

57th 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, 2022

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 Klein, Ph.D.
Alyson J. McGregor, M.D.
Thelma Mielenz, Ph.D.
Alexandra Noël, Ph.D.
Judy Regensteiner, Ph.D.
Michelle Robinson, D.M.D.
Yoel Sadovsky, M.D.
Phyllis Sharps, Ph.D.

Melissa Simon, M.D.

Kimberly J. Templeton, M.D.

ORWH Leadership Present

Janine Clayton, M.D., FARVO, Director
Samia Noursi, Ph.D., Associate Director for
Science Policy, Planning, and Analysis
Sarah Temkin, M.D., Associate Director, Clinical
Research

Other NIH Leadership Present

Lindsey A. Criswell, M.D., M.P.H., D.Sc.,
Director, National Institute of Arthritis and
Musculoskeletal and Skin Diseases (NIAMS)
Rick Woychik, Ph.D., Director, National Institute
of Environmental Health Sciences (NIEHS)

Call to Order

Samia Noursi, Ph.D., ACRWH Executive Secretary and ORWH Associate Director, Science Policy, Planning, and Analysis, called the online meeting to order at 9:31 a.m. She introduced new ACRWH members Stephen Higgins, Ph.D., University of Vermont; Hendrée Jones, Ph.D., University of North Carolina; Thelma Mielenz, Ph.D., Columbia University; Alexandra Noël, Ph.D., Louisiana State University; and Phyllis Sharps, Ph.D., M.S.N., RN, Johns Hopkins University. Committee members introduced themselves and approved the minutes of the 56th ACRWH meeting held on April 6, 2022.

ORWH Director's Report

Dr. Noursi introduced Janine A. Clayton, M.D., FARVO, Director, ORWH. Dr. Clayton delivered the Director's Report. Dr. Clayton began by announcing the upcoming retirement of Anthony M. Fauci, Director, National Institute of Allergy and Infectious Diseases (NIAID) in December 2022. She highlighted Dr. Fauci's contributions to advancing women's health, e.g., identifying sex differences in immune response to the flu and the inclusion of pregnant people in COVID-19 research.

ORWH and NIH Update. Dr. Clayton announced the appointment of Balkissa M. Abdoulaye, M.A., as Assistant Director of the ORWH Management, Reporting, Operations and Communications Section.

NIH Strategic Plan for Research on the Health of Women. Development of the 2024-2028 strategic plan is underway, informed by ACRWH recommendations following the 2021 ORWH-led Women's Health Conference and by 187 comments from NIH Directors', NIH scientists and administrators, as well as

advocacy and patient communities and the public in response to a Request for Information (RFI) (NOT-OD-22-186).

Changes in Biennial Report. At the request of NIH Leadership, ORWH has reduced the FY 2021-2022 Biennial Report to under 100 pages. To accommodate the reduction, ORWH will leverage its existing digital content from current activities. ACRWH members will be asked in early 2023 to review sections of the FY 2021-2022 Biennial Report.

Personnel Updates. Dr. Clayton announced the appointment of Monica Bertagnoli, M.D., as Director of the National Cancer Institute (NCI), bringing the total number of female IC directors to 12. She also announced the appointments of Robert W. Eisinger, Ph.D., as Acting Director of the Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI); Nina F. Schor, M.D, Ph.D., as Acting Deputy Director for Intramural Research; and Kevin D. Williams, J.D., as Director of the Office of Equity, Diversity, and Inclusion. James M. Anderson, M.D., Ph.D., NIH Deputy Director for Program Coordination, Planning, and Strategic Initiative and DPCPSI Director, has retired, as will Andrea Norris, NIH Chief Information Officer and Director of the Center for Information Technology, in December 2022.

COVID-19 Update. A literature review by Shirley Sylvester and colleagues published in *Current Medical Research and Opinion* (2022) reported sex differences in COVID-19 sequelae and Long COVID Syndrome (LCS). Women were significantly more likely than men to develop LCS. Of 4,000 publications identified by the researchers, only 23 reported sex disaggregated data in sequelae, and only 12 did so for LCS.

Researching COVID to Enhance Recovery (RECOVER). NIH's RECOVER initiative will examine sex differences in both acute infections and LCS via clinical cohort studies. Pregnant women comprise one acute infection cohort and one post-infection cohort. Data collection for these cohorts will include pregnancy and pregnancy-related outcomes, e.g., COVID effects on menstruation, menopause symptoms, fertility, and sexual function.

COVID-19 Portfolio Analysis. The COVID-19 Working Group of the Coordinating Committee on Research on Women's Health (CCRWH) conducted a portfolio analysis of NIH grants made between March 2020-June 2022 using research, condition, and disease categorization keywords related to disorders and conditions that preferentially affect women. The analysis included 523 grants supported by 21 ICOs. Outcomes included publication of "Guiding Principles: Sex and Gender Influences in COVID-19 and the Health of Women" ([available on the ORWH website](#)); issuance of an RFI related to the intersection of the pandemic and health of women; and contributions to "Sex/Gender-Specific COVID-19 Outcomes and Management Relevant for Heart, Lung, Blood, and Sleep Disorders: From Bench to Bedside," a workshop sponsored by the National Heart, Lung, and Blood Institute (NHLBI).

Diverse Voices. COVID-19 and the health of women were addressed in the July 2022 webinar in ORWH's new quarterly lecture series called "Diverse Voices: Intersectionality and the Health of Women."

Community Partnership to Advance Science for Society (ComPASS). A new, innovative initiative funded by NIH's Common Fund, ComPASS aims to catalyze, deploy, and evaluate community-led health equity structural interventions that employ multi-sector partnerships to reduce disparities, and to develop health equity research models for community-led, multisectoral structural intervention research across NIH and other federal agencies. What makes the program particularly innovative is that it will fund community organizations directly to develop multi-sector partnerships among community organizations, researchers, and other sectors. Two funding opportunities have been announced to kick off the initiative: "ComPASS Program: Community-Led, Health Equity Structural Interventions Initiative" (OTA-

22-007; Letter of Intent Due: Nov. 18, 2022) and “Community Partnerships to Advance Science for Society: Coordination Center” (RFA-RM-23-001; Application Due: Jan. 27, 2023).

