

59th Meeting of the National Institutes of Health (NIH)
Advisory Committee on Research on Women's Health (ACRWH)
Office of Research on Women's Health (ORWH)
Bethesda, MD
October 18, 2023

Members Present

Garnet L. Anderson, Ph.D.
Irene Aninye, Ph.D.
Amanda Bruegl, M.D.
Stephen Higgins, Ph.D.
Scott J. Hultgren, Ph.D.
Reshma Jagsi, M.D., D.Phil.
Hendrée Jones, Ph.D.
Sabra L. Klein, Ph.D.
Alyson J. McGregor, M.D.
Thelma Mielenz, Ph.D.
Judith G. Regensteiner, Ph.D.
Michelle Robinson, D.M.D.
Yoel Sadovsky, M.D.
Phyllis Sharps, Ph.D., M.S.N.
Melissa Simon, M.D., M.P.H.
Kimberly J. Templeton, M.D.

Ad Hoc Members Present

Chloe Bird, Ph.D., M.A.
Ayush Giri, Ph.D., M.S.
Aza Nedhari, M.S.
Ighovwerha Ofotokun, M.D., M.Sc.
Fatima Stanford, M.D., M.P.H., M.P.A.

ORWH Leadership Present

Janine A. Clayton, M.D., FARVO, Director
Chair, ACRWH
Vivian Ota Wang, Ph.D., Deputy Director
Samia Noursi, Ph.D., Associate Director for
Science Policy, Planning, and Analysis
Executive Secretary, ACRWH
Sarah Temkin, M.D., Associate Director for
Clinical Research
Xenia Tigno, Ph.D., Associate Director for
Careers

Other NIH Leadership Present

Jon R. Lorsch, Ph.D., Director, National Institute
of General Medical Sciences (NIGMS)

Call to Order

Samia Noursi, Ph.D., ACRWH Executive Secretary and ORWH Associate Director for Science Policy, Planning, and Analysis, called the online meeting to order at 9:31 a.m. Committee members introduced themselves. Dr. Noursi acknowledged the following ACRWH members who are retiring: Scott Hultgren, Ph.D.; Sabra Klein, Ph.D.; Alyson McGregor, M.D.; Judith Regensteiner, Ph.D.; Michelle Robinson, D.M.D.; and Neel Shah, M.D. She also welcomed ad hoc members Chloe Bird, Ph.D., M.A.; Ayush Giri, Ph.D., M.S.; Aza Nedhari, M.S.; Ighovwerha Ofotokun, M.D., M.Sc.; and Fatima Stanford, M.D., M.P.H., M.P.A. ACRWH members unanimously voted to approve the minutes of the 58th ACRWH meeting on April 12, 2023.

ORWH Director's Report

Dr. Noursi introduced Janine A. Clayton, M.D., FARVO, Director of ORWH, who delivered the ORWH Director's Report. Dr. Clayton began her presentation with a snapshot of recent cancer research, noting that 1.5 million deaths from cancer could have been prevented through primary prevention or early detection, with an additional 800,000 deaths could have been prevented if women everywhere had

access to optimal cancer care. A new American Cancer Society study reported the incidence of lung cancer in women under 50 is higher than among their male counterparts, highlighting the importance of including sex as a biological variable (SABV) in cancer research.

ORWH and NIH Updates. Dr. Clayton announced the appointment of Vivian Ota Wang, Ph.D., as Deputy Director of ORWH. She also announced an opening for the position of ORWH Associate Director for Interdisciplinary Research Section.

There are now 11 women institute and center (IC) directors at NIH. They include Maria Bertagnolli, M.D., National Cancer Institute (NCI), who has been nominated by President Joseph Biden to be NIH Director; Jeanne Marazzo, M.D., M.P.H., National Institute of Allergy and Infectious Disease (NIAID); and Janine Simmons, Ph.D., NIH Deputy Director for Behavioral and Social Sciences Research (OBSSR). She also announced the retirement of Patricia Flatley Brennan, RN, Ph.D., from the National Library of Medicine (NLM) directorship.

NIH Mission Statement. NIH plans to update its mission statement with the following proposed language: “To seek fundamental knowledge about the nature and behavior of living systems and to apply that knowledge to optimize health and prevent or reduce illness for all people.” Public comment on the new mission statement may be submitted through November 24, 2023 ([NOT-OD-23-163](#)).

NIH Revitalization Act of 1993. NIH celebrated the 30th anniversary of this legislation during the summer of 2023. The Act established the inclusion of women and minority groups as a requirement in research.

Health Disparities. People living with disabilities are now considered a health disparities population according to a decision by NIH in consultation with the Agency for Healthcare Research and Quality, the National Advisory Council on Minority Health, and the Health Disparities Working Group on Persons Living with Disabilities [report](#); disability community input; and a review of science and evidence.

Scientific Integrity. NIH is seeking public comment on its [draft scientific integrity policy](#) that articulates the procedures and processes in place at NIH that help maintain rigorous scientific integrity practices. Comments will be accepted until November 9, 2023.

Menopause. World Menopause Day was observed on October 18, 2023. NIH has funded menopause research for 30 years, beginning with the Women’s Health Initiative and continuing with the Study of Women’s Health Across the Nation (SWAN), Menopause Strategies: Finding Lasting Answers for Symptoms and Health (MsFLASH) trials, and the ongoing Menopausal Vasometer Symptoms and Brain Aging in Women (MsBRAIN) trial. [MyMenoplan.org](#) is a website that was developed with support from NIH that includes a tool to find treatment options based on specific symptoms. ORWH’s [7th Annual Vivian Pinn Symposium](#) focused on “Menopause and Optimizing Midlife Health of Women” and “Research on Menopause” was the theme of its [In Focus on Women’s Health \(5.2\) publication](#). ORWH has also created a new travel award for the North American Menopause Society meeting and produced a report on [“Menopause: What You Need to Know”](#) in MedlinePlus (September 7, 2023).

ComPASS. Dr. Clayton updated the Committee on the NIH Community Partnerships to Advance Society (ComPASS) 10-year initiative to address health disparities and health equity. ComPASS planned budget is approximately \$153 million over the next five years, which will fund up to 25 community-led structural interventions, five health equity research hubs, and a coordination center. The 25 Community-Led Health Equity Structural Interventions (CHESIs) ([OTA-22-007](#)) will develop, implement, assess, and

disseminate co-created community-led, health equity structural interventions in partnership with research organizations. Scientific review of CHESI applications incorporated community members and those with lived experience.

NIH Build Up Trust Challenge. The NIH Build UP Trust Challenge will award a total of up to \$1.25 million for solutions that increase research participation and the adoption of medical care by building trust and improving engagement with minority health populations and populations with health disparities. The National Heart, Lung, and Blood Institute (NHLBI) is administering this challenge competition with cross-NIH support. The deadlines for the required registration are November 14, 2023, at 5 p.m. Eastern time; submissions are due December 5, 2023, 5 p.m. Eastern time.

Social Determinants of Health (SDOH) Research. NIH has established an SDOH Coordinating Committee to advance SDOH research through cross-NIH collaboration. This effort is being led by co-chairs Eliseo J. Pérez-Stable, M.D., National Institute on Minority Health and Health Disparities (NIMHD) and Shannon N. Zenk, Ph.D., M.P.H., RN National Institute of Nursing Research (NINR).

Policy and Scientific Updates. Congress has requested an assessment of NIH research on women's health, including NIH research priorities; NIH training and education efforts to build and sustain a robust women's health research workforce; NIH structure, systems, and review processes to optimize women's health research; NIH-wide workforce needed to effectively support women's health research; definition of women's health in today's social and cultural climate; and allocation of funding such that NIH women's health funding is reflective of the burdens of disease among women. The National Academies of Sciences, Engineering, and Medicine (NASEM) will convene an ad hoc committee with specific scientific, ethical, regulatory, and policy expertise to develop a framework for addressing the persistent gaps that remain in the knowledge of women's health research across all ICs.

