotes the use of best methods in prevention research and the development of better methods. Among other efforts, ODP has created a publicly available online course on pragmatic and group randomized trials in public health and medicine, created an online research methods resource, and developed a prevention research expertise survey. ODP is also providing resources to program and review staff to ensure that applications with strong methods are distinguished from those with weak methods. ODP also identifies experts in prevention research methods for recruitment to review panels and has created informational and interactive tools for prevention researchers.

ODP has provided input to the strategic plans of the ICs and has created new scientific interest groups, including the Childhood Screening Interest Group and the Genetics of Prevention Interest Group. The ODP will continue to foster prevention research across NIH and with other public and private prevention partners. The Office expects to release its strategic plan in September 2018.

Council Discussion

Dr. Richard Krugman asked whether ODP has worked with foundations that may be interested in prevention research. This might be a way to leverage NIH dollars. Dr. Murray said that most of his efforts have been focused on NIH processes, but he will take Dr. Krugman's suggestion back to his team.

Dr. Rivara asked about working with CDC. Dr. Murray said that ODP works with CDC through its work with the Community Preventive Services Task Force (CPSTF) and other joint activities.

Dr. Saade asked that Dr. Murray help educate IRBs about group cluster randomized trials. IRBs do not understand them. Dr. Murray said that ODP has not attempted to educate IRBs individually, but the research methods website at NIH provides tools and information on these types of trials that IRBs could use. ODP also helps find the appropriate expertise for review panels.

Dr. Bianchi asked how ODP interacts with the ICs. Dr. Murray said that there is a research coordinating committee with representatives from each IC along with representatives from other federal agencies such as CDC. The committee meets about eight times a year.

IX. OPIOIDS AND PUBLIC HEALTH

Nora D. Volkow, M.D., Director of NIDA, said that NIDA shares many interests with NICHD, including work on the opioid crisis. The number of opioid overdose deaths has continued to grow, having increased 22 percent between 2015 and 2016. In 2016, there were more deaths from opioid overdoses than from motor vehicle accidents.

The opioid crisis has been emerging since the late 1990s, when it became clear that opioids were being overprescribed. While opioids are effective at managing acute severe pain, they also depress respiratory function and are highly addictive. In addition, while individuals need increasing amounts of opiates to control pain because of the development of tolerance, the respiratory depressant effects of opioids do not develop tolerance at the same rate.

The NIH opioid research initiative has worked on reversing overdoses and developing treatment for addiction. Basic science approaches have provided new understanding of cell signaling pathways that could lead to developing a new generation of pain therapeutics that provide relief without blocking respiration and with less tolerance.

As an example of partnerships with the pharmaceutical industry, NIDA supported development of an intranasal form of naloxone that is very effective. Naloxone can immediately block opioids, including fentanyl, a highly addictive opioid involved in many overdose deaths, but it to be effective it must be administered quickly into the bloodstream. The nasal spray delivers naloxone to the bloodstream, quickly reversing an overdose without the necessity of an injection.

NIDA is also working to help develop new formulations for medication-assisted treatment (i.e., buprenorphine or naltrexone) to improve compliance and thus decrease opioid use and deaths. One approach is to develop extended release formulations, including a buprenorphine implant that lasts six months. Another approach is to develop compounds that target the neurocircuitry to interfere with the drug's ability to reach the brain's reward centers. NIDA is funding work to develop vaccines against fentanyl and heroin that has worked well in animal models. The vaccine stimulates formation of antibodies that bind to the opioid in the blood and prevent it from reaching the brain.

In addition, a NIDA-funded randomized clinical trial showed that buprenorphine administered in the hospital with and immediate referral to treatment reduced illicit opioid use and increased the patient's engagement in addiction treatment.

About 17 percent of pregnant women are prescribed an opioid during pregnancy, exposing the fetus to the drug and driving an increase in NICU admissions for neonates suffering withdrawal. Research has found that treating an addicted pregnant woman with buprenorphine reduces the likelihood that her newborn will need treatment in the NICU, compared with treating pregnant women with methadone.

Council Discussion

Dr. Catherine Gordon noted that adolescents are a highly vulnerable population for opioid addiction. Dr. Volkow agreed and said that pregnant adolescent girls have a higher rate of

marijuana and tobacco smoking than adolescent girls who are not pregnant. Adolescents will need tailored interventions, in part because their brains are still developing.

X. CONCEPT CLEARANCE REVIEW AND DISCUSSION

The Council considered the following concepts and concurred with each of them:

- Using Archived Data and Specimen Collections to Advance Maternal and Pediatric HIV/AIDS Research
- Development of Novel Non-Steroidal Contraceptive Methods
- Chemical Screening and Optimization Facility
- Pediatric Critical Care and Trauma Scientist Development Program
- Reproductive Medicine Network Clinical Sites and Data Coordinating Center
- Intellectual and Developmental Disabilities Research Centers
- Newborn Screening Translational Research Network

XI. COMMENTS FROM RETIRING MEMBERS

Dr. Bianchi thanked the retiring Council members, all of whom thanked her for the opportunity to serve on the Council. The following members are retiring:

- Dr. Patricia M. Flynn
- Dr. Gregory S. Kopf
- Dr. Stephen A. Petrill
- Dr. George R. Saade
- Dr. Richard K. Shields
- Ms. Sheila C. Zimmet

Dr. Bianchi thanked members of the public for attending the meeting, either in person or through the videocast. She adjourned the open session of the meeting at 12:05 p.m.

XII. CLOSED SESSION

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

XIII. 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 496 HD-primary applications requesting $133,251,087 in direct costs and $180,809,756 in total costs.

XIV. ADJOURNMENT

There being no further business, the meeting adjourned at 3:00 p.m. on Thursday, January 18, 2018. The next meeting is scheduled for June 7, 2018.

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

SIGNED 3/23/2018

Diana W. Bianchi, M.D. Date
Chair, National Advisory Child Health and Human Development Council
Director, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development

Eugene Hayunga, Ph.D.
Acting Committee Management Officer
Eunice Kennedy Shriver National Institute of Child Health and Human Development

Attachment: Council Roster

[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.