Scientific Collaborations. Dr. Clayton reported on numerous new developments in the areas of policy and scientific collaboration:

Research Performance Progress Report (PRRP). The “NIH and Other PHS Agency PRRP Instructional Guide” was updated on May 13, 2022, to include project outcome instructions specifying that valid analyses for sex and gender and race and ethnicity for Phase III clinical trials must be reported.

Improving Representation in Clinical Trials. In 2022, the National Academies of Sciences, Engineering, and Medicine (NASEM) published *Improving Representation in Clinical Trials: Building Research Equity for Women and Underrepresented Groups* that examined the long-term medical and economic impacts of lack of inclusion of women and underrepresented minority groups in clinical research and subsequent translational work. It concluded that “large swaths of population,” including those who face the greatest health challenges, are not adequately represented in clinical research. Underrepresentation compounds health disparities and compromises the generalizability of research. On May 4, 2022, the report was presented by Dr. Clayton and NASEM Committee Chair Kirsten Bibbins-Domingo, M.D., Ph.D., University of California, San Francisco, to the NIH Inclusion Governance Committee. Recommendations from the consensus study report that are relevant to NIH include establishing an intradepartmental task force on research equity, standardizing submission of demographic characteristics for trials in ClinicalTrials.gov, incorporating considerations of participant representativeness in score-driving criteria in proposal reviews, assessing study progress in meeting enrollment goals of representativeness, developing guidelines to direct Institutional Review Boards (IRBs) on equitable compensation for research participants and caregivers, and investing in funding a community research infrastructure to expand the research capacity of community health centers and safety net hospitals.

Sex as a Biological Variable (SABV). A recent article (September 13, 2022) in *Nature* described the ongoing quest to apply SABV requirements in scientific studies and reports, detailing missed opportunities when sex differences are not disaggregated, e.g., pooled data indicates the risk for cardiovascular diseases increases when systolic blood pressure exceeds 120–129 millimeters of mercury (mmHg), but sex-specific analyses show the risk begins to climb for women when systolic blood pressure tops 110 mmHg.

An example of SABV in action is a new Funding Opportunity Announcement (FOA) from the National Institute on Aging (NIA) to investigate sex differences on molecular determinants of Alzheimer's Disease (AD) risk. “Integrative Research to Understand the Impact of Sex Differences on the Molecular Determinants of AD Risk and Responsiveness to Treatment” (PAR-22-228 | Reissue of RFA-AG-21-029) invites applications that apply a cross-disciplinary and team science approach to gain comprehensive mechanistic understanding of impact of sex differences on molecular trajectories of brain aging relevant to AD. The earliest submission date is November 11, 2022.

Specialized Centers of Research Excellence on Sex Differences (SCORE). The FOA for the SCORE Centers (RFA-OD-22-014 | Reissue of RFA-OD-19-013) was reissued earlier in 2022 with the participation of eight ICs. The next application receipt date is July 15, 2024.

Sex and Gender R01. “The Intersection of Sex and Gender Influences on Health and Disease (R01 Clinical Trial Optional)” (RFA-OD-22-028) has also been reissued with support from ten ICs and the Sex and Gender Minority Research Office (SGMRO). The first application receipt date is December 19, 2022.

Animal Model Research. The Advisory Council to the Director (ACD) Working Group published “Enhancing Rigor, Transparency and Translatability in Animal Research Report” (2021) to advise on how NIH can help researchers increase confidence in the quality and applicability of their research and ensure animal subjects are used with consideration of ethics and harm–benefit analysis. A new study (*Brain*, 2022) based on animal research showed for the first time that neurons in women’s spinal cord process pain differently than men. In contrast to most pain research that uses only male rodents, this study used female and male spinal cord tissue from both rats and humans. It found neuronal growth factor plays a major role in amplifying spinal cord pain signaling in male humans and male rats, but not in female humans or female rats. This research represents a foundational step toward treating pain.

Clinical and Public Health Research. Dr. Clayton shared alarming data showing steeper declines in female life expectancy in the United States over the past two years compared to other high-income countries. The declines were more severe for Black and Hispanic women than for White women. Dr. Clayton cited several studies that document persistent gaps between men and women in the treatment of debilitating chronic conditions, including myocardial infarctions, chronic kidney disease, and stroke.

Galvanizing Health Equity Through Education. ORWH addresses health equity challenges through education, such as its new GENDER 25: Galvanizing Health Equity through Novel and Diverse Educational Resources (RFA-OD-22-015) and its e-learning course Bench to Bedside: Integrating Sex and Gender to Improve Human Health. Other NIH initiatives to address health equity include Pathways to Prevention of poor postpartum health outcomes, an ORWH and IC collaborative effort. “Identifying Risks and Interventions to Optimize Post-Partum Health” is a virtual workshop scheduled for November 29–December 2022, that will address risk indicators for poor postpartum health outcomes at different time points in pregnancy and delivery.

In FY 2022, the President’s Budget included \$30 million for the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) to expand the “Initiative Maternal Health Research Centers of Excellence” (IMPROVE) and to launch Centers of Excellence that support research projects that will incorporate local community needs and perspectives. New initiatives include a Dissemination and Implementation NOSI addressing evidence-based findings with an emphasis on strategies for populations with health disparities; a Community Partnerships Challenge to build research infrastructure that helps address structural barriers for community and advocacy organizations conducting maternal health research; RADx-Tech for Maternal Health Challenge to innovate point-of-care and home-based diagnostics that predict/diagnose risk of severe maternal morbidity and maternal mortality (SMM/MM) for postpartum individuals; Connectathon to identify, create, and standardize maternal health-related data elements; and the IMPROVE Community Implementation Program to support community-engaged implementation projects for evidence-based interventions in disproportionately impacted populations and maternity care deserts.

Funding. Dr. Clayton presented an overview of ORWH’s budget history, noting its total budget increased from \$45.46 million in FY 2020 to \$51.48 million in FY 2021, a difference of \$6.02 million. ORWH’s FY 2021 extramural budget was allocated to SCORE (31 percent); Building Interdisciplinary Research Careers in Women’s Health (BIRWCH) (24.1 percent), IC co-funds (20.3 percent), career programs (7.5 percent), Understudied, Underrepresented, and Underreported (U3) Administrative Supplements (7.5 percent), Sex and Gender R01 (5.2 percent), and Sex and Gender Administrative Supplements (4.5 percent).

Careers. Dr. Clayton reported on new developments supporting women researchers:

Anti-Harassment Enforcement and Reporting. NIH has expanded anti-harassment enforcement and reporting requirements. NIH now has the authority, under Section 239 of the Consolidated

Appropriations Act for FY 2022, to require institutions to report personnel changes (on a grant) related to harassment.