The focus of the National Academy of Medicine (NAM) annual meeting on October 9, 2023, was Women's Health: From Cells to Society. The meeting featured four panel discussions on sex and gender differences, maternal and reproductive health, health across the lifespan, and the future of women's health policy and research.

Chronic Conditions in Women. NASEM has established an ad hoc workgroup to develop a Framework for the Consideration of Chronic Debilitating Conditions in Women. The workgroup is charged with 1) Reviewing the existing literature on chronic debilitating conditions specific to women; 2) Assembling evidence-based findings on chronic debilitating conditions in women, incorporating the influence of social determinants of health; and 3) Producing a report that describes current gaps in evidence and provides a suggested research agenda for the future.

ORWH has issued [RFA-OD-23-013v](#) and [RFA-OD-23-014](#): Understanding Chronic Conditions Understudied Among Women (R01/R21) in collaboration with the National Institute of Aging (NIA), National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), NCI, the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), and NHLBI. The purpose is to invite applications on chronic conditions understudied among women and/or that disproportionately affect populations of women who are understudied, underrepresented, and underreported in biomedical research. The application due dates are June 20, 2023 and June 20, 2024.

Reproductive Health and Equity. NASEM has established a new standing committee on Reproductive Health, Equity, and Society to evaluate the health, social, and economic implications of access to

reproductive health care in the U.S. and globally to inform related program and activity development at NASEM and to exchange ideas among leading stakeholders.

Career Burnout. Burnout among medical professionals is higher among women and younger clinicians. ORWH is sponsoring a NASEM Workshop on the impact of burnout on gender equity in science, technology, engineering, mathematics, and medicine (STEMM). NASEM will convene a panel of experts to participate in a 2-day public workshop that will take an intersectional approach; place emphasis on women of color, women with disabilities, sexual and gender minority women; consider the disciplinary differences in burnout across STEMM fields; and give particular attention to groups (*e.g.*, caregivers) that research has shown are disproportionately affected by burnout.

Women's Health Innovation Opportunity Map. ORWH collaborated with the Bill and Melinda Gates Foundation to hold the Innovation Equity Forum (IEF) on July 6–7, 2023, to mobilize and accelerate innovations to improve women's health and foster cross-sector multinational partnerships to advance R&D efforts in women's health innovation. The [Women's Health Opportunity Map 2023](#) was published in early October 2023. Aligned with the goals of the IEF, NIMHD published two new funding opportunities in Latin America: Unveiling Health and Healthcare Disparities in Non-Communicable and Chronic Diseases in Latin America: Setting the Stage for Better Health Outcomes Across the Hemisphere (R01 - Clinical Trials Not Allowed) ([PAR-23-303](#)), and Interventions on Health and Healthcare Disparities on Non-Communicable and Chronic Diseases in Latin America: Improving Health Outcomes Across the Hemisphere (R01 - Clinical Trial Required) ([PAR-23-304](#)).

Women and HIV. The NIH Office of AIDS Research (OAR) and ORWH launched the joint HIV and Women Signature Program in February 2023. Its objectives include 1) Ensuring all women receive evidence-based HIV care, prevention, and treatment tailored to their own needs, circumstances, and goals; and 2) Supporting women in science careers to reach their full professional potential. On September 6, 2023, a workshop and listening session was held at the U.S. Conference on HIV and AIDS. A virtual scientific workshop is scheduled for March 21-22, 2024. There is a new Request for Information (RFI) on Research Opportunities Related to HIV and Women's Health ([NOT-OD-24-011](#)), with comments due by December 31, 2023.

Office of Autoimmune Disease Research (OADR). Many autoimmune diseases disproportionately affect women. Congress mandated that ORWH create a new [Office of Autoimmune Disease Research \(OADR\)](#) within ORWH with these objectives: 1) Coordinate the development of a multi-IC strategic research plan with concrete, meaningful milestones to set priorities; 2) Identify emerging areas of innovation and research opportunity; 3) Coordinate and foster collaborative research across ICOs; 4) Annually evaluate the autoimmune research portfolio to determine progress made across NIH; 5) Provide resources to support planning, collaboration, and innovation; and 6) Develop and oversee a publicly accessible central repository for autoimmune disease research (ADR). ORWH briefed Congress on its progress in establishing the OADR on October 19, 2023. First-year activities included establishment of the new office; ORWH support for 28 applications with co-funding from 10 ICOs covering a range of conditions; six **Exposome in Autoimmune Disease Collaborative Teams PLANning** (EXACT-PLAN) program awards ([NOT-OD-23-112](#); see below); five intramural fellowships; and two Accelerating Medicines Partnership® Autoimmune & Immune-Mediated Disease (AMP® AIM) Leadership Scholar Program (LSP) awards (see below). In addition, the Coordinating Committee for Autoimmune Disease Research (CCADR) was established and held its first meeting where it created four working groups: Operations and Management, Strategic Plan Development, Annual Portfolio Analysis, and Data Repository.

ORWH has divided current and future planned activities of OADR into four categories: Infrastructure, Scientific Direction, Public Engagement, and Funding Opportunities, which build upon each other. Major activities within each category include 1) *Infrastructure*: An OADR Core was established to stand up the office; two full-time positions, including OADR Director, were created. ORWH is tapping into NIH platforms such as Office of Intramural Training and Education (OITE) and AMP® AIM to train the future workforce and host comprehensive scientific workshops focused on ADR, and is coordinating with NIH to develop a core set of ADR Common Data Elements that will become recognized NIH terms used to identify and track research efforts, investments, and communications. 2) *Scientific Direction*: The CCADR was established to provide a structured forum to leverage the autoimmune disease research expertise housed across different ICs. All NIH IC directors received communication announcing the new CCADR and have begun responding to its request that they identify scientific experts to serve as IC representatives. High priority next steps include developing an OADR Strategic Plan and conducting a portfolio analysis to fully understand the funding landscape. 3) *Public Engagement*: ORWH has met with patient advocate groups and expects to have ongoing conversations with these groups. Future efforts include development of an RFI to solicit input from public and community constituents and development of messaging and stakeholder engagement plans to establish effective communication processes. 4) *Funding Opportunities*: ORWH has issued an open call for ADR meritorious applications through existing co-funding platforms and through the NIH-wide Coordinating Committee for Women's Health. Fiscal Year (FY) 2023 funding pathways have been identified and are being evaluated for FY 2024.

Awards have been made for the EXACT-PLAN program supporting exploratory, early, and conceptual stage research projects to advance the study of the exposome in autoimmune diseases through development and implementation of a future national, interdisciplinary, collaborative team science research network.

Maternal Health. The U.S. Centers for Disease Control and Prevention (CDC) reports that one out of five women report mistreatment during maternal care with higher numbers of Black, Hispanic, and multiracial women and those with no insurance or public insurance reporting such mistreatment.

Pathways to Prevention (P2P) uses an unbiased, evidence-based process to identify research gaps in a scientific area of broad public health importance via P2P workshops. ORWH, with support from several ICs, organized a workshop on Identifying Risks & Interventions to Optimize Postpartum Health held between November 29 and December 1, 2022. In October, an invitation-only Federal Partners Meeting of agency staff working within this space will be held to help NIH assess current federal initiatives, resources, and potential partnerships relevant to the topic area and to develop an action plan to guide next steps.

Dr. Clayton presented an update on FY 2022 and FY 2023 initiatives in the **Implementing a Maternal health and PRenancy Outcomes Vision for Everyone (IMPROVE)** program, including the launch of ten Centers of Excellence, one data innovation and coordination hub, and one implementation science hub. Other new activities include a Notice of Special Interest (NOSI) for dissemination/implementation, Connecting the Community for Maternal Health Challenges, and a Rapid Acceleration of Diagnostics Technology (RADx® Tech) for Maternal Health Challenge.

OBSSR has released two Notices of Funding Opportunity (NOFOs) focused on intimate partner violence research, a leading cause of maternal mortality: Career Enhancement Award to Advance the Study of Intimate Partner Violence (IPV) in the Context of Maternal Morbidity and Mortality Research (K18

Clinical Trial Not Allowed) ([RFA-OD-24-001](#)) and R25 for Short Courses on Techniques for Measuring Intimate Partner Violence (IPV) in Different Populations (R25 Clinical Trial Not Allowed) ([RFA-OD-24-002](#)). December 1, 2023, is the due date for both opportunities.

A new Task Force on Maternal Mental Health, co-led by the U.S. Department of Health and Human Services (HHS) Office on Women's Health and the Substance Abuse and Mental Health Services Administration (SAMHSA), will identify, evaluate, and make recommendations to coordinate and improve activities related to maternal mental health and co-occurring substance use disorders.

ORWH and the National Institute of General Medical Sciences (NIGMS) joined with 16 other participating NIH ICs in FY 2023 to award 26 administrative supplements to 16 Institutional Development Award Program (IDeA) States to expand their research and research capacity to address women's health and health disparities across the lifespan with an emphasis on maternal mortality and morbidity. Since FY 2020, this collaboration has awarded \$15.4 million dollars in funding to 60 grants in 20 IDeA States and Puerto Rico. ORWH co-funded 16 applications.

Specialized Centers of Research Excellence (SCORE). SCORE is a signature ORWH program that is the only disease agnostic NIH-wide program focusing on biomedical conditions affecting women. A [recent special issue](#) (6 August 2023, Vol. 22 No. 8) of the *Journal of Women's Health* featured articles from each SCORE and highlighted the new Career Enhancement Center (CEC) that supports early career faculties or established investigators who seek to enhance or refocus their careers on translational research. SCORE's annual meeting on November 3, 2023 will feature keynote speaker Claire Pomeroy, M.D., President of the Albert and Mary Lasker Foundation.

Sex and Gender. Objective 2.2 of Strategic Goal 2 of the 2019–2023 Trans-NIH Strategic Plan for Women's Health Research is to develop and adapt reliable and valid measures relevant to the health of women. Today ORWH will present for clearance a concept on gender to support research testing gender terminology for measuring current gender identity as part of the two-step method of data collection. Multiple ICs have expressed interest in this concept, including the Sex and Gender Minority Research Office (SGMRO), NLM, OBSSR, NIA, and NICHD.

ORWH's educational efforts to promote health equity include a new and enhanced Sex and Gender webpage that relaunched in January 2023. It includes "[Understanding the Influences of Sex and Gender in Health and Disease](#)" that explores topics such as mental health, substance use disorders, cardiovascular health, autoimmune diseases, and more. ORWH is funding **Galvanizing Health Equity** through **Novel and Diverse Educational Resources (GENDER) R25** ([RFA-OD-22-015](#)) with multiple ICs to support sex and/or gender-related educational activities that complement and/or enhance training of diverse workforce to meet nation's health research needs. Round 1 funding is completed.

Funding. ORWH's total budget increased from \$51.5 million in FY 2021 to \$60.6 million in FY 2022, an increase of \$9.1 million. For FY 2022, its total extramural grant investments equaled \$43,222,779, excluding R&D Contracts, inter-agency agreements, and Loan Repayment Program (LRP) awards. ORWH's signature programs received most of the funding. FY 2022 investments by program included the Building Interdisciplinary Research Careers in Women's Health (BIRCWH) program: \$10,820,409, including BIRCWH supplements; Career Programs: \$3,009,110; SCORE: 11,707,976; other IC Co-Funds: \$8,815,706; Sex/Gender Administrative Supplements: \$1,877,128; Sex/Gender R01: \$3,830,594; and Understudied, Underrepresented and Underreported (U3) Administrative Supplements: \$3,161,856. FY

2023 budget appropriations include \$76,480,000 for ORWH; \$10,000,000 for OADR-ORWH; \$5,000,000 for BIRCWH; and \$2,000,000 for the NASEM study.

Careers. The NOSI titled Research Supplements to Promote Re-Entry, Reintegration into, and Retraining in Health-Related Research Careers ([NOT-OD-23-170](#)) announced three programs that enable administrative supplements to be given to existing NIH research grants and are intended to support full or part-time research by researchers returning to the scientific workforce or those wishing to expand their skill sets. While reentry and reintegration supplements have been in place previously, the retraining/retooling opportunity represents an expansion of the program. It resulted from recommendations at the NIH Partnership Summit: Reimagining Women in the Bioengineering, Technology, and Data Science Ecosystem.

NASEM Study. ORWH is supporting a new NASEM study on “Policies & Practices for Supporting Family Caregivers Working in Science, Engineering & Medicine.” The report that will provide leaders in academia and government with evidence-based guidance on how to implement policies and programs to support the retention, reentry, and advancement of students and professionals working in science, engineering, and medicine who have family caregiving responsibilities.

Building Interdisciplinary Research Careers in Women’s Health (BIRCWH). ORWH’s signature BIRCWH program currently consists of 19 active programs. Since its inception, ORWH has supported over 750 BIRCWH Scholars. ORWH and the ICs contribute over \$15 million per year to support this career development program. Most recently, BIRCWH expanded its scope by adding its fourth scholar and fifth trainee as well as including predoctoral trainees. The BIRCWH Program Annual Meeting will be held on December 5, 2023.

Team Science Leadership Scholar Program (LSP). This \$4 million pilot program is intended to train people to lead future large, multi-pronged projects like the Human Genome Project, the Human Microbiome Project, and The Cancer Genome Atlas. LSP has a growing relationship with the Accelerating Medicines Partnership Autoimmune & Immune-Mediated Disease (AMP® AIM). The first cohort of AMP® AIM 2023 LSP awardees includes April Lynn Barnardo, M.D., MSCI, a former BIRCWH scholar.

Upcoming Events. Dr. Clayton announced the following upcoming events related to women’s health research: 1) The Long-Term Effects of Pregnancy on Aging Workshop on November 1, 2023 from 8:00 a.m. – 6:30 p.m.; 2) Specialized Centers of Research Excellence on Sex Differences (SCORE) 2023 Annual Meeting Keynote Address on November 3, 2023 from 8:45 a.m. – 9:30 a.m. (virtual only); 3) Building Interdisciplinary Research Careers in Women's Health (BIRCWH) 2023 Annual Meeting on December 5, 2023 from 8 a.m. – 5 p.m.; 4) Diverse Voices: Graphic Medicine on January 25, 2024 from 3 p.m. – 4 p.m.; and 4) HIV & Women Scientific Workshop on March 21 – 22 , 2024 from 10 a.m. – 5 p.m.

Closing Remarks. Dr. Clayton encouraged ACRWH members to keep in touch with ORWH through its publications, social media channels, events, and e-learning opportunities.

NIGMS’ Role in Supporting Women’s Health Research

Dr. Clayton introduced Jon R. Lorsch, Ph.D., Director, National Institute of General Medical Sciences (NIGMS), who provided an overview of NIGMS activities that support workforce diversity and women’s health research. Dr. Lorsch reviewed the NIGMS mission, emphasizing that the institute supports basic research that increases understanding of biological processes and lays the foundation for advances in disease diagnosis, treatment, and prevention.

In 2016, NIGMS initiated its Maximizing Investigators' Research Awards (MIRA) Program that has become its flagship initiative and is expected to be the Institute's dominant form of support by 2025. MIRA's purpose is to empower researchers to undertake more creative and ambitious research by providing a single grant to Principal Investigators (PIs) to support their NIGMS-related research program. These MIRA grants are longer and on average larger than NIGMS R01s and are characterized by their flexibility, i.e., no specific aims are required, and research can change direction. Those eligible to apply for a MIRA grant include Early-stage investigators (ESIs), established investigators (EIs) with at least one single PI NIGMS R01-equivalent grant, and new investigators (NIs). Applications from ESIs and EIs are reviewed by separate panels. Women and men applicants have done equally well in peer review in both the EI and ESI programs. Further, NIGMS has more than tripled the number of ESIs it funds each year since 2013, primarily due to the MIRA program. Notably, ESI MIRA applicants and awardees are typically about a year younger than ESI R01 applicants and awardees.

Training, Workforce Development, and Diversity. NIGMS has the largest NIH portfolio of training, workforce development, and diversity programs, spanning the entire career spectrum from pre-K to post doctorates to independent faculty careers. Dr. Lorsch highlighted NIGMS' Science Education Partnership Awards (SEPA) that represent partnerships between educators and scientists to get students and the general public interested in science, technology, engineering, and medicine (STEM) careers. Operating primarily in the K-12 space, examples of SEPA-funded projects include one at Xavier University of Louisiana-Mobile Outreach for Laboratory Enrichment (XULA-MOLE) that is co-funded with ORWH and provides a comprehensive training and mentoring program for New Orleans high school students and teachers. Seeds of Success: Empowering Girls in STEM Through Mentoring, Access, and Leadership is a Yale University program that provides an out-of-school intervention designed to inspire girls in grades seven to nine to consider careers in STEM.

The Maximizing Opportunities for Scientific and Academic Independent Careers (MOSAIC) program is part of NIGMS's efforts to enhance diversity within the academic biomedical research workforce by targeting the transition from late-stage postdoctoral studies to independent research. The program provides diversity focused K99/R00s and UE5 Mentoring Hubs at professional societies that provide mentoring to participants in areas such as navigating the job application process and grant writing. Over 130 K99s were awarded in FY 21-FY 23 by 17 ICs. Of the MOSAIC scholars, approximately 75 percent are women and about 70 percent are underrepresented minorities.

New NIGMS training, workforce development, and diversity programs include Advancing Research Careers (ARC) that is like MOSAIC in structure but targets the earlier transition from graduate student to postdoc, as well as Leading Equity and Diversity (LEAD), a second branch of the Medical Scientist Training Program (MSTP) that trains physician-scientists across multiple disciplines at Historically Black Colleges and Universities (HBCUs), Tribal Colleges and Universities (TCUs), and IDeA State institutions. In addition, NIGMS is providing undergraduate and graduate training grants for Tribal Organizations.

Institutional Development Awards (IDeA). NIGMS' IDeA Program is a Congressionally mandated initiative that provides over \$420 million per year to states that are traditionally underrepresented in NIH funding. The program includes three components: IDeA Networks of Biomedical Research Excellence (INBRE) that link one or more research-intensive institution in an IDeA State to Primarily Undergraduate Institutions in the state; Centers of Biomedical Research Excellence (COBRE) that develops research capacity in broad scientific areas with a focus on early-career independent researchers; and IDeA Clinical and Translational Research Programs. NIGMS has partnered with ORWH on IDeA initiatives, including a

NOSI on Supporting Women's Health Research in IDeA States ([NOT-GM-23-012v](#)) that will support a COBRE focusing on women's health and a NOSI for Administrative Supplements for Research on Women's Health in the IDeA States ([NOT-GM-22-005](#)).

UNITE. Dr. Lorsch is co-chair of the E Committee within the NIH [UNITE Initiative](#), charged with addressing the "Extramural Research Ecosystem: Changing Policy, Culture, and Structure to Promote Workforce Diversity." Three of the UNITE funding opportunities emerged from the E Committee include: 1) **Research With Activities Related to Diversity (ReWARD)** ([PAR-23-122](#)); 2) Instrumentation Grant Program for Resource-Limited Institutions (RLI-S10) ([PAR-23-138](#)); and 3) the **ST**rengthening **R**esearch **O**pportunities for **NIH** **G**rants (STRONG) program ([PAR-23-144](#)) to help resource-limited institutions expand their research capacity.

Discussion. The following key points were made following Dr. Lorsch's presentation:

- There is a need to get youth, especially American Indian/Alaska Native (AIAN) youth, excited about STEM at an early age. Dr. Lorsch encouraged organizations to apply for the SEPA program, noting there is one in Montana that targets AIAN youth. He also encouraged applications to NIGMS' Bridges to Baccalaureate program that supports community college students to complete a four-year STEM degree.
- MIRA awards differ from merit awards in that they are not intended specifically for meritorious or elite researchers. NIGMS terminated its merit program after starting MIRA because it showed it was not changing scientists' career trajectories.
- Eligibility for a MIRA ESI is defined by the institution; however, the review panel will assess the investigator's independence.
- People in their mid-to-late career who want to transition from teaching to research are eligible for MIRA grants as new investigators. Another funding opportunity from NIGMS available to those at eligible institutions is the **Support for Research Excellence (SuRE)** R16 program that supports research capacity building at institutions that are underrepresented in NIH funding or that serve underrepresented students. Dr. Clayton noted that ORWH's new retraining path on career grants would be another pathway for this group.

Open Discussion

Dr. Clayton facilitated an open discussion among ACRWH members about the following key points. In which the following comments were made:

- Comorbidities in chronic disease research, such as the high risk for urinary tract infections in women with multiple sclerosis (MS), is a major interest for ORWH; ORWH is highlighting the comorbidities issue for the NASEM committee. OADR is also highlighting the need for interdisciplinary research and for multi-IC partnerships to address this topic.
- There is a continuing need to improve reporting of research results by sex and gender by both researchers and journals; the shortcoming is not in current guidelines but in their enforcement. One recommendation is to require publications to address the population to which the reported research is applicable and to require sex and gender in systematic reviews. Dr. Templeton will host an invitation-only meeting of the top 30 journals in the musculoskeletal field to identify key issues in this area and develop recommendations; these will be published in a journal next year.
- There also is a need to integrate sex and gender concepts into undergraduate medical education (UME) and continuing medical education (CME) curricula. This includes revising medical textbooks to acknowledge that the evidence base to date is highly skewed toward men and requires targeting a different set of editors and publishers, as well as educating federal agencies and national

societies about the need to include sex and gender in information provided to clinicians and patients. The University of Colorado is currently developing an in-depth curriculum on sex and gender.

- Per a National Academy of Medicine meeting, there is a huge funding gap on research on women's health that is essential to address. Among the problems: Panel reviews at NIH considering applications about the impact of disease known to affect men on women's health often consider such studies to be replications. The small percentage of grants (about 11 percent) addressing women's health are disproportionately reviewed by special panels. One strategy may be to require a statement in applications about the impact of proposed clinical research on women's health. Overall, a multipronged approach to this problem is required.
- Although men and women are at parity in K award funding, women are less likely than men to apply for a Research Project Grant (RPG). Similarly, there are far fewer senior female leaders than men in medicine. ORWH is planning to develop a toolkit based on interventions that work and institutions that have made changes. The issue in the field is uptake and implementation, not lack of evidence.
- Dr. Clayton's "braided river" is a good analogy about how people flow in and out of their careers. NASEM published a report in 2020 called "[Promising Practices for Addressing the Underrepresentation of Women in Science, Engineering, and Medicine](#)" for retaining women in STEM careers and held a meeting in August 2023 to examine where women are in senior leadership positions. It's time to shift the conversation to policy issues and additional interventions.
- Caregiving is a lifelong commitment for women that affects their careers. Even when caregiving policies are in place, the lived reality is often different from the stated policy. Some policies assure paid leave without specifically protecting research time. There is a need to identify institutions that have a robust family caregiving policy that is sustained beyond a grant period. Some exemplars are expected in the anticipated NASEM report. Overall, there needs to be a cultural shift in perceptions of family caregiving from stigma to validation.
- ORWH has offered continuity supplements since 2020 that support women in balancing career and family caregiving responsibilities. The National Research Service Awards also have a childcare stipend available. ORWH will continue to work on these issues.

Panel: Women's Health and the Institutional Development Awards (IDeA) States Programs

Dr. Noursi introduced Regine Douthard, M.D., M.P.H., Senior Medical Officer, ORWH, who welcomed the three speakers on this panel: Tia Brodeur, M.D., Ph.D., Indiana University; Emily Harville, Ph.D., Tulane School of Public Health and Tropical Medicine, and Emily Haozous, Ph.D., RN, FAAN, Pacific Institute for Research and Evaluation, Southwest Center.

Ovarian Stimulation with Gonadotropins Promotes Unique Dynamics of Ovarian Immune Microenvironment

Dr. Douthard introduced Dr. Brodeur who presented work that she began with support from an IDeA States Program women's health research award and that is the foundation for her ongoing investigations.

Background. Women are born with all the eggs they are ever going to have. But oocyte loss occurs rapidly because these cells die by atresia, leading to apoptotic debris that needs to be efficiently cleared; macrophages are responsible for this task. Not only do they clear debris and bacteria, but macrophages also mediate tissue repair. Uptake of apoptotic debris by macrophages is not a passive process, but one that promotes a tolerogenic phenotype in phagocytes, providing some resistance to autoimmunity. Inefficient clearance of apoptotic debris may lead to secondary necrosis, and thus be partially

responsible for the initiation/propagation of systemic autoimmunity. Therefore, a relevant question is: What cell is responsible for uptake of apoptotic debris and how is this process affected by the use of ovarian steroid hormones that are in high concentration in the ovary? There is a condition called primary ovarian insufficiency that affects about one percent of women overall; there is an autoimmune version of it that is characterized by oophoritis or ovarian inflammation. The etiology of this condition is not understood.

In the classical model of autoimmune disease, there is a presumed genetic predisposition and some environmental triggers that lead to activation of the innate immune system that includes cells like macrophages because they have fewer checkpoints to promote tolerance. This, in turn, leads to activation of the adaptive immune system which includes autoreactive T and B cells. This spiral is responsible for the full spectrum of clinical disease.

Research Strategy and Findings. Dr. Brodeur hypothesized that pre-ovulatory peak estradiol levels promote increased uptake of apoptotic debris by ovarian resident phagocytes and prevent secondary necrosis that would promote oophoritis, and that this would also lead to a tissue-remodeling phenotype of macrophages in the ovary. Dr. Brodeur identified the following key markers in the ovaries that she would study: CD45, a marker of haematopoietically-derived cells, including leukocytes; CD19 and TCR- β indicating T and B cells; and CD11b and F4/80, typically associated with macrophages. The goal of her study was to determine if these cells were truly ovarian resident or simply passing through. She began her research by injecting mice intravenously with an antibody against CD45 which was conjugated to fluorochrome PE. If the animals were intravascularly stained with CD45-PE, that would help the investigators differentiate the cells circulating through blood vessels from those resident in the tissue itself. After three minutes of circulation, the animals were sacrificed, and the ovaries extracted for ex-vivo staining for CD45 and flow cytometry. Dr. Brodeur found that the ovarian cells in animals exposed to CD45 were double-positive while the cells of saline-injected control animals were not. This suggests that the leukocytes were resident in the tissue rather than circulating through.

The next step was to understand how these ovarian-resident immune cells responded to high estrogen levels. To assure robust results, the investigators induced super-physiologic levels of estradiol with human menopausal gonadotropin, isolated the cells, and then stained the tissue for immunofluorescence and flow cytometry. The tissue staining revealed highly expressed levels of CD206, a macrophage marker. Flow cytometry showed high T and B cells levels under all conditions and an increase in CD11b, another macrophage marker, in the animals exposed to the gonadotropins.

What would occur with natural ovarian aging and a presumed low estrogen state? Comparing young ten-week-old mice with old 40-week-old mice, Dr. Brodeur observed an increase in the number of macrophages in the older animals. Next, she zoomed in on the transcriptome of the cells exposed to the high estrogen state via single cell RNA sequencing. The plots of the distinct cell clusters present in the ovary revealed two cell types that distinguished between the saline-injected (controls) and gonadotropin-injected (treatment) mice. These were an increase in natural killer (NK) cells in the gonadotropin-treated mice, coupled with a decrease in mature B cells.

In her analysis, Dr. Brodeur noted MerTK⁺ macrophages because this protein has been shown to be important in male fertility; male mice deficient in MerTK are infertile. In this study, the mice high in MerTK highly expressed a molecule that is involved in cell death. Dr. Brodeur also examined T and B cells in wild type controls in MerTK-deficient mice, observing a decrease in B cells in the ovaries of MerTK-deficient mice which had not been previously reported for other tissues studied for autoimmune

diseases. No significant differences in T cells were observed. Because the protein is highly expressed in macrophages, the investigators looked at CD206 levels and found similar levels in both the control and MerTK-deficient mice.

Dr. Brodeur summarized her key findings: 1) CD206+ macrophages are abundant in the ovary, but expression does not appear to be significantly impacted by a high estrogen state. 2) MerTK function in maintaining fertility in the testis is not applicable to the ovary. 3) Despite possible association with male factor infertility, MerTK does not appear to be a crucial target in ovarian remodeling (in young mice). 4) B cells and NK cells unexpectedly respond to “estrous” in super ovulated mice.

Future Directions. Dr. Brodeur’s team have generated mice that are estrogen receptor deficient in the macrophage lineage and are pursuing further investigation of macrophages as potential mediators of “inflammaging,” *i.e.*, investigating their cytokine and metabolic profile, accumulation of apoptotic debris, fecundity, and ovarian lifespan (oocyte loss, fibrosis).

Collecting Pregnancy Data in the Strong Heart Study

Dr. Douthard introduced Dr. Harville, whose presentation focused on the challenges of collecting pregnancy data in the Strong Heart Study, the largest epidemiologic study of American Indians ever undertaken. Three of the four authors of this research initiative are from IDeA States; they received an IDeA women’s health supplement to examine pregnancy data in the Strong Heart Study.

Background. Pregnancy complications, such as hypertensive disorders of pregnancy (gestational hypertension and preeclampsia) and gestational diabetes mellitus (GDM), predict cardiovascular morbidity and mortality. Most studies addressing the relationship between cardiovascular disease (CVD) and pregnancy have been conducted in White populations, even though studies suggest racial variation in the likelihood of progression from GDM to Type 2 diabetes or from prehypertension to hypertension. American Indian women are at high risk for pregnancy complications and adverse birth outcomes, although there is substantial variation by state and tribe. AIAN women are at particularly higher risk for complications linked to higher body mass indices (BMIs): GDM, preeclampsia, and macrosomia. However, there are few or no large-scale studies that address reproductive health in this population.

The longitudinal Strong Heart Study, supported by NHLBI and initiated in 1988, examined CVD and its risk factors among American Indian men and women. The study included 12 American Indian tribes and communities in three geographic areas: an area near Phoenix, Arizona; the southwestern area of Oklahoma; and western and central North and South Dakota. It was carried out in multiple phases with different types of data collection at each phase.

Methods. The aims of the women’s health supplement were to assess the quality of self-report of reproductive health in an American Indian cohort and to characterize preeclampsia and gestational diabetes in the cohort. The investigators pulled pregnancy data from multiple sources. In Phases I, II, IV, and V of the Study, female participants were asked about the number of times they had given birth, living children, and “lost pregnancies” (miscarriage and stillbirth). When participants were asked about high blood pressure and diabetes, “only during pregnancy” was one option. In Phase III, participants were asked about high blood pressure during pregnancy. In Phase IV participants were asked if they were currently pregnant/breastfeeding. In Phase V, participants were tasked about their history of hypertension during pregnancy and preeclampsia. And in Phase VI, the participant’s medical history included parity, gravidity, stillbirth, preeclampsia in first or later pregnancies, GDM in first or later pregnancies (also dates of first pregnancy and complicated pregnancies). Other sources of pregnancy

information included medical records (requested for cases of preeclampsia and a subset as controls); these were abstracted and reviewed. National Data Warehouse of the Indian Health Service (IHS) records allowed comparisons of blood pressure readings during the period a woman was pregnant. The study is currently seeking birth certificates but has not yet obtained them. The researchers are trying to integrate these disparate data sources to examine the pregnancy histories of women. Data were collected retrospectively from all female participants and prospectively from women of childbearing age.

Findings. The first objective the research team sought to accomplish was to validate the preeclampsia data by comparing self-reports to recorded data such as medical records (which were often incomplete). There did not appear to be much overlap on preeclampsia information across the data sources. On the other hand, GDM appears to have more reliable data and became a focus of investigation. Among the group of about 300 women for whom pre-pregnancy data was available, almost eight percent had GDM (comparable to other ethnic groups) and another seven percent had diabetes diagnosed prior to pregnancy (higher than other groups). Among cardiovascular risk factors for GDM, only glucose stood out as a predictor. Looking at GDM as a predictor for developing other cardiovascular diseases in the future, only diabetes stood out. At age 50, about a doubling of risk for Type 2 diabetes was reported among women with a history of GDM in the study. The only risk factors that appeared to affect the progression from GDM to later Type 2 diabetes were HbA1c or glucose at post-pregnancy visit and BMI.

In summary, the investigators found that accessing pregnancy data, even with records and appropriate permissions, is difficult. Further, developing an accurate retrospective diagnosis of preeclampsia is difficult. Major predictors and consequences of GDM relate to glucose and BMI, with limited associations with other CV risk factors. There was a high prevalence of diabetes among the women, suggesting that early-life studies may be necessary. Factors limiting this study included self-reports of GDM, a limited number of cases, limited pre-pregnancy data, and incomplete pregnancy histories of participants.

Trends in Premature Mortality with a Focus on Women's Health

Dr. Douthard introduced Dr. Haozous, who participated in an IDeA INBRE in Montana where she learned grant writing. Dr. Haozous' presentation focused on a collaboration between intramural researchers in the Division of Epidemiology and Genetics at NCI whose studies revealed alarming findings about the disparities in deaths between the AIAN population and others. Therefore, they sought Dr. Haozous' expertise on American Indian data concerns.

Deaths of Despair. The phrase "deaths of despair" (due to poisonings, alcohol-related deaths, and suicides) was originally used in relation to a rise in death rates among White men and women without a college degree. Economists believed that the root cause of these increased deaths was societal, driven by growing unemployment and financial insecurity. However, increases in death rates due to these "deaths of despair" have not been restricted to middle-aged Whites in non-urban America. In fact, death rates from these causes increased from 2015 to 2016 across all racial/ethnic groups.

Dr. Haozous also defined another cause of premature death (*i.e.*, death before age 65) as death by intent, a categorization that provides important nuance to specific external causes of death (suicide, homicide, unintentional injury). She explained that it is important to study cause of death because it allows researchers to build meaningful benchmarks, helps the public understand the context for health outcomes, and identifies reasonable and practical interventions that fit the data and the populations.

Publications. Dr. Haozous' first collaboration with the NCI scientists resulted in a paper in *The Lancet*¹ that drew on data from the National Center for Health Statistics (NCHS) and the Census to look at cause of death. The mortality data were broken into age cohorts and compared by sex, race, and ethnicity. The results showed dramatic disparities in premature mortality for American Indian and Alaska Native populations. Increases in mortality were highest in women and in people between the ages of 25-30. AIAN mortality rates increased in all age cohorts born after 1948, with specifically high rates of mortality from liver disease and opioid-related causes. Dr. Haozous called out two implications of the data for women's health: 1) AIAN populations are guaranteed healthcare through IHS, yet access to behavioral health services is scant; and 2) Women needing treatment for mental health and drug and alcohol-related concerns have few options, contributing to high rates of mortality in this population.

A subsequent study² used death certificate data to project premature mortality for the U.S. population for the most common causes of premature death (cancer, heart disease, accidents, suicide, and chronic liver disease/cirrhosis). The projections suggested a ten percent increase in premature mortality in non-Hispanic White women and AIAN men and women, as well as increased accidental death rates in all populations except Asian and Pacific Islander (API) women. Suicide rates were projected to increase in all groups. Dr. Haozous identified the following implication of these findings for women's health: Adopting prevention, education, treatment, and recovery legislation to address opioid addiction can effectively eliminate drug poisonings and reduce accident-related mortality by two percent.

In a study of death certificate data for those aged 1 to 24 published in *JAMA Pediatrics*,³ the investigators found that mortality for U.S. youth is declining slowly in comparison to youth in Canada and England/Wales. However, mortality remains high for AIAN and Black/African American youth. There were concerning increases in suicide and drug poisoning deaths in the youth population. The 2015 infant mortality rate in the US was disproportionately high in Black/African American individuals (11/1,000) and AIAN individuals (9.7/1,000). In fact, in this study, the U.S. had the highest infant mortality rate.

Two separate studies published in *JAMA Network Open*^{4,5} examined deaths of despair between 2000–2026 and 2000–2017. These studies reported that alcohol-related death rates increased the most in AIAN men and women and in White women over the study period. Rates of increase varied by racial group and age group, with large increases taking place in mid-life for White men and women and AIAN

¹ Shiels MS, Chernyavskiy P, Anderson WF, Best AF, Haozous EA, Hartge P, Rosenberg PS, Thomas D, Freedman ND, de González AB. Trends in premature mortality in the USA by sex, race, and ethnicity from 1999 to 2014: an analysis of death certificate data. *The Lancet*; 2017. DOI: 10.1016/S0140-6736(17)30187-3.

² Best AF, Haozous EA, de González AB, Chernyavskiy P, Freedman ND, Hartge P, Thomas D, Rosenberg PS, Shiels MS. Premature mortality projections in the USA through 2030: a modelling study. *The Lancet Public Health*; 2018. DOI: 10.1016/s2468-2667(18)30114-2.

³ Khan SQ, de González AB, Best AF, Chen Y, Haozous EA, Rodriguez EJ, Spillane S, Thomas DA, Withrow D, Freedman ND, Shiels MS. Infant and Youth Mortality Trends by Race/Ethnicity and Cause of Death in the United States. *JAMA Pediatrics*; 2018. DOI: 10.1001/jamapediatrics.2018.3317.

⁴ Shiels MS, Tatalovich Z, Chen Y, Haozous EA, Hartge P, Nápoles AM, Pérez-Stable EJ, Rodriguez EJ, Spillane S, Thomas DA, Withrow DR, de González AB, Freedman ND. Trends in Mortality From Drug Poisonings, Suicide, and Alcohol-Induced Deaths in the United States From 2000 to 2017. *JAMA Network Open*; 2020. DOI: 10.1001/jamanetworkopen.2020.16217.

⁵ Spillane S, Shiels MS, Best AF, Haozous EA, Withrow DR, Chen Y, de González AB, Freedman ND. Trends in Alcohol-Induced Deaths in the United States, 2000-2016. *JAMA Network Open*; 2020. DOI: 10.1001/jamanetworkopen.2019.21451.

women. Mortality rates increased overall over time, although rates and causes varied by region, indicating each community requires its own tailored intervention.

The researchers also examined excess deaths due to COVID and deaths not due to COVID from March 2020 to December 2020, looking at race, ethnicity, sex, age, and cause of death.⁶ They found that excess deaths were two to four times higher in Black/African American, AIAN, and Latino populations than in non-Hispanic White populations during the first nine months of the COVID-19 pandemic. Black/African American, Latinas, and AIAN women had higher rates of excess mortality from heart disease, diabetes-related causes, cerebrovascular disease, and Alzheimer's disease.

An analysis of “deaths from external causes” published in *JAMA Internal Medicine*⁷ included deaths from intentional and unintentional injury and poisoning (e.g., drug overdose) and firearms, drawing on NCHS data for adults 20 and older between 1999–2020. The results showed that death rates due to drug poisonings, firearms, and other injuries of intent increased greatly. Drug poisoning rates tripled in 2019–2020, despite a decrease in opioid prescribing. Mortality due to firearms increased over time, with an overall increase of 1.1 percent annually. The implications for women's health: 1) focused public health interventions are necessary to address rising mortality rates from preventable causes; and 2) women are particularly vulnerable to homicide deaths from firearms, requiring direct and urgent attention to counteract this serious public health threat.

Dr. Haozous summarized her presentation by noting the following key points: 1) Premature mortality and deaths of despair are important public health concerns; 2) There is a specific need to address firearm deaths and drug poisonings through public health and policy changes; 3) New analyses are needed to update projections following the COVID-19 pandemic; and 4) AIAN women's health is a specific health disparity population. Dr. Haozous commented that there is a pressing need to bridge academic research and public health interventions, including the behavioral health care gap..

Discussion: Dr. Douthard moderated a discussion among the panelists that addressed the following topics:

- Bridging the policy-to-practice gap will require more support for people working in prevention. More attention should be paid to dissemination and implementation of prevention strategies.
- Participation in IDEa initiatives helped these researchers build professional relationships, provided an opportunity to work on AIAN health issues, and made a scientific research career possible by providing financial resources.
- Better understanding of infections of the female reproductive tract could have public health implications, e.g., the increase observed in Dr. Brodeur's research in NK cells could indicate a need for protection from ovary-trophic viruses, including mumps, which can lead to oophoritis in women and infertility in males. The sex differences in autoimmunity are one of the possible explanatory factors for the decrease in B cells.

⁶ Shiels MS, Haque AT, Haozous EA, Albert PS, Almeida JS, García-Closas M, Nápoles AM, Pérez-Stable EJ, Freedman ND, de González AB. Racial and Ethnic Disparities in Excess Deaths During the COVID-19 Pandemic, March to December 2020. *Annals of Internal Medicine*; 2021. DOI: 10.7326/m21-2134.

⁷ Lawrence WR, Freedman ND, Mcgee-Avila JK, de González AB, Chen Y, Emerson MA, Gee GC, Haozous EA, Haque AT, Inoue-Choi M, Jackson SS, Lord B, Nápoles AM, Pérez-Stable EJ, Vo JB, Williams F, Shiels MS. Trends in Mortality From Poisonings, Firearms, and All Other Injuries by Intent in the US, 1999-2020. *JAMA Internal Medicine*; 2023. DOI: 10.1001/jamainternmed.2023.2509.

- Patients with lupus are characterized by double negative T cells. Currently, the differentiation pathway of downregulation of CD8 that leads to double negative T cells in the ovary is unknown. There are potential therapeutics that could be used for ovarian insufficient patients if these cells reveal themselves to be important in the treatment of autoimmune disease.
- Waist circumferences may be a better indicator of obesity than BMI in the Strong Hearts study.
- It may be the case that pregnant AIAN women with GDM in the Strong Hearts Study already had diabetes without diagnosis.
- Because of incomplete medical records and the reliability of self-reports, the pregnancy-related data from the Strong Hearts Study may be considered suggestive rather than definitive. Missing data is not uncommon for AIAN populations. Dr. Harville's study team is seeking to overcome this challenge by looking at the overlap across four sources of data to establish a likelihood estimate among them.
- There is currently no example in the published literature of a multidisciplinary approach that has been successful in addressing the health issues faced by AIAN women. It is unlikely that what works for one tribe will work for another, as each tribe is culturally distinct.
- More can be done to protect women from the harms posed by tobacco. Successful evidence-based interventions are being underutilized.

Concept Clearance: Building Interdisciplinary Research Careers in Women's Health (BIRCWH) Request for Applications (RFAs)

Xenia Tigno, Ph.D., Associate Director for Careers, ORWH, introduced Lisa Begg, Dr.P.H., RN, Senior Research Program Officer, ORWH, who presented a concept clearance for Building Interdisciplinary Research Careers in Women's Health (BIRCWH) Request for Applications (RFAs). ORWH requested approval to reissue [RFA-OD-19-020](#), and [RFA-OD-21-006](#) for Building Interdisciplinary Research Careers in Women's Health, (K12, Clinical Trial Optional) simultaneously. The purpose of these RFAs is to invite institutional career development award applications to the BIRCWH program. Each award will support the mentored research career development of junior faculty members known as BIRCWH Scholars. Contingent upon NIH appropriations, \$7.5 million for each application deadline (for FY 2025 and for FY 2027) will be available to support up to a total of 20 meritorious five-year BIRCWH awards across both RFA deadlines.

Background. The BIRCWH Program was created in FY 1999 with a special Congressional appropriation. The RFAs are re-issued every five years. IC co-funding can vary with each RFA re-issuance. Twelve of the current 19 grantees have multiple Principal Investigators (MPIs), and 14 have Physician PIs (solo or MPIs). More than 750 Scholars have completed the program. Of these, 88 percent have remained in research, and 46 percent are physician-scientists. Over half (51 percent) hold a Ph.D. and 35 percent hold an M.D. Eighty percent of the Scholars are women and 20% are men. Over 13 percent of Scholars across all cohorts of the program were underrepresented minorities.

Innovation. Examples of innovations within BIRCWH include 1) the Harvard BIRCWH Innovation Project that will elevate the scientific mission of the SCORE and Career Enhancement Core by formulating a biomedical-science pipeline that infuses consideration of sex differences across the brain and body to create a SCORE Translational Workforce Innovation Network (TWIN), building on academic-industry partnerships; and 2) the Team Science Leadership Scholar Program, previously described by Dr. Clayton.

2025 Evaluation Plans. On the 25th anniversary of the BIRCWH program in the fall of 2025, ORWH will launch a major evaluation of the program. The primary evaluation questions include 1) Was the BIRCWH program able to build a cadre of scientists pursuing women's health research? 2) What are the other

program outcomes of the BIRCWH program? 3) What do BIRCWH Scholars (past and present) and PIs see as the most valuable aspect of the program?

Discussion: The following key points were raised during a discussion of this concept clearance:

- A supplement for BIRCWH Scholars with individual K awards that would allow them the opportunity to reenter their careers in the event of family caregiving or other leaves would put them at parity with other K awards. This is an area that can be explored; however, there are standard policy rules that apply to T32 programs by which ORWH must abide.
- Because the government is operating on a Continuing Resolution, it is unlikely that Congress will approve new funds in the near term to extend training for a 4th trainee beyond two years. Institutions are free to extend their terms for regular trainees with no additional supplemental funding.

Note: The concept for Building Interdisciplinary Research Careers in Women’s Health, (K12, Clinical Trial Optional) RFA-OD-19-020, and RFA-OD-21-0060 was approved with a vote of 12 in favor and one abstention.

Concept Clearance for Reissuance: Research on the Health of Women of Understudied, Underrepresented and Underreported (U3) Populations Administrative Supplement and Program Evaluation

Dr. Noursi introduced Miya Whitaker, Psy.D., M.A., Health Scientist Administrator/Program Officer, ORWH, who presented a concept clearance for the FY 2024 reissuance of the Health of Women of Understudied, Underrepresented and Underreported (U3) Populations (Admin Supp Clinical Trial Optional) program. The U3 programs supports supplemental research projects that explore the impacts of intersectionality (the lived experience of an individual’s multiple identities) and social determinants of health (SDOH) on women in the United States who are understudied, underrepresented, and underreported (U3) in biomedical research. Funding is contingent upon NIH appropriations and ICO partnership, estimated at \$2 million. The award project period is for one year.

Program Evaluation. Between FY 2017–FY- 2023, 105 awards to 30 states and the District of Columbia totaling \$20.41 million across 19 ICs were funded as part of the U3 program. NICHD and NCI funded the largest number of U3 grants. Analysis of the U3 portfolio revealed that African Americans and Hispanic/Latinos were the focus of most U3 research. The R01 was the most common funding mechanism. Women’s health, SDOH, and mental health were the topics most often addressed. Seventy percent of the funded investigators were female, and more than half of funded PIs held a Ph.D. degree.

In both 2022 and 2023, U3 investigators appeared in four of ORWH’s Diverse Voices: Intersectionality and the Health of Women virtual lecture series. Other U3 program achievements include research across a broad array of topics; an increasing number of investigators from diverse backgrounds; and productivity among U3 PIs, as measured by the number of scientific presentations, publications, etc.

In summary, U3 may be considered a successful program because: 1) U3 continues to support research considering the intersection of social and biological factors and women’s health across the life, using an SDOH and intersectionality lens in clinical, behavioral, and translational studies; 2) U3 continues to support inclusion in interdisciplinary research focused on women’s health by supporting a broad range of priority topics, including chronic disease and autoimmunity, that disproportionately affect U3 women;

and 3) U3 continues to support diverse perspectives and diverse investigators, leading to work that accelerates knowledge. The funded portfolio comprises more than 25 percent MPI awards.

Discussion: The following key points were raised during a discussion of this concept clearance:

- ORWH is investigating the factors that led to a dip in awards in 2020 subsequently followed by a gradual increase to 2023.

Vote: The concept for Research on the Health of Women of Understudied, Underrepresented and Underreported (U3) Populations Administrative Supplement was approved with a vote of 14 in favor.

Concept Clearance: NOSI on Health Influences of Gender as a Social and Structural Variable

Dr. Noursi introduced Elizabeth Barr, Ph.D., Social and Behavioral Scientist Administrator, ORWH, who presented a concept clearance for a NOSI on the health influences of gender as a social and structural variable. Its purpose is to highlight interest in receiving research and training grant applications focused on the health impacts of gender-related social and structural variables. Funding and the anticipated number of awards is contingent upon NIH appropriations and IC partnerships. The award project period will be determined by mechanism.

Dr. Barr explained that gender is a social and structural variable that encompasses multiple domains, each of which influences health: gender identity and expression, gender roles and norms, gender relations, and systems and structures of power. Additional research is needed to continue delineating and untangling the effects of gender from the effects of sex and other biological variables. Interest in further research on the health influences of gender grew out of a Gender and Health Scientific Workshop in October 2022 that had wide support within NIH and the extramural community.

In preparation for the Gender and Health Workshop, ORWH and NICHD analyzed gender-related research at NIH that focused on the relationships between gender roles, relations, power dynamics, or (in)equity and health during FY 2017–FY 2022. They identified 204 competing awards focused on gender and health, with 16 of the 27 ICs issuing at least one new gender-related award. Among the recent gender-related awards, HIV prevention and mental health were the most common topics addressed, followed by sexual assault, cancer, and unintended pregnancy. A post-workshop commentary in *Translational Behavioral Medicine*⁸ summarizing NIH research perspectives related to gender and health noted: “A second critical opportunity is continued and expanded support for research that considers the multiple social, structural, biological, and behavioral factors that influence the health of women and individuals assigned female at birth, and the intersections of these factors.”

Thus, the focus of this new concept clearance is on gender roles, norms, relations, power, equity, equality, and sexism. Intersectional approaches in these research and training grants are encouraged. Examples of responsive topics include: 1) Development, testing, or validating measures and methods; 2) Observational studies; and 3) Development, testing, implementation, dissemination, and/or evaluation of interventions.

Discussion: The following key points were raised during a discussion of this concept clearance:

⁸ Barr E, Popkin R, Roodzant E, Jaworski B, Temkin, SM. Gender as a social and structural variable: research perspectives from the National Institutes of Health (NIH). *Translational Behavioral Medicine*; 2023. DOI: 10.1093/tbm/ibad014.

- It is challenging but necessary to integrate SABV and gender, *e.g.*, women often don't receive the same medications as men (a gender variable) but there is also a biological aspect of how the medications work in the body (SABV). Teasing out the differences may depend on the research question being addressed.
- Training in sex and gender is available via ORWH resources but is not currently required.

Vote: The concept clearance for a NOSI on Health Influences of Gender as a Social and Structural Variable was approved with a vote of 13 in favor and one abstention.

Concept Clearance: Women and HIV

Dr. Barr presented a concept clearance for a NOSI titled HIV and Women. Funding and the anticipated number of awards is contingent upon NIH appropriations and IC partnership. The award project period will be determined by the funding mechanism.

Dr. Barr reviewed key global statistics (2021) about women and HIV, noting that 54 percent (~20 million) of all people with HIV are women. In the United States, 23 percent (258,000) of people with HIV are women; Black and African American women are overrepresented among new HIV diagnoses.

There were 1.3 million pregnant people living with HIV across the globe in 2021, of which an estimated 81 percent received antiretroviral therapy (ART) to prevent vertical transmission. The most recent report from the World Health Organization (WHO) in 2017 indicated 1.2 percent of maternal deaths globally are estimated to be HIV-related. Additionally, HIV is associated with an increased risk of comorbidities that compound the risk of death during pregnancy.

For the NOSI under consideration, the proposed areas of focus include research and training grants. High priority topics will be identified through literature review, external engagements, a Request for Information (RFI), and portfolio analysis. Intersectional approaches will be encouraged. Examples of high priority topics include community-led research; HIV, pregnancy, lactation, and postpartum; early childhood consequences of HIV exposure; HIV and aging; HIV and menopause; intersections of HIV and comorbidities, multimorbidity, and polypharmacy; implementation science; interdisciplinary approaches and gender-affirming and trauma-informed HIV care and research; and sex and gender influences in treatment, prevention, and cure-related research.

Discussion: The following key points were raised during a discussion of this concept clearance:

- Women have a different constellation of comorbidities than do men; it would be desirable to incorporate language about these differences into the NOSI.
- Like other viruses, HIV remains in the body, leading to chronic inflammation, organ damage, and comorbidities. Thus, the proposed research provides a window into how viral infections in women work and the potential for prevention.

Vote. The concept clearance for a NOSI on Women and HIV was approved with a vote of 14 in favor.

Open Discussion

Dr. Clayton facilitated an open discussion in which the following comments were made:

- More work is needed to build a broader recognition of women's health issues beyond reproductive health. An important strategy for prioritizing women's health research would be to elevate ORWH to an institute within NIH. While this "top down" effort is important, a "bottom up" strategy at the

grassroots level is also needed, *i.e.*, bringing up sex and gender at every opportunity. Further, while infrastructure may change, the focus and types of research addressed are also important.

- Recommended priority topics and their impact on women’s health include tobacco; infectious diseases; alcohol and cannabis; lactation; abortion access/care; menopause; pain; and the maintenance of chronic disease treatments during family planning, pregnancy, and postpartum. Opportunities exist in each of these areas for collaboration across NIH.
- Lack of clinical practice guidelines for women’s health care is an issue that needs greater recognition and attention. An evidence base for establishing such guidelines is needed; guidelines should expressly state which people were included in the studies that formed the evidence base for each guideline. Development of an evidence base requires collaborative cross-disciplinary conversations, possibly facilitated by an organization such as NASEM. If ORWH were an institute, it would have greater authority to advance the evidence base, perhaps using NCI’s strategy of funding P50 Centers of Excellence that develop “transdisciplinary research models that can more rapidly advance the science beyond earlier paradigms” (per [NCI website](#)).
- ORWH and ACRWH members should use success stories to market ORWH and promote its potential as an institute.
- The forthcoming 2024–2028 NIH-Wide Strategic Plan for Research on the Health of Women, currently being finalized, will address how ICs implement the plan. ACRWH members will have the opportunity to provide input on the implementation process to assure there is true understanding of the importance of creating the evidence base that will advance the science supporting women’s health.
- Geographic regions that lack funding or health care deserts is a topic that may be addressed in a future ACRWH meeting. One potential strategy for addressing funding deserts is collaborating with the Association of American Medical Colleges (AAMC) and the deans of institutions in those areas.

Closing Remarks

Dr. Clayton adjourned the meeting at 3:35 p.m. The next meeting, scheduled for April 9, 2024, will be a hybrid meeting.

Certification

We certify that the contents above are accurate and complete.

Janine Clayton, MD

Janine Austin Clayton, M.D., Director
Office of Research on Women’s Health

Samia D. Noursi

Samia Noursi, Ph.D., Executive Secretary
Advisory Committee on Research on Women’s Health

Date 12/19/2023

Date 12/19/2023