



*Eunice Kennedy Shriver* National Institute  
of Child Health and Human Development

NATIONAL ADVISORY CHILD HEALTH  
AND HUMAN DEVELOPMENT  
COUNCIL

*MEETING MINUTES*

June 7–8, 2021

**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  
MEETING SUMMARY  
June 7–8, 2021<sup>1</sup>**

The National Advisory Child Health and Human Development (NACHHD) Council convened its 176th meeting at 12:30 p.m. on Monday, June 7, 2021, by National Institutes of Health (NIH) VideoCast. The meeting was open to the public on June 7 from 12:30 to 5:27 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 on June 8, 2021, from 12:30 p.m. until 4:30 p.m.

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

**Council members present:**

Diana W. Bianchi, M.D. (Chair)

Shari L. Barkin, M.D.

Susan Bookheimer, Ph.D.

Christina M. Bucci-Rechtweg, M.D.

Michele Caggana, Sc.D.

John P. Coughlin, M.D.

Kathleen B. Egan, Ph.D.

Lucky Jain, M.D.

Catherine E. Lang, Ph.D.

Missy Lavender, M.B.A.

Martin Matzuk, M.D., Ph.D.

Genevieve S. Neal-Perry, M.D., Ph.D.

Carmen L. Neuberger, J.D.

Adam C. Resnick, Ph.D.

David H. Rowitch, M.D., Ph.D.

Annette Sohn, M.D.

Alan Thenevet N. Tita, M.D., Ph.D., M.P.H.

Rebeca Wong, Ph.D.

Anthony J. Wynshaw-Boris, M.D., Ph.D.

**National Advisory Board on Medical Rehabilitation Research Council liaison:**

Arthur English, Ph.D.

**Department of Defense:**

COL (Ret.) Paul F. Pasquina, M.D. (absent)

***Ex officio* members present:**

Patricia Dorn, Ph.D.

Aaron M. Lopata, M.D., M.P.P.

**Executive secretary:**

Eugene G. Hayunga, Ph.D.

---

<sup>1</sup> 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.

**Others present:**

Members of NICHD staff

Members of NIH staff

Members of the public

**I. CALL TO ORDER AND INTRODUCTORY REMARKS**

Dr. Bianchi welcomed members of the NACHHD Council and other participants to this meeting.

**Review of Confidentiality and Conflicts of Interest**

Dr. Hayunga reminded Council members 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. Before the meeting, Council members had received a conflict-of-interest certification form, which they were required to sign. Dr. Hayunga also reminded Council members that they are required to recuse themselves and leave the virtual meeting before any discussion involving any organizations or universities for which they are in conflict, in addition to those listed in the Council Action document. Council members are not allowed to serve on the 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.

**Council Minutes**

A motion to approve the February 2–3, 2021, NACHHD Council meeting minutes carried.

**Future Meeting Dates**

Dr. Hayunga reviewed the future Council meeting dates:

September 9–10, 2021

January 11–12, 2022

**II. NICHD DIRECTOR’S REPORT**

Dr. Bianchi delivered the director’s report.

**Fiscal Year 2022 Appropriations**

NACHHD Council members had received a two-page summary of NICHD’s justification to Congress for its proposed budget. This document provides a useful snapshot of the institute’s work over the past year.

President Biden released his proposed fiscal year (FY) 2022 budget on May 28, 2021. This budget includes \$51 billion for NIH, a \$9 billion increase from FY 2021. The proposed NIH budget includes \$6.5 billion to establish the new Advanced Research Projects Agency for Health (ARPA-H) and \$1.94 billion for NICHD, including \$30 million for Implementing a Maternal health and Pregnancy Outcomes Vision for Everyone (IMPROVE) and \$15 million for research

on the effects of SARS-CoV-2 infection in children. The proposed budget also includes a plan to move two programs from the NIH Office of the Director to NICHD:

- [Environmental influences on Child Health Outcomes \(ECHO\) Program](#)
- [INvestigation of Co-occurring conditions across the Lifespan to Understand Down syndromE \(INCLUDE\) Project](#)

ECHO has two major components: use of data from cohort studies with more than 90,000 participants, including more than 57,000 children, and the Institutional Development Awards States Pediatric Clinical Trials Network. ECHO staff will provide valuable expertise to NICHD in such areas as pediatric epidemiology, longitudinal research, clinical trials, and toxicology. Examples of recent ECHO research findings include identification of a chromosomal variant associated with wheezing phenotypes in childhood and assessment of childhood obesity in the United States.

Dr. Bianchi testified at both the House of Representatives and Senate appropriation subcommittee hearings for the FY 2022 budget. House members asked about COVID-19 in children, medications taken by breastfeeding women, pediatric nephrology, and environmental influences on child health outcomes. The Senate was more interested in the long-term effects of COVID-19 in children, including on their mental health.

At the time of the Council meeting, very little information was available on the proposed ARPA-H. However, Eric Lander, Ph.D., the new director of the White House Office of Science and Technology Policy, was scheduled to discuss this agency at the Advisory Council to the Director meeting on June 11, and this meeting will be open to the public.

### **2020 NICHD Research Advances**

NICHD has invested more than \$91 million in the [Human Placenta Project \(HPP\)](#) over the past 7 years. HPP aims to develop new tools to study the human placenta in real time and learn how it develops and functions during pregnancy. One HPP project found that wave reflection measurements change in the presence of placental pathology, and these changes could be good biomarkers of the risk of stillbirth. Another HPP team developed an acoustic microfluidic approach to study placental vesicles from maternal blood. NICHD also continues to support a large portfolio of basic placenta research.

### **COVID-19 Research Updates**

NICHD recently issued a notice of special interest ([NOT-HD-21-035](#)) for administrative supplement applications to investigate the impact of COVID-19 vaccination on menstruation. These studies will include participants from diverse and understudied populations or leverage existing large cohorts, datasets, or biorepositories. Applications are due June 17.

An NICHD [intramural study](#) showed that the human placenta expresses the main SARS-CoV-2 entry factors angiotensin-converting enzyme 2, transmembrane protease serine 2, and furin. The study offers a possible mechanism to explain the apparent lack of vertical transmission of SARS-CoV-2 from the pregnant person to the fetus. Another NICHD [intramural study](#) found that the SARS-CoV-2 RNA replicase requires iron sulfur clusters as cofactors. TEMPOL, an

experimental drug, inhibits the activity of the SARS-CoV-2 RNA replicase, and the investigators are exploring the possibility of a clinical trial of TEMPOL to treat COVID-19.

As part of NIH [Rapid Acceleration of Diagnostics \(RADx\)<sup>TM</sup>](#)–Underserved Populations (RADx-UP), NICHD is assessing diagnostic testing approaches to enable students and staff to return safely to in-person schooling. The Phase 1 projects, which have already been funded, focus on underserved and vulnerable populations. The Phase 2 projects, which are being reviewed, will expand the geographic area, age range, and racial and ethnic groups included in the initiative, as well as address the impact of vaccine availability for middle schoolers and educate students, families, and staff about the importance of COVID-19 vaccines.

### **NICHD Staff Updates**

Dr. Bianchi announced the appointments of several new extramural and intramural staff members. Open positions at NICHD, including the NICHD scientific director and director of the Division of Intramural Population Health Research, are listed at [Jobs at NICHD](#).

### **Discussion**

Dr. Resnick asked about plans to integrate HPP data with other NICHD datasets. Dr. Bianchi explained that funded investigators will share their datasets with one another and that HPP will connect data on pregnant people with data collected subsequently on their children. NICHD is working to connect datasets from multiple NIH institutes and centers (ICs) for its multisystem inflammatory syndrome in children (MIS-C) research.

Dr. Egan asked whether NICHD's efforts in INCLUDE are increasing the number of researchers interested in studying Down syndrome. In addition, she noted that she had not seen many applications for INCLUDE among the applications for Council review. Dr. Bianchi explained that INCLUDE is NIH-wide and that many other ICs fund INCLUDE studies, so the NACHHD Council does not see all of the INCLUDE research. INCLUDE has received a large number of applications and brought new investigators into this field, and this program might be a good topic for a future NACHHD Council meeting. Sujata Bardhan, Ph.D., Intellectual and Developmental Disabilities Branch, added that the INCLUDE funding continues to generate a great deal of excitement in the community, including among trainees and investigators who do not typically study Down syndrome.

Dr. Jain asked how the increase in proposed budget for NICHD compares with the increases for other ICs and how NICHD is coordinating its RADx-UP research with the work of other ICs involved in RADx. Dr. Bianchi explained that the proposed NIH budget includes increases of 2% to 3% for base funding for most ICs, not including dedicated funds. She added that RADx programs are NIH-wide and that several NICHD leaders (including herself) are members of committees that administer RADx and discuss the integration of the various RADx programs. Alison Cernich, Ph.D., NICHD Deputy Director, added that NICHD works with RADx-Tech, the National Institute of Biomedical Imaging and Bioengineering, and other Department of Health and Human Services colleagues to coordinate testing supplies for the return-to-school activities.

Dr. Wong asked about the relationship between the data-rich projects that Dr. Bianchi had described and the *All of Us* Research Program, as well as whether *All of Us* collects placenta

data. Dr. Cernich replied that *All of Us* does not collect placental data, but NICHD is actively involved in *All of Us* and works to synchronize its data with those of *All of Us*. Dr. Bianchi added that *All of Us* does not yet enroll children, although it does include pregnant people. Dr. Wong said that HPP could offer vast expertise to *All of Us* on enriching its national data collection.

Dr. Barkin asked what NICHD has learned about data sharing and data linking from the research it funds (such as ECHO) that could be useful for advancing research. Dr. Bianchi explained that ECHO has not yet been integrated into NICHD, because this plan is subject to congressional approval. However, NICHD does already manage ECHO grants. Dr. Cernich added that NICHD is increasingly using existing data sources, making them interoperable, and working on other ways to give NIH researchers access to several datasets through eRA Commons. Questions that need to be addressed include how to protect the data, use them in ways that are consistent with participants' informed consent, and encourage novel secondary data use.

Dr. Lang asked how different the proposed NICHD budget is likely to be from the final budget. Dr. Bianchi explained that congressional negotiations on the budget will continue. Both parties in Congress have shown a great deal of excitement about the work of NIH and appreciation for its role in developing COVID-19 vaccines and preparing them for emergency use approval.

Dr. Jain asked whether NACHHD Council members may share the two-page NICHD budget summary with colleagues. Alexis Clark, NICHD budget officer and chief of the Financial Management Branch, encouraged Dr. Jain and others to share this summary, which is part of the [NIH congressional justification overview](#). Page 95 of this document has a table summarizing the FY 2022 President's budget request for each IC. [NICHD's portion of the proposed budget](#) is also available online. Issel Anne Lim, Ph.D., team lead for science policy and planning, explained that NICHD updates the congressional budget justification each year to highlight the breadth of NICHD-supported research. This was the first time that NICHD also produced the fact sheet, and the institute will probably update this document regularly as well.

### **III. NATIONAL INSTITUTE ON DEAFNESS AND OTHER COMMUNICATION DISORDERS DIRECTOR'S INVITED PRESENTATION**

Debara Tucci, M.D., M.S., Director of the National Institute on Deafness and Other Communication Disorders (NIDCD), explained that the institute's mission is to conduct and support research and research training in the normal and disordered processes of hearing, balance, taste, smell, voice, speech, and language. In FY 2020, NIDCD used approximately half of its budget to support research on hearing and another quarter to support research on language and on smell.

Dr. Tucci provided several examples of recent research in each of the institute's priority areas.

#### **Hearing and Balance**

NIDCD's research on hearing and balance includes studies on tinnitus and hyperacusis, auditory and vestibular processing, hearing aids, cochlear implants, and management of hearing impairments in infants and children. Ongoing NIDCD studies are:

- Testing delivery of normal copies of mutated genes into a deaf mouse model of hereditary hearing loss to restore hearing and balance
- Studying cochlear implantation in children with asymmetric hearing loss or single-sided deafness
- Assessing the link between the arctic *CPT1A* variant and childhood hearing loss by leveraging an NICHD-funded prospective cohort study on the impact of diet and the arctic *CPT1A* variant on Alaska Native children
- Conducting a community-engaged, effectiveness implementation trial of a patient navigator intervention to reduce infant hearing diagnosis non-adherence after a positive newborn hearing screening result

### **Taste and Smell**

NIDCD research on taste and smell ranges from studies of sinusitis and rhinitis to research on chemical senses and disease, impact of genes and the environment on food preferences, and tissue engineering.

NIDCD is funding administrative supplements to determine whether anosmia (loss of smell) is an early indicator of COVID-19, identify genetic variations associated with anosmia in individuals with COVID-19, and examine mechanisms underlying persistent smell loss in people with long COVID-19. Through RADx Radical (RADx-rad), NIDCD has funded four studies to determine whether chemosensory loss is an early indicator of COVID-19 and can predict disease severity, disease persistence, or other neurological manifestations.

Other NIDCD research is determining whether individual and genetic variations in taste predict side effects and medication adherence and whether the palate can be used to identify medicines likely to present taste issues for some patients. Another institute trial in children ages 3 to 6 and their mothers is evaluating whether repeated exposure to foods containing less sugar will reduce preferences for sweet foods and increase liking and intake of less sweet foods.

### **Voice, Speech, and Language**

NIDCD has several portfolios that complement those of NICHD. For example, applications for studies on normal language development are assigned to NICHD, whereas those for research on disordered language development go to NIDCD. Other topics in this category addressed by NIDCD are motor speech production, sign language, literacy and deafness, and language impairment in autism.

NIDCD studies on voice, speech, and language are:

- Developing longitudinal models of speech and language development in cerebral palsy that can be used to predict outcomes, test interventions, and guide treatment decisions
- Evaluating effects of hypoglossal nerve stimulation on cognition and language in individuals ages 10 to 21 with Down syndrome and severe, untreated, obstructive sleep apnea
- Developing tools to improve outcomes of toddlers with communication delays
- Identifying language-based markers of autism spectrum disorder that can be detected during social interactions

## **Discussion**

Dr. Barkin asked whether NIDCD is studying different communication strategies for people with autism. Dr. Tucci replied that NIDCD has a large autism portfolio, and she offered to obtain more information on this portfolio for Dr. Barkin.

Dr. Resnick asked whether NIDCD is studying vestibular schwannoma associated with neurofibromatosis type 2. Dr. Tucci replied that NIDCD is funding research to develop molecular therapies for this challenging combination of diseases.

Dr. Resnick asked whether NIDCD is studying ways to deliver medications through the nose that cannot pass through the blood–brain barrier. Dr. Tucci said that NIDCD is not conducting this type of research at this time. No convincing evidence shows that SARS-CoV-2 can reach the brain through the olfactory system, but this system might be a conduit for delivering certain drugs.

Dr. Bianchi noted that Dr. Tucci had made three important points:

- NICHD does not fund all of the pediatric research conducted by NIH, and NIDCD is just one of many ICs conducting research in this area.
- Dr. Tucci gave examples of studies funded by several ICs. Many studies cannot be funded by one IC alone.
- Dr. Tucci had provided an example of an INCLUDE study in which NICHD is not involved.

## **IV. STRATEGIES TO ENRICH INCLUSION AND ACHIEVE EQUITY**

Charisee Lamar, Ph.D., M.P.H., Director of the NICHD Office of Health Equity, described the Strategies to enRich Inclusion and achieVe Equity (STRIVE) initiative. STRIVE is developing three five-year action plans with comprehensive, actionable policy recommendations and outcome metrics to:

- Enhance equity, diversity, and inclusion in the NICHD workforce.
- Increase the diversity of the NICHD extramural scientific workforce with an emphasis on trainees and program directors and principal investigators (PD/PIs)
- Establish research priorities to address health disparities, including systemic racism, that will facilitate more equitable health for all.

The three STRIVE committees include more than 50 NICHD staff members who have scientific and administrative positions as well as diverse skills and viewpoints. STRIVE efforts are tailored to the institute’s mission but are informed by the NIH UNITE initiative and other NIH-relevant activities, and it consults external stakeholders. Once the action plans are ready, they will be presented to Dr. Bianchi for approval.

The committees have started collecting and analyzing baseline data. These activities include:

- Surveying NICHD employees about equity, diversity, and inclusion at the institute



- Analyzing demographic data on 44,000 extramural program directors and principal investigators (PD/PIs) funded by NICHD between 1996 and 2020
- Analyzing the FY 2020 NICHD health disparities research portfolio

The data show that although the numbers of Black and Hispanic PIs funded by NICHD have increased in the last 25 years, these numbers are still small. Most of NICHD’s health disparities research in FY 2020 focused on racial and ethnic minority populations, but the institute also funds research on low–socioeconomic status, sexual and gender minority, and rural populations. Health disparities research accounts for 21% of the NICHD research portfolio. The most common diseases and conditions in the NICHD health disparities research portfolio are HIV/AIDS, maternal health, and preterm birth.

The portfolio and survey results analyses are ongoing. The committees will also evaluate demographic employee and personnel action data before identifying ways to improve career growth at NICHD. The institute will host a research workshop series that will take a life course approach to mitigate disparities; will also host a conference designed to identify new strategies for increasing diversity in the scientific workforce; and will continue to identify opportunities to engage internal and external stakeholders (e.g., a series of listening sessions). Dr. Lamar hoped that the STRIVE recommendations would be approved and incorporated into the NICHD strategic plan in early 2022. Progress will then be monitored, and changes will be made when needed.

## **Discussion**

Dr. Coughlin asked whether NICHD has defined “structural racism” and how this concept is manifested at NICHD. Dr. Cernich explained that NICHD uses the NIH definition: “organizational structures, policies, practices, and social norms that perpetuate bias, prejudice, discrimination, and racism limit the pace of scientific progress.” STRIVE is determining how these factors affect recruitment, retention, and advancement in the NICHD workforce; which individuals receive training through NICHD intramural and extramural programs; and the institute’s health disparities research funding. STRIVE will use the results as a basis for recommendations.

Dr. Barkin wondered whether the reason for the small numbers of Black and Hispanic investigators with NICHD funding is the low volume of applications from these individuals or low rates of successful applications. Dr. Cernich explained that NICHD will share these data as soon as possible, and both issues often play a role in the low numbers of researchers from underrepresented populations who receive NIH funding.

Dr. Coughlin asked whether reviewers know the identities of the PIs of the applications they review. Dr. Cernich said that reviewers do receive information on the PIs and their institutions, but applicants are not required to report their race, ethnicity, or disability status.

Dr. Lang noted that differences in responses to the STRIVE survey by employment level need to be considered in the analyses. Dr. Lamar replied that the STRIVE committees are taking this

type of factor into account. STRIVE will also hold listening sessions for NICHD staff and will issue a more in-depth survey in the future. To make staff comfortable, STRIVE is providing opportunities to offer input anonymously.

Dr. Lang asked how the STRIVE committees will handle data on research on both low-income and racial and ethnic minority populations so that they avoid overcounting in certain disparity categories. Dr. Lamar explained that the NICHD portfolio analysis is a computerized process that searches the text in each application, and the health disparity categories of NICHD's health disparities research are not mutually exclusive. A study that is relevant to more than one disparity population will be counted in all relevant categories.

Dr. Lamar emphasized that the analyses she described are still at an early stage, and she will give more reports to the NACHHD Council as STRIVE makes progress.

## **V. VOICE OF THE PARTICIPANT**

Victoria Seng Nelson, M.P.H., described her decision to receive the COVID-19 vaccination during her pregnancy. Ms. Nelson lives in Fort Worth, Texas, is a 33-year-old mother of a 21-month-old daughter and is 35 weeks pregnant. She holds an undergraduate degree in cell biology and molecular genetics and a master's degree in public health. She is responsible for corporate and community engagement at a nonprofit organization focused on ending poverty.

Ms. Nelson qualified for the vaccine in January 2021 because of her pregnancy. At her 13-week obstetric checkup, she told her obstetrician that she had registered to receive the vaccine. Although her obstetrician did not instruct Ms. Nelson not to receive the vaccine, the physician did not encourage Ms. Nelson to do so.

Because she was offered the vaccine, Ms. Nelson trusted that vaccination was in her best interest. In Texas, the vaccine was offered to people in her priority group because of strong and consistent evidence that COVID-19 increases their risk of severe illness or death. Because she found COVID-19 frightening, Ms. Nelson viewed the risk of COVID-19 as worse than the risk of the vaccine. She had more information than most mothers because of her education, which enabled her to evaluate the pros and cons of vaccination for herself and her family. She was not frightened by the newness of the vaccines, but she acknowledged that other mothers might not understand their safety.

Ms. Nelson received her two doses of the Moderna COVID-19 vaccine in January and February 2021. After each dose, her arm was sore, and she developed insomnia and flu-like symptoms. These symptoms were preferable to developing the disease. Since she became fully vaccinated, Ms. Nelson's mental health has improved, which benefits her daughter. She has also resumed certain aspects of her normal life with more comfort than if she were not vaccinated. Ms. Nelson's husband is now fully vaccinated as well, and they are pleased that they are unlikely to transmit the virus to their daughter and can safely take her out of the house for her education, socialization, and development.

After receiving her second dose, Ms. Nelson registered for the Centers for Disease Control and Prevention's V-safe After Vaccination Health Checker and was delighted to be part of a longitudinal study. She also reached out to NICHD about participating in research.

Ms. Nelson considered some hypothetical factors that might have affected her decision to receive the COVID-19 vaccine. She believes that she would have participated in a vaccine clinical trial. However, she would have had to consider the possibility that she might be given a placebo and the fact that she has a toddler and will soon have an infant, neither of whom is eligible for vaccination. Ms. Nelson located most of the information she wanted before being vaccinated, although she would have liked more information on the mRNA vaccine delivery method. A recommendation from her physician to receive the vaccine would have been helpful, and many other pregnant and lactating women have been seeking this type of encouragement.

Ms. Nelson hoped that children will be included in COVID-19 vaccination trials, and she would be happy to enroll her children in such a trial. Questions that Ms. Nelson still has include:

- Could she transmit the infection to her children now that she is vaccinated?
- How long will her immunity last?
- How long will the immunity she will transmit to her infant last?
- How could her vaccination status affect her infant while she is breastfeeding?

The scientific community needs to determine how to increase vaccination rates to protect pregnant and lactating people and children and prepare for the next pandemic. Ms. Nelson suggested that scientists use social media influencers, science-savvy parents, and even children as vaccine ambassadors to combat misinformation and address hesitancy. She also recommended that the research community to include pregnant and lactating people in studies.

## **Discussion**

Dr. Bianchi explained that good data now show that pregnant people transmit SARS-CoV-2 antibodies after vaccination to their infants. These antibodies are also present in breastmilk, so lactating parents can transmit antibodies to their infants. She wished that this message would come through more strongly. Ms. Nelson offered to help spread the word.

Dr. Bookheimer asked what Ms. Nelson tells individuals who express vaccine hesitancy. Ms. Nelson said that she would encourage these individuals to receive the vaccine, while respecting their reasons for hesitating. Because she is not a healthcare provider, she would hesitate to recommend that others receive the vaccine. The most persuasive argument is that people can protect not only themselves but also others through vaccination. Ms. Nelson would also point out that data increasingly show that the vaccines are safe.

Dr. Tita reported that his clinic has started documenting patient intentions to receive the COVID-19 vaccine. Clinic providers are educating patients about the pros and cons of vaccination, and the clinic is tracking delivery of this education.

Dr. Neal-Perry commented that social media reports are claiming that the vaccine increases the risk of infertility. She asked whether Ms. Nelson has shared her story on social media. Ms. Nelson said that building trust in people who do not trust the healthcare system is challenging.

She is willing to share her story on social media, because mothers do seek advice from other mothers.

Dr. Jain noted that members of the public are swayed by messages about the risks of COVID-19 vaccination, such as the small number of cases of myocarditis in adolescents who received the vaccine. The risk-to-benefit ratio strongly favors vaccination.

## **VI. THE MATERNAL AND PEDIATRIC PRECISION IN THERAPEUTICS HUB: ADVANCING FRONTIERS IN HEALTH THROUGH MATERNAL AND PEDIATRIC PRECISION IN THERAPEUTICS**

Aaron C. Pawlyk, Ph.D., chief of the NICHD Obstetric and Pediatric Pharmacology and Therapeutics Branch, described several NICHD programs that support clinical trials in children and in pregnant and lactating people. He also explained that the Pediatric Research Equity Act and the Best Pharmaceuticals for Children Act (BPCA) help ensure that the medications used for children have been tested in children.

The NICHD [Pediatric Trials Network](#), funded through the BPCA, studies the formulation, dosing, efficacy, and safety of drugs and medical devices used in pediatric patients. The T32 [Pediatric Clinical and Developmental Pharmacology Training Network](#), also funded through the BPCA, provides training in pediatric clinical pharmacology. NICHD is expanding its training and career development program by combining training, individual fellowship, and career development awards and expanding these awards to include maternal clinical pharmacology.

The Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC) submitted its [implementation report](#) to the Secretary of Health and Human Services in August 2020. This report identifies strategies to implement the recommendations in the PRGLAC [2018 report](#).

The aim of the new [Maternal and Pediatric Precision in Therapeutics \(MPRINT\) Hub](#) is to aggregate, present, and expand the available knowledge, tools, and expertise in maternal and pediatric therapeutics to the broader research, regulatory science, and drug development communities. Activities include:

- Providing knowledge and expertise to the scientific community
- Catalyzing and accelerating maternal and pediatric therapeutic development
- Creating synergies with other resources and networks
- Building on other NICHD clinical trial programs and laying the foundation for future efforts

The MPRINT Centers of Excellence in Therapeutics will conduct cutting-edge clinical, translational, basic, and data sciences research and generate novel tools and approaches to advance and accelerate research and regulatory science in maternal and pediatric therapeutics. Each center will conduct at least two research projects, one of which must be clinical. Studies by these centers could, for example, assess the effects of drugs on breastmilk composition, develop new devices and methods for precision dosing, or build new pharmacometric models to predict the safety and efficacy of drugs in children and pregnant people.

The MPRINT Knowledge and Research Coordination Center will coordinate and support the operations of the MPRINT Hub, collaborate with the MPRINT Centers of Excellence in Therapeutics, and develop a Web portal to provide access to a curated knowledge base of maternal and pediatric pharmacology and therapeutics data. Subject matter experts will review the MPRINT Hub once a year.

The spokes of the MPRINT Hub will include:

- Existing NICHD networks
- Other government agencies
- Foundations, universities, and other private-sector entities
- Investigator-initiated grants

The Bill & Melinda Gates Foundation is launching a program in modeling drug effects during pregnancy that will work with the MPRINT Hub as one of its first spokes.

## **Discussion**

Dr. Bianchi reported that NICHD created the MPRINT Hub to fill some of the gaps identified by PRGLAC, including the lack of evidence on medications taken by pregnant people and even more so by lactating people.

Dr. Sohn approved of the plan to form partnerships between the MPRINT Hub and low- and middle-income countries. Bangkok has at least three universities conducting precision medicine studies, and investigators in these countries have the potential to contribute to the research supported by this new NICHD program.

Dr. Bucci-Rechtweg was excited by the new preclinical opportunities to leverage data for determining appropriate doses for pediatric, pregnant, and lactating patients. In spite of all the work done and the progress made in pediatric research over the last two decades, foundational research to inform smart program designs for developing pediatric medications is still lacking. Assumptions that data on other populations can be extrapolated to children are not an appropriate basis for decisions about medication use in children, and preclinical studies in pediatric and pregnancy disease models are needed to collect the best-quality evidence.

Dr. Resnick asked whether other data-driven NICHD initiatives that focus on infrastructure, such as the Gabriella Miller Kids First Pediatric Research Program and INCLUDE, will be strategic partners of the MPRINT Hub. He also noted that Research to Accelerate Cures and Equity (RACE) for Children Act activities, which focus on pediatric cancers, could provide valuable collaborative opportunities for the MPRINT Hub. Dr. Pawlyk explained that the MPRINT Hub can be the “glue” for a variety of NICHD initiatives and networks. He also noted that NICHD is working with the Foundation for NIH to develop public–private partnerships to work on RACE for Children Act activities.

Dr. Tita was pleased by the potential synergies between the MPRINT Hub and various NICHD networks, which will increase these networks’ vibrancy and impact. He asked about plans to expand training opportunities offered through the networks. Dr. Pawlyk replied that NICHD is

working to prevent early-career investigators from dropping out of research before they become established investigators. The institute plans to bring fellows and other trainees from different networks together for cross-fertilization, which is a first step in enhancing career development and training opportunities. Dr. Barkin suggested including early-stage investigators in the new MPRINT Centers of Excellence to accelerate their training and career development. Dr. Pawlyk approved of this idea.

## **VII. FROM PARASITES TO PUPPIES: TOWARD NONINVASIVE DIAGNOSIS OF PEDIATRIC SARS-COV-2 INFECTION AND MIS-C**

Audrey R. Odom John, M.D., Ph.D., Stanley Plotkin endowed chair at the University of Pennsylvania and chief of infectious diseases at Children's Hospital of Philadelphia (CHOP), described the case of a healthy 5-year-old girl who was admitted to the CHOP intensive care unit with a fever, very low blood pressure, a rash, conjunctivitis, cracked lips, and diarrhea. Her echocardiogram showed abnormalities of the coronary arteries, and her SARS-CoV-2 antibody test result was positive. The girl was treated with intravenous immunoglobulin and steroids, and her condition resolved within a few days. Her diagnosis was MIS-C, and her physicians believe that this diagnosis was associated with a previous SARS-CoV-2 infection.

Most children infected with SARS-CoV-2 have very mild symptoms and do quite well, but approximately 4,000 children in the United States with COVID-19 have developed MIS-C. Many questions about MIS-C remain unanswered, including questions about its pathophysiology, why certain children develop it, and how best to treat it.

CHOP received an award from the Predicting Viral-Associated Inflammatory Disease Severity in Children with Laboratory Diagnostics and Artificial Intelligence (PreVAIL kIDs) initiative, which is part of RADx-rad. The goals of this initiative are to understand the spectrum of pediatric COVID-19, rapidly diagnose and characterize MIS-C associated with SARS-CoV-2, and predict the longitudinal risk of disease severity after exposure to or infection by SARS-CoV-2.

The challenge that the CHOP PreVAIL kIDs project is addressing is to determine which children and teenagers with fever have MIS-C. Clinicians want to avoid misdiagnosing fever in children who come to the emergency department, because misdiagnoses can lead to delays in treatment for MIS-C or other conditions, and accurate diagnoses are important for identifying effective treatments.

Dr. John's research has focused on the development of noninvasive diagnostic technologies for pediatric infections. People carry a wide variety of volatile organic compounds, and these compounds can provide a great deal of information about a person's health and disease. Any given breath sample has approximately 200 to 300 compounds that can be used to distinguish one disease from another. In addition, breath can be measured noninvasively several times in the same child.

Dr. John typically enrolls children with and without a given disease, collects breath samples, uses mass spectrometry to compare the composition of the samples, and looks for biomarkers

that are characteristic of children with the disease. She has validated biomarkers that are characteristic of children with malaria, demonstrating the feasibility of this approach.

The Breath, Urine, Saliva (BUS) COVID-19 Biomarker Study collects BUS samples from children, adolescents, and young adults ages 4 to 20 who do and do not have a SARS-CoV-2 infection. The laboratory is using unbiased metabolite profiling to identify compounds in the specimens of study participants with the infection. Cindy Otto, D.V.M., Ph.D., director of the Penn Vet Working Dog Center, is determining whether dogs can use their strong sense of smell to identify study participants with infection. Studies have shown that dogs can detect SARS-CoV-2 infection in children and adults with high specificity and sensitivity.

The BUS COVID-19 Biomarker Study's mass spectrometry analyses identified six biomarkers that are characteristic of children with SARS-CoV-2 infection. These biomarkers, which overlap with but are not identical to those in adults, have 84% accuracy and 91% sensitivity to detect SARS-CoV-2 infection. Dr. John hopes to develop a rapid and easy diagnostic screening test for pediatric SARS-CoV-2 infection using these biomarkers. She will also collect samples from other respiratory viruses to determine whether the six biomarkers are specific to SARS-CoV-2. The metabolites might provide useful information on the biology of the infection and of breath volatile compounds in general.

The CHOP PreVAIL kIds study has similar goals to those of the BUS COVID-19 Biomarker Study, but it focuses on MIS-C. This study is enrolling children at CHOP who have had a temperature higher than 38°C for at least three days and at least two clinical or histological features suggesting MIS-C. The study will use data from BUS samples and electronic medical records to develop a candidate diagnostic biomarker or algorithm for use in the clinic to diagnose MIS-C in children with a fever when a clinician suspects MIS-C.

## **Discussion**

Dr. Caggana asked whether the mass spectrometry approach or dogs could identify individuals in areas of need around the world who have other infections; such options might prove useful in the next pandemic. Dr. John said that she hoped to use this approach to detect other infectious diseases, including malaria. However, preparing to use this approach for the next pandemic is challenging, because the algorithm needs to be trained on the disease, which requires a gold standard test to determine whether a person has the disease. Dr. Sohn reported that a few COVID-19-sniffing dogs are used in Thailand.

Dr. Barkin asked about differences among volatile organic compounds in MIS-C and other conditions, such as toxic septic shock or Kawasaki disease. Dr. John said that her study is designed to detect these differences. MIS-C involves different immune regulation from severe COVID-19, toxic shock, and Kawasaki disease, and Dr. John suspects that these different diseases will have different metabolic profiles.

Dr. Rowitch asked whether the study will also conduct genomic profiling. Dr. John replied that the CHOP PreVAIL kIds study is not collecting genomic data, but other PreVAIL kIds studies are. Collecting genomic data would require many more samples than will be available at CHOP.

Dr. John reported that the PreVAIL kIDs investigators meet monthly and are interested in collaborating to learn more about the post-acute sequelae of COVID-19 and long COVID-19 in children.

## VIII. COUNCIL STATEMENT OF UNDERSTANDING

Dr. Hayunga said that the Statement of Understanding between NICHD and the NACHHD Council is posted on the Council website and provides a short synopsis of the Council and its membership and structure. Council members voted to approve the statement of understanding.

## IX. CONCEPT CLEARANCE

The NACHHD Council reviewed the following eight concepts and voted to approve each one:

- **Research Enhancement Award Program for Health Professional Schools and Graduate Schools** (Mahua Mukhopadhyay, Ph.D., Developmental Biology and Structural Variation Branch)
- **Advancing Research to Understand Congenital Malformations** (Reiko Toyama, Ph.D., Developmental Biology and Structural Variation Branch)
- **Elucidation and Validation of the Transmembrane Transporter Proteins in Nutrient and Drug Disposition** (Alison Harrill, Ph.D., Obstetric and Pediatric Pharmacology and Therapeutics Branch)
- **Bioprinted Tissue Constructs for OB/GYN and Pediatric Applications** (Antonello Pileggi, M.D., Ph.D., Obstetric and Pediatric Pharmacology and Therapeutics Branch)
- **Integrative Research Resources for Advancing Maternal & Pediatric Therapeutics** (Zhaoxia Ren, M.D., Ph.D., Obstetric and Pediatric Pharmacology and Therapeutics Branch)
- **Promoting Reproductive Health for Adolescents and Adults with Disabilities** (Rosalind King, Ph.D., Population Dynamics Branch)
- **Innovative Therapies and Tools for Screenable Disorders in Newborns** (Mollie Minear, Ph.D., Intellectual and Developmental Disabilities Branch)
- **Opportunities for Collaborative Research at the NIH Clinical Center** (Eugene Hayunga, Ph.D., Division of Extramural Research)

### Advancing Research to Understand Congenital Malformations

Dr. Bucci-Rechtweg asked whether Advancing Research to Understand Congenital Malformations will exclude the more commonly studied structural defects. Dr. Toyama explained that the program will include all types of structural defects, but those that have received little attention will be given higher priority. She also confirmed that teams will need to include clinical and basic researchers.

### Integrative Research Resources for Advancing Maternal & Pediatric Therapeutics

Dr. Barkin asked about the relationship between the proposed Integrative Research Resources for Advancing Maternal & Pediatric Therapeutics and the MPRINT Hub. Dr. Ren explained that this concept will leverage the MPRINT Hub as well as other resources, such as databases and biospecimens, from NICHD-supported research networks to develop information that will be



useful for the development of therapies for children and for pregnant and lactating people. Dr. Pawlyk added that the new initiative will pull together existing resources, including biospecimens stored in various biobanks, for research in understudied areas and make them usable for research. The initiative will also offer training and infrastructure for using biospecimens. In contrast, the MPRINT Hub will provide access to tools and technologies.

### **Promoting Reproductive Health for Adolescents and Adults with Disabilities**

Dr. Tita asked about the accomplishments of previous cycles of Promoting Reproductive Health for Adolescents and Adults with Disabilities and what changes will be made in the next cycle. Dr. King replied that previous program announcements for this initiative focused on pregnancy, whereas this concept focuses on the period before pregnancy in adolescents and adults with disabilities who plan to become pregnant and those who have an unplanned pregnancy. A separate NICHD [notice of special interest](#) focuses on studies of reproductive health, pregnancy, and parenting in people with disabilities.

Dr. Sohn commented that the types of data to collect and how to implement interventions will depend on when the individual developed a disability (e.g., at birth, as a young child, later in life). Dr. King said that this concept is broad, and NICHD wants investigators to propose a wide range of studies. A meeting planned by NICHD and the Administration for Community Living in the fall will address disability timing issues. The types of issues that this initiative might address are whether the same approaches are effective for people with different types of disabilities and how different the screening approaches must be for individuals with different types of disabilities.

### **Innovative Therapies and Tools for Screenable Disorders in Newborns**

Dr. Caggana said that the availability of only a few technologies limits the use of newborn screening, and that inexpensive, high-throughput technologies are needed. New technologies, such as antisense oligonucleotides and gene therapy, will increase the need to expand the newborn screening panel.

### **Opportunities for Collaborative Research at the NIH Clinical Center**

John Gallin, M.D., chief scientific officer and scientific director of the NIH Clinical Center provided additional details on Opportunities for Collaborative Research at the NIH Clinical Center. This trans-NIH program has made at least 37 awards to open the doors of the Clinical Center to the extramural community and to establish collaborations between intramural and extramural investigators.

Dr. Wynshaw-Boris asked whether this program can support studies in young children and pregnant people. Dr. Gallin explained that the Clinical Center does not admit children younger than 2 or deliver babies. However, healthy infants and young children can come to the Clinical Center to participate in studies, and NIH is exploring ways to bring infants to the Clinical Center through a collaboration with Children's National Hospital.

Dr. Barkin asked about the diversity of patients and conditions studied at the Clinical Center. Dr. Gallin explained that research at the Clinical Center consists of first-in-human trials of new

treatments and studies of patients with rare diseases. The Clinical Center has had patients from every U.S. state and many other countries, and its patients are representative of the U.S. population.

Dr. Gallin explained that the purpose of this initiative is to bring more patients to the Clinical Center and enable extramural investigators to take advantage of the special opportunities available. For example, care is provided at the Clinical Center at no cost to patients, and their travel costs are covered. Furthermore, the Clinical Center can keep patients for a year, when necessary. Because of these unique capabilities, studies can be conducted at the Clinical Center that could not be done elsewhere.

Dr. Resnick asked whether intramural datasets are stored in the same place as extramural ones. Dr. Gallin replied that all intramural data and medical records related to the Clinical Center are stored in the NIH Biomedical Translational Research Information System. Extramural collaborators have access to data from the study in which they are involved, and Dr. Gallin hopes to make all Clinical Center research data available to any researcher.

## **X. ADJOURNMENT**

Dr. Bianchi announced the upcoming retirement of Dr. Hayunga. She invited several colleagues to describe Dr. Hayunga's accomplishments at NICHD and to share some personal recollections or their interactions with Dr. Hayunga. NACHHD Council members used the chat function to praise Dr. Hayunga's contributions and thank him for all he has done for NICHD. Dr. Hayunga said that he was touched and humbled by all of the kind words and that he has done so well only because of the good team that has worked with him.

## **XI. CLOSED SESSION**

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

## **XII. REVIEW OF APPLICATIONS**

The session included a discussion of procedures and policies regarding voting and confidentiality of application materials, committee discussions, and recommendations. Members absented themselves from the meeting during discussion of and voting on applications from their own institutions or other applications in which there was a potential conflict of interest, real or apparent. Members were asked to sign a statement to this effect. The Council considered and approved 511 HD-primary applications requesting \$178,297,809 in direct costs and \$249,045,969 in total costs.

## **XIII. ADJOURNMENT**

There being no further business, the meeting adjourned at 4:30 p.m. on Tuesday, June 8, 2021. The next meeting, which will again be virtual, is scheduled for September 9–10, 2021.

I hereby certify that, to the best of my knowledge, the foregoing minutes and attachments are accurate and complete.<sup>2</sup>

---

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

---

Date

---

Eugene G. Hayunga, Ph.D.  
Executive Secretary, National Advisory  
Child Health and Human Development  
Council

---

Date

Attachment: Council Roster

---

<sup>2</sup> 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.