Sexual Harassment. A 2022 NASEM report titled *Exploring Sanctions and Early Interventions for Faculty Sexual Harassment in Higher Education* reported that 38 percent of women graduate students experience sexual harassment from faculty/staff. The report called for research on coordination, transparency, and consistency in sanctioning and early intervention to hold faculty accountable and to support those harmed. ORWH has funded two R01 awards on sexual harassment research in response to “Research on Interventions that Promote the Careers of Individuals in the Biomedical Research Enterprise” (PAR-21-269). Awards were made to Stanford University (\$404,000 for 5 years fully funded by ORWH) and to Indiana/Purdue (ORWH funded 10% total cost [\$43,000] for 5 years).

Women’s Health Research Events. ORWH, in partnership with nine ICs and the Office of Behavioral and Social Science Research (OBSSR), will present the first-ever workshop on “Gender and Health: Impacts of Structural Sexism, Gender Norms, Relational Power Dynamics, and Gender Inequities” on October 26, 2022. The workshop will review conceptual frameworks, examine measurement and methods, identify points of intervention to mitigate health disparities, highlight interventions, and identify opportunities to advance research and foster collaboration, within the gender inequities domain.

The SCORE annual meeting will be held on November 1, 2022, and the BIRCWH annual meeting on November 2, 2022.

ORWH shares research to improve women’s health its e-newsletter, The Pulse; the quarterly publication, Women’s Health in Focus; its e-learning courses, and its website and social media.

Accelerating Medicine Partnership® Autoimmune and Immune-Mediated Diseases (AMP® AIM Program)

Dr. Clayton introduced Lindsey A. Criswell, M.D., M.P.H., D.Sc., Director, National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS). The Accelerating Medicine Partnership (AMP) is a public-private partnership launched in 2014. It consists of nine programs supported by 15 ICOs (including ORWH), 28 industry partners, and 29 nonprofits. Clinical topics addressed include Alzheimer’s Disease, Type 2 diabetes, rheumatoid arthritis (RA), Systemic Lupus Erythematosus (SLE), Parkinson’s Disease, schizophrenia, gene therapy for rare diseases, and heart failure. The projects focus on the precompetitive research phase, including disease mechanisms, biomarkers, and intervention targets.

RA and SLE were the initial diseases addressed by AMP. The initiative focused first on disease “deconstruction” by identifying cells of interest; identifying and tracking markers using single-cell analytics and cross-validate expression in subsets; identifying intracellular pathways, cell subset and state, ligand/receptor expression, and clinical correlations; and identifying cell populations and effector pathways, including biomarkers, targets for therapy, and molecular classifications of the diseases. This process represented a transformative approach to precision medicine, including an infrastructure for target tissue research biopsies, disaggregation of standard operating procedures, rapidly evolving single cell technologies, and new bioinformatics strategies that are widely used today. A significant legacy of this work is the rich data set it generated that is now available to the broader research community.

AMP AIM builds on the key outcomes of this RA and SLE work by indexing and mapping cells and pathways in SLE, Sjögren’s Disease, RA, and Psoriatic Spectrum Disorder, and studying how these

pathways and cells interact through new analytics in different diseases to identify specific and shared mechanisms. Both Sjögren's Disease and Psoriatic Spectrum Disorder disproportionately affect women.

Team Science Leadership Scholars Program (LSP). NIAMS and ORWH announced in September 2022 that they are partnering to launch a pilot program to support and train mid-career research scholars by helping them acquire and hone team science leadership and mentoring skills. LSP is being funded by ORWH and will be embedded within AMP AIM. The program reflects the partners' joint interest in women's health and women's career development. A national search for four to five Scholars will be launched shortly. These Scholars will be selected for two to three-year terms with responsibilities to lead projects that are synergistic with AMP AIM goals; gain training and experience in leadership and mentoring; and interact with senior and junior investigators within the Network and with scientists and leaders from industry and non-profit organizations represented on the AMP AIM steering committee.

Discussion. The following key points were discussed following Dr. Criswell's presentation:

- Sjögren's Disease can be a painful and disabling condition. Because it is multifactorial, diagnosis is challenging. Research on Sjögren's has fallen behind that of other autoimmune diseases.
- Partnerships play an important role in advancing research, but they can be challenging to implement. As a public-private partnership, AMP has played a critical role in linking industry partners to the ICs and other organizations. Increasingly, it has become evident that including the patient perspective in research partnerships is critical.
- Diseases and conditions that impact women's health are fundamental to NIAMS' work, e.g., there are sex and gender differences in osteoarthritis that have been understudied. The new partnership with ORWH is critical to the Institute's success. Training for women's health leadership role in team science, for example, is an important element not addressed elsewhere.
- Learning how to educate policymakers and the public about evidence-based science is extremely important, but not taught in most institutions. To educate scientists to accomplish it successfully requires mentoring teams and mentoring environments. There is an opportunity for greater collaboration between NIH and academic organizations to encourage more training/fellowships on health policy/science communication.

How Climate Change Impacts Women and Their Health

Dr. Clayton introduced Roy Woychik, Ph.D., Director of the National Institute of Environmental Health Sciences (NIEHS), who described the broad spectrum of work undertaken by NIEHS as well as work being conducted across NIH and other HHS agencies on how climate change affects women's health.

NIEHS. The mission of NIEHS is to discover how the environment affects people in order to promote healthier lives. In carrying out its mission, NIEHS emphasizes innovation and prevention of adverse health effects. NIEHS' strategic plan is built around three themes: 1) advancing environmental health science across lifespans; 2) promoting translation, i.e., moving data to knowledge to action by policymakers, and the public; and 3) enhancing environmental health science through stewardship and support.

The enormity of NIEHS' challenge in achieving its mission may be found in the huge variety of environmental exposures that need to be considered, e.g., green spaces; the microbiome; infectious agents; air, water, and soil; agricultural chemicals and pesticides; synthetic materials; disasters and wildfires; lifestyle factors such as diet, exercise, and stress; as well as personal care products. An important theme running throughout NIEHS' work is health disparities and structural racism.

There is inter-individual genomic and biological heterogeneity and therefore people respond to their environments in different ways. This fundamental understanding leads to an emerging new concept, precision environmental health, that incorporates consideration of genetics and epigenetics to explain why people have different responses to specific environmental exposure that make some people sick. This understanding of how environmental signals activate genes includes why women respond differently than men to the same exposure.

An important idea to help explain the impact of the environment on health is the exposome concept, first introduced in 2005, which considers the totality of environmental exposures over the life course. However, the scientific community is lacking guidance on how to conduct an exposomic experiment. Therefore, NIEHS supported five workshops last summer to consider how to operationalize the exposome in order to collect, share, and harmonize exposomic data and make it translatable. An operational model may be completed within the next few months.

Women's Health. Women's health is an essential part of the NIEHS research agenda. Women are especially susceptible to environmental exposures during specific periods over the life course. Pregnancy represents a particularly sensitive window of susceptibility, as there are physiological changes to every major organ system that increase susceptibility to environmental exposures. Thus, environmental scientists study hypertensive disorders during pregnancy, such as gestational hypertension, preeclampsia/eclampsia, chronic hypertension, all leading causes of maternal morbidity and mortality. NIEHS scientists have discovered that air pollution from traffic emissions is a hazard for hypertension in women; NIEHS grantees have discovered that exposure to cadmium and other heavy metals contribute to preeclampsia. Pregnancy is also a period when the fetus is particularly susceptible to environmental exposures. NIEHS-supported studies have demonstrated that environmental exposures during pregnancy can contribute to adverse health effects in offspring much later in life.

Childhood and early puberty are other important windows of susceptibility as the body is still growing and hormonal systems are active. Work being conducted in Dr. Woychik's laboratory have demonstrated how exposure during early development can influence how genes are expressed much later in life. Investigators treated pregnant mice with a chemical pesticide that is known to affect specific parts of the electron transfer chain with a dose that had no adverse effects on the mother. However, this exposure had remarkable effects on the epigenome of the offspring, affecting hundreds of gene loci, that were observed at weaning, 6-, 12-, and 18-months of age. Thus, environmental exposures have the capacity to alter gene activity negatively, both during development and much later in life.

Health Disparities. Through its environmental justice initiative, NIEHS addresses health disparities resulting from environmental exposures. Minority racial and ethnic populations live in different physical and social environments compared to the majority White population. Racial differences in chemical exposures lead to different health outcomes across the lifespan. In April 2022, NIEHS conducted a workshop on "Environmental Impacts on Women's Health Disparities and Reproductive Health." Workshop participants recommended that NIEHS develop equal access to tools and opportunities to improve health equity, shift to a translational and environmental epidemiological health research framework, and develop trans-disciplinary, community-driven, and comprehensive research programs that lead to action and to informed policy.

NIEHS has also implemented Women's Health Awareness workshops to empower women to take charge of their own health, especially in communities of color. NIEHS oversees the Women's Health Awareness Community Resiliency, Environmental Action, and Collaborations for Health (REACH) Equity in North

Carolina, co-funded by ORWH, to identify predisposing factors and COVID-19-related factors that contribute to adverse health outcomes within the Women's Health Awareness population in order to develop effective interventions.

Climate Change Effects on Women. The health effects of climate change are wide-ranging and include impacts on cardiovascular, mental, and respiratory health, among others. While many of these effects are direct (e.g., rising global temperatures resulting in heat-related conditions), others are indirect. These indirect effects include changes such as chemical releases into the environment; changes in air, water, and food quality and quantity; population displacement; and disruptions to the healthcare system. Underserved populations already experiencing health disparities are disproportionately impacted by climate change, as are exposed workers (e.g., farmers using pesticides), disabled persons, and those living in low-to-middle-income countries. Vulnerability to climate change also varies by life stage and the presence of chronic conditions.

Climate change also affects women differently. For example:

- Women experience greater deposition of particles from air pollution in their lungs, resulting in a greater likelihood of respiratory illness. Chronic exposure to air pollution during pregnancy has been shown to lead to miscarriage and stillbirth.
- Changes in ambient temperature have been shown to contribute to increased cardiovascular risk for women during labor; non-Hispanic Black women were particularly susceptible.
- Hotter temperatures may be a novel risk factor for lower fetal growth. A study of nearly 30 million births in the U.S. between 1989 and 2002 revealed that higher ambient temperatures across pregnancy, particularly in the second and third trimesters, were associated with higher risk of term small for gestational age (SGA) and lower birth weight.
- Higher temperatures have also been linked to reduced ovarian reserve measured by antral follicle count (AFC), suggesting that the steady increase in ambient temperature due to climate change may result in accelerated reproductive aging in women.

Examples of indirect climate change on women include:

- A study of the impact of Hurricane Harvey on pregnant women revealed that women delivering after the storm suffered 27 percent higher maternal morbidity and 50 percent higher neonatal morbidity than did women who delivered before the storm.
- Breast cancer patients living through Hurricane Katrina had a 15 percent higher mortality rate than patients who did not experience the storm, most likely due to disruptions in healthcare delivery caused by the storm.

In 2021, President Joseph Biden signed Executive Order 14008, "Tackling the Climate Crisis at Home and Abroad," and charged NIH with leading the effort to address the health effects of climate change. An NIH Executive Committee on Climate Change and Health (CCH), consisting of the directors of seven ICs and the Fogarty International Center (FIC), has re-energized a long-standing NIH Working Group with over 100 members from all of the ICs. Among the Working Group's activity is development of an NIH-wide strategic framework on climate change and health. The centerpiece of the framework is transdisciplinary transformational research, supported by four core elements: health effects research, health equity, intervention science, and training and capacity-building. Examples of research questions that might be addressed include the identification of new and emerging health risks, who is most at risk, and how communities can best adapt to a changing climate. Four FOAs have been funded with FY 2022 funds from the seven NIH Initiative partner ICs. There is a complementary intramural program in progress as well.

The new 2022-2023 NIH Climate and Health Scholars Program is designed to bring climate and health scientists from outside the federal government to work with NIH staff to share knowledge and build capacity in the scientific domains outlined in the strategic framework. Applications are due on September 15, 2022.

In addition to an NIH Climate Change and Health Initiative webpage and a public seminar series on the topic, NIEHS supports a searchable data of literature on climate change and health on its website.

Discussion. Key discussion topics following Dr. Woychik's presentation included:

- In response to a question about maternal smoking as a risk factor for adverse effects of other environmental exposures and climate change on pregnancy outcomes, NIEHS shared information about a review of global studies conducted by its intramural Pregnancy and Childhood Epigenetics (PACE) consortium that indicated direct changes in offspring methylation that could lead to altered phenotypes.
- Climate change may impact immunity to infections. For example, some studies have suggested that exposure to harmful PFAS chemicals following a weather event can suppress the immune system and a person's ability to respond to vaccination. However, it's a multifaceted issue involving genes, environmental effects, and increases in infectious agents working together synergistically. More researchers need to be engaged in studying climate change from a systems perspective.
- To build community resilience in the face of climate change, more and better health messaging guidance about environmental health risks for the public and for providers is needed.
- Training healthcare providers on environmental health issues is a priority for NIEHS. Most medical schools now include environmental health in their curricula. The Institute has launched a pediatric and reproductive health fellows training program, works closely with professional societies to promote the importance of environmental health to their members, and funds traditional training grants, including for practitioners.
- Both NIEHS and ORWH look forward to greater collaboration on environmental health research.

Open Discussion

Key topics in the open discussion included:

- NIEHS is or has been a participating IC in the BIRCWH, U3, and R01 Sex and Gender opportunities and will participate in the new SCORE RFA. ACRWH members encouraged greater collaboration with NIEHS.
- The integration of the microbiome and women's health is an important emerging area but remains relatively unexplored. ORWH has provided valuable support on this topic through its partnerships with ICs. For example, NIAID, which has a microbiome research program, has provided robust support to both issuances of ORWH's R01 and has co-funded several R01 applications with ORWH. More complex models to utilize varied types of data are needed for such studies.
- Potential priority topics for ORWH include the intersection of precision medicine and women's health. Previous discussions of embedding sex and gender into precision medicine have evolved into the All of Us (AoU) program which Dr. Clayton advises. Similarly, NIEHS is working with AoU leadership to include precision environmental health that would impact women's health into the AoU framework. ORWH also works in the precision medicine space by investing in educational materials and resources in interprofessional education and expanding its relationship with the National Institute of General Medical Sciences (NIGMS).

- The integration of women's health across ICs and the broad recognition of the complexities of women's health issues are exciting and should continue to be promoted as the ORWH perspective. The next biennial report will highlight the broad array of IC activities in this domain.
- ORWH should continue to support women's health awareness as women are the gatekeepers of family and community health, as well as support meaningful engagement with communities.

Panel: Epidemiological Contribution to Understanding the Environmental Impact on Women's Health

Dr. Noursi introduced Regine Douthard, M.D., Senior Medical Officer, ORWH, who moderated the panel discussion. Dr. Douthard introduced Kristen Upson, Ph.D., M.P.H., Assistant Professor of Epidemiology and Biostatistics, Michigan State University, who served as Panel Chair.

Women's Risk of Endometriosis (WREN) Study. Endometriosis refers to the presence of lesions in different genital areas. Its symptoms include chronic and acyclic pelvic pain, painful menstruation, painful urination and bowel movements, fatigue, and pain during intercourse. It is not clear why some people develop endometriosis and others do not. No single theory has been able to explain all manifestations of the condition. The most widely accepted theory of its pathogenesis posits that the lining of the uterus shed with each menses is refluxed into the peritoneal cavity leading to the implantation of endometrial tissue and endometriosis. Other theories propose that endometriosis may result from local tissue that undergoes changes or metaplasia; alternatively, tissue misplaced outside the uterus during intrauterine development develops into endometriosis. Different types of endometrioses may arise from different processes and mechanisms. However, it's generally agreed that estrogen plays a key role in regulating pathological developmental processes. Exposure to endocrine-disrupting chemicals (EDCs), i.e., those that interfere with any aspect of hormone action in the body, may also have an impact. EDCs can be found in pesticides, metals, etc., but also in everyday products, including food, beverages, personal care products and a range of consumer products.

Endometriosis can be challenging to study because it can only be diagnosed by surgical visualization. Therefore, there are no epidemiological studies of the disease, but only case control studies. Most studies of endometriosis have identified cases among those undergoing surgery who are then compared to other surgical cases who are not diagnosed with endometriosis. The problem with this approach is that the comparison group already have an indication for surgery, such as menstrual problems or fibroids, that may also be affected by endocrine-disrupting chemicals. Thus, these patients may not represent the frequency of chemical exposure in the underlying population that gave rise to cases, obscuring the interaction between environmental chemicals and endometriosis in epidemiological studies.

The Women's Risk of Endometriosis (WREN) study ameliorated this methodological drawback. Led by Victoria Holt, Ph.D., Fred Hutchison Cancer Research Center, and Delia Scholes, Ph.D., Group Health Cooperative, and funded by NICHD, this population-based case control study used a sample drawn from members of Group Health Cooperative, now part of Kaiser Permanente. In WREN, the study population was identified first: premenopausal participants aged 18-49 with an intact uterus, at least one ovary, and no prior history of endometriosis who were enrolled in the plan for at least six months prior to their first visit for symptoms suggesting endometriosis between 1996-2001. From the study base, an age-matched comparison group was then randomly selected.

Sample Characteristics and Methods. WREN had 310 endometriosis and 727 population-based controls. The median age of both cases and controls was 39 years old. The sample was mostly white (83-85

percent). Almost half the cases (46 percent) and 41 percent of the controls had graduated from college. Overall, the socio-economic characteristics of the WREN population was similar to both the clinic and surrounding populations. Female study staff conducted an in-person structured interview at each participant's home or at Fred Hutchinson Cancer Center. The questions covered a range of health histories (e.g., menstruation, reproductive, pregnancy, contraception) and various methods were employed to aid recall.

Key Findings. Many of the chemicals detected in the endometriosis cases were found in all participants, suggesting chronic exposure. However, a few findings stood out: The risk of endometriosis doubled as a result of exposure to organochlorine pesticides; increased by 30 percent from exposure to PCBs (e.g., from animal and dairy product consumption); tripled as a result of exposure to BPA; and decreased by 70 percent from exposure to phthalate metabolites. Soy formula infant feeding doubled the risk for endometriosis, as did in-utero diethylstilbestrol (DES) exposure. A 50 percent increase in risk for endometriosis was observed for night shift work, which disrupts circadian rhythm.

Study Strengths and Limitations. Strengths of the study include its population-based sampling; collection of biologic samples; years of biologic sample collection (before EDCs became widely known); and data on ovarian and non-ovarian pelvic endometriotic lesion locations. Limitations include biologic sample collection after case diagnosis; single sample for non-persistent chemicals (BPA, phthalates); research having been conducted before recent developments in mixtures analyses; and the presence of undiagnosed disease among controls.

Recommendations. In a comprehensive review of EDCs and endometriosis, Dr. Upson found discrepant results with no consensus on findings given inconsistencies in definitions and methodological approaches. In the past decade, there has been a rise in studies using innovative, population-based approaches that have yielded some more consistent findings. To move the field forward, Dr. Upson recommend population-based sampling, measuring exposure during etiologically relevant windows (e.g., birth, pregnancy), disaggregating endometriosis, considering environmental exposures unique to menstruators (e.g., menstrual product use), and using team science approaches.

Discussion: A brief discussion of the value of population-based studies of endometriosis in establishing consistent findings followed Dr. Upson's presentation. She emphasized the need for repeated measures over time to characterize exposure to environmental chemicals.

Study of Environment, Lifestyle, and Fibroids (SELF). Dr. Upson introduced Quaker E. Harmon, M.D., Ph.D., Staff Scientist, Women's Health Group, NIEHS, who described the SELF study, a longitudinal cohort study in Detroit with mostly Black women, the population at highest risk of fibroids.

Uterine leiomyoma, i.e., fibroids, are non-cancerous smooth tumors of the uterus. Symptoms may include heavy menstrual bleeding; pain (during menstrual period, pelvic, back, during sex); abdominal bloating /pressure; bladder and bowel symptoms; fatigue; and difficulty getting pregnant or pregnancy complications. Treatment options include medications or other interventions; however, fibroids often return following treatment. Fibroids can be cured by hysterectomies and are the most likely reason for a woman to have this surgery. Almost 50 percent of premenopausal women have a fibroid they don't know about. Black women, however, experience earlier onset and higher prevalence of fibroids.

Research into risk factors for fibroids has been slow. Many risk factors, including age, race/ethnicity, and early onset of menarche, are non-modifiable. Modifiable risk factors include physical activity, dietary

exposures, smoking, and the use of DMPA (brand name Depo-Provera®), an injectable, progestin-only contraceptive, that has been shown to be a protective factor. There have been animal and human tissue studies to learn about fibroids, but clinical case control studies have been hampered by methodological issues, such as misclassification of cases and controls and misclassification of exposure. Existing human studies have failed to identify the early development of fibroids. Until researchers understand the natural history of the disease, it can be hard to identify important exposures.

Sample and Methods. The SELF Study enrolled 1,693 Black or African American women between 23-35 years of age in the Detroit, MI area, who had no clinical diagnosis of fibroids. Their mean age was 29. The majority (78 percent) had some college education, 60 percent were employed, 45 percent had a household income below \$20,000, and 60 percent had given birth. Environmental exposures examined in the SELF study included DMPA, soy milk infant feeding, and the natural history and impact of birth. During four research visits scheduled 18-20 months apart, ultrasound examinations to detect new fibroids, questionnaire, clinical measurements to track fibroid growth, and biospecimens were collected from the research participants. Response rates per visit varied from 86 percent to 91 percent.

This study design allowed for exposures to be measured before new fibroids developed. Understanding the natural history of a condition is fundamental because it helps identify population burden, when and who to screen, and knowing when to treat. It also allowed researchers to find exposures which slow the growth of small fibroids, which is important to understand how to reduce or delay symptoms and the need for invasive treatments. Finally, identifying exposures which increase the risk of new fibroids or increase the growth of small fibroids informs identification of opportunities to avoid or reduce exposure and how to prioritize screening.

Key Findings. The study reported:

- The incidence of fibroids increases with age, while fibroid growth rates decreased with age.
- Exposure to DMPA within the past two years was associated with a 40 percent reduction in fibroid incidence and 45 percent reduced fibroid growth.
- Women who were fed soy-based formula beginning within two months of birth and used for more than four months had a 48 percent increased risk of fibroids. (Soy-based formula has high levels of phytoestrogens and has been linked to reproductive conditions, including early/late menarche, menstrual irregularities, and endometriosis).
- Women who gave birth were less likely to have fibroids. Giving birth within the previous five years reduced fibroid growth by 30 percent; the effect was strongest among women who breastfeed for six or more months.

SELF is investigating other exposures including personal care products, sleep quality, early life adversity, and measured metals/endocrine disrupting compounds on a wide variety of outcomes, including menstrual cycle characteristics, birth outcomes, infertility, and COVID experiences, among others.

SELF's highly engaged cohort and collaborative science provides a model for similar studies. Its findings need to be replicated in other populations with high-quality study designs. Research on life-course diseases like fibroids requires a long-term investment.

Discussion. In response to questions from ACRWH members, Dr. Harmon noted that there are no parallel studies elsewhere that she's aware of, noting that it is difficult to get natural history studies funded extramurally. There could be an opportunity to conduct future sub-studies of fibroids within the

AoU program, but the condition is difficult to study well using electronic health records which is a primary data source for AoU.

The NIEHS Sister Study. Dr. Upson introduced Dale Sandler, Ph.D., Senior Investigator, Chronic Disease Epidemiology Group, NIEHS, who reported on the Sister Study that looks at environmental exposures among women who have a sister with breast cancer. Breast cancer remains the leading type of incident cancer, accounting for 30 percent of all incident cancers in women. Incidence is higher among White women; mortality is higher among Black women. In 2012-2013, commissioned reports called for more environmental research into breast cancer that was multi-disciplinary, considered genomics and gene x environment interactions, and adopted a life-course approach. Previous research had focused on lifestyle, hormones, and reproduction, rather than environment. The Sister study had just completed enrollment and was therefore positioned to meet this need. Growing concern about the health impacts of climate change added new urgency to the issue.

Study Design. The goal of the study was to enroll 50,000 volunteer women with a sister with breast cancer to address concerns about environmental exposures. Sisters have a two-fold risk and higher prevalence of relevant genes or exposures, providing increased power to detect associations. Further, sisters are highly motivated to participate, and response rates are high. The study utilized a prospective design that addressed limitations of prior case-control studies, provided an opportunity to study survival as well as a range of health outcomes.

Sample and Methods. The study enrolled 50,884 women between 35-74 years of age representing each of the 50 states and Puerto Rico. Despite targeted outreach and restricted enrollment, the final sample is less diverse than the U.S. as a whole: 83 percent self-reported non-Hispanic White ethnicity, 51 percent completed college, average household income exceeded the U.S. average by \$20,000 per year, and 37 percent reported themselves in excellent health, compared to 17 percent for the U.S. as a whole. Data collection began with a home visit followed by annual and triennial questionnaires. Enrollment questionnaires collected data on health and exposures, reproduction, diet, and family history. Follow-up questionnaires addressed reproduction, hormones, health, exposures, stress, and quality of life. A second home visit was scheduled for those women in the study who developed breast cancer. The study collected tissue samples and validated medical records for certain cancer. Between 2003-2020, 4,427 cases of incident breast cancer were diagnosed among the research participants. This is approximately twice as many as would be expected from the general population. In addition, study investigators collected environmental data from other sources, including biological samples, household dust from home visits, and Geographic Information System (GIS) data. More recently, metalomics and exposomic, as well epigenetics (e.g., methylation exposure signatures, such as smoking) have been added to the study methods.

Some Key Findings. The SISTER study has encompassed a wide-ranging set of topics, including chronic diseases and other cancers. Since 2009, the study has generated 270 papers and 17 extramural grants. Examples of key findings include:

- Breast cancer is associated with living on/near a road with heavy traffic, generating air pollution.
- Increased physical activity between ages 5-19 decreases the risk of breast cancer.
- Exposure to secondhand smoke during childhood and in utero increases the risk of breast cancer.
- High early life trauma is associated with decreased breast cancer risk, but sexual trauma may be associated with increased risk.

- Frequent use of hair straighteners in adolescence is associated with a two-fold higher risk of premenopausal breast cancer, whereas frequent use of hair straighteners in the year before enrollment was associated with 50 percent increase in postmenopausal risk.
- Adult use of permanent hair dye associated with 9 percent higher overall breast cancer risk and a 45 percent higher for Black women.
- Following a healthy dietary pattern is associated with lower breast cancer risk.
- Self-reported exposure to any indoor light, especially sleeping with light or TV on, is associated with increased obesity at enrollment (BMI, waist circumference, other). Sleeping with the light or TV on was also linked to hypertension and increased risk of breast cancer.
- Green space reduces the odds of depressive symptoms in historically redlined neighborhoods.

Final Thoughts. Prospective cohort studies can be valuable for studying the environment and health outcomes; however, more diverse cohorts are needed. New technologies have expanded options for exposure assessment, but questionnaires are sometimes the best/only way to capture personal or historical/early life exposures. Where possible, questionnaires should be validated with GIS, monitoring or biomarker/'omics data. The impacts of multiple exposures, chemical mixtures, and the external and internal exposome should be studied, as well as the social and community environment.

State of the Science. Dr. Harmon briefly reviewed the three conditions addressed in the panel presentation. She noted that breast cancer has been widely researched, whereas endometriosis and fibroids have not been. There are ongoing public awareness campaigns for breast cancer (pink ribbon) and fibroid (white dress), but no coordinated efforts to inform the public about endometriosis. She reviewed the following recommendations from the panel:

1. Focus funding on non-fatal conditions that substantially affect quality of life.
2. Include women in the study of common conditions.
3. Identify factors that contribute to disparate environmental exposures (e.g., personal care products, menstrual blood loss, hormonal contraceptive use, occupational exposures).
4. Promote strong epidemiologic study design for robust results (Limit bias in participant selection, case definition and exposure assessment).
5. There is an urgent need to understand basic epidemiology (age of onset, disease trajectory, disease subtypes, major risk factors).
6. Support development of non-invasive diagnostic tools (currently, definitive diagnosis of endometriosis and adenomyosis requires surgery).
7. Build capacity to investigate exposures over the life-course (novel data linkages, biologic specimen collection, prospective data collection).
8. Incorporate upstream influences on measured exposures (e.g., systemic racism, sexism, environmental racism; neighborhood context).
9. Employ team science (i.e., multidisciplinary teams).

Discussion. Dr. Douthard facilitated a discussion that included the following key points:

- Hormonal contraception is associated with outcomes of endometriosis, fibroids, and breast cancer. Thus, progestin contraception may be an important exposure to measure; the SISTER study is currently examining hormonal intrauterine devices.
- Structural racism has not been sufficiently addressed in studies on environmental health; it should be added to the list of recommendations for future research.

- The barriers to more funding for women's health issues include finding a home within NIH for them and finding the right study section with epidemiology expertise and women's health outcomes.
- There is a need to fund more studies on the impact of heavy menstrual bleeding and pain on daily activities and to create more awareness of this issue among clinicians who tend to dismiss these symptoms.

2024-2028 NIH-Wide Strategic Plan for Research on the Health of Women: Content Area Discussion and Member Vote

Dr. Noursi provided an update on the 2024-2028 NIH-wide *Strategic Plan for Research on the Health of Women* that aims to provide a road map to guide NIH-wide research on the health of women; it will be launched in January 2024. To date, ORWH has engaged all ICOs, many of the federal agencies that have a focus on women's health, as well as private, non-profit groups and individuals (via an RFI), to help to inform development of the Report.

ORWH established an ACRWH Working Group to guide development of the Report. Co-chaired by Dr. Noursi and ACRWH member Alyson McGregor, M.D., the Working Group was charged with addressing the current state of science on the health of women, determining research gaps, and identifying goals and objectives that ORWH needs to prioritize from 2024 – 2028. In addition, the Working Group was to review the implementation of the 2019 – 2023 Trans-NIH Strategic Plan on Research on Women's Health by the ICOs and the evaluations of their implementation.

Kelly Chandler, Ph.D., Health Science Policy Analyst, ORWH, provided an overview of the process model that ORWH created to guide development efforts for the Plan. On June 30, 2022, initial findings from ORWH's data collection efforts were presented to the Strategic Plan Working Group which then developed strategic plan content areas based on all input that had been collected. Once these have been approved by ACRWH, ORWH will recruit members of the CCRWH, ICO subject matter experts, planning and evaluation (P&E) representatives, and NIH Working Group Members to participate in topic specific ThinkTank Groups that will draft strategic goals, objectives and metrics. ORWH will then develop a draft of the Strategic Plan, as well as an accompanying implementation and evaluation guide.

Data sources that informed the development of the proposed content areas included discussion at the working group kick-off meeting, inputs from ICO directors who were asked to identify the most important women's health issues addressed within their scientific missions, 120 comments gathered in response to the RFI published on July 22, 2022, and feedback from ORWH staff.

Ching-yi Shieh, Ph.D., Statistician/Health Science Policy Analyst, ORWH, summarized key findings from the content analysis of data collected. She pointed out that since the FY 2024 – FY 2028 strategic plan aims to provide a road map to guide NIH-wide research on the health of women, it should recommend broader research areas to inform the development of strategic goals, objectives, and evaluation metrics; not target specific diseases or health conditions, as ICOs will address those topics based on their scientific mission; and respect ICOs' decisions in terms of how to define any terminologies and operationalize the study designs. She also noted that the identified content areas may not be mutually exclusive, and that data coding accounted for inter-rater consistency.

The following content areas were identified:

1. Consider how the intersection of social and biological factors affect the health of women.

2. Support the development of data science, innovative research methods and measurements, and cutting-edge technologies for the health of women.
3. Support biomedical workforce training and promote female scientists' career development to advance health of women.
4. Advance basic science and translational research to improve the health of women:
5. Encourage community engagement and promote implementation science for the health of women.

In addition to content areas, ORWH identified cross-cutting topics (comorbidity and multimorbidity, inclusion of women in clinical trials, and prevention care and services) and specific topics (diseases that affect or predominately affect women and girls; maternal morbidity, mortality, and pregnancy; mental health; sexual and reproductive health; substance use and misuse; and lactation and breastfeeding). Dr. Noursi concluded the presentation by articulating the overarching principles that emerged from the content analysis: Encourage cross-ICO partnership and collaboration; prioritize interdisciplinary research; and consider the NIH Diversity, Equity, Inclusion, and Accessibility (DEIA) goals wherever appropriate.

Discussion: The following key points were made in the discussion:

- Research on gender is included in Content Area 1.
- Debilitating chronic conditions in women will be included in the strategic plan; these should be explicitly defined so that they can be more easily studied. These conditions should include not only those that affect women and girls (including menopause), but also those such as cardiovascular disease and osteoporosis that affect women in unique ways.
- Cultural humility or responsiveness are better terms than cultural competence since no one can ever be competent in every culture.
- It is important for the ACRWH to address changes in access to reproductive health care including around abortion which is an evidence-based safe procedure; this is especially true considering high maternal morbidity and mortality rates in the U.S.
- Include career re-entry for women in discussions about supporting women's biomedical careers.
- More studies on pregnancy are needed, especially from a community health care perspective.
- Address the dyad composed of the birthing parent and baby, not just the individual woman. Link this emphasis to the health of the family/community/society (i.e., to the greater good).
- An important theme is the progression from basic to translational to clinical research. However, on page 49 of the document sent to ACRWH members, there is a discussion of research opportunities in cervical cancer, debilitating chronic conditions, and maternal morbidity and mortality. The maternal health recommendation does not include basic and translational research; there are important basic and translational research opportunities in this area that should be included.

Vote: Dr. Noursi called for a vote via electronic poll approving the content areas for the 2024-2028 strategic plan with the incorporation of the comments made by ACRWH members. The poll results showed 17 members in favor of approval.

Concept Clearance: Gender and Measurement

Sarah Temkin, M.D., Associate Director, Clinical Research, ORWH, introduced Elizabeth Barr, Ph.D., Social and Behavioral Scientist Administrator, ORWH, who presented this concept clearance. Dr. Barr explained that sex, a biological variable, and gender, a sociocultural variable, are distinct concepts, but the terms are often used interchangeably, including in biomedical literature and popular culture. This imprecise language can cause ambiguity and confusion among scientists, policymakers, government agencies, and the public.

In 2021, NIH commissioned NASEM to convene a panel of experts to review the existing knowledge base related to sex-, gender identity-, and sexual orientation-related measurement, to make recommendations for specific measures, and to provide guidance for their use. The lead ICO for this initiative was SGMRO; the initiative had 18 other ICO co-funders, including ORWH. Recommendations by the expert panel may be found in *Measuring Sex, Gender Identity, and Sexual Orientation* (NASEM, 2022).

The NASEM panel concluded that accurate definitions and appropriate terminology are essential to rigorous research. For measuring gender identity, it recommended the two-step method of data collection that is widely utilized and collects data about sex assigned at birth and current gender identity. To that end, ORWH is proposing a new concept on Gender and Measurement to support research testing gender terminology (e.g., woman, man, nonbinary) for measuring current gender identity as part of the two-step method of data collection (sex assigned at birth and current gender identity). This concept is responsive to Objective 2.2 in the Trans-NIH Strategic Plan for Women's Health Research: Develop and adapt reliable and valid measures relevant to the health of women. Multiple ICOs, including SGMRO, NIA, NICHD, and OBSSR have expressed interest in supporting the concept.

Discussion: ACRWH members made the following points:

- It's important to use the correct terminology in discussing sex and gender. There is a need to collect data about both without making people fearful.
- The prevailing political climate in some states may prevent researchers in state-funded institutions from conducting research on gender. ORWH provides evidence-based inter-professional education and media outreach to educate clinicians, policymakers, and the public about sex and gender, but recognizes that it is a complex space. This concept should help improve measure of gender to help society address the issue.
- Include de-implementation (i.e., identifying and removing harmful, non-cost-effective, or ineffective practices based on tradition and without adequate scientific support) that may be impacting race, gender, and intersectional identities, in the FOA.

Vote: Dr. Noursi called for a vote to approve the "Gender and Measurement Concept Clearance" ACRWH members approved the motion via an online poll with 14 in favor and 1 opposed.

ORWH E-Learning Courses: Overview and Live Demonstration

Dr. Barr reviewed findings from research published in the *Journal of Women's Health* (2019) that less than 25 percent of medical school lectures raised the topic of sex or gender influences on physiology and disease; only 8.1 percent included an in-depth discussion of sex or gender differences and even these discussions failed to address available data on sex- and gender-specific influences on diagnosis, treatment prognosis, and drug effects. Training is needed on the application of SABV and sex and gender considerations across all aspects of biomedical research and clinical care.

ORWH has sought to close this training gap via the provision of e-learning courses, including Bench to Bedside: Integrating Sex and Gender to Improve Human Health, the SABV Primer, and Introductory Training. As of August 31, 2022, a total of 1,917 individuals have registered for the ORWH Course Dashboard for these online courses. Learners reported affiliations with institutions in 56 countries, and 81 percent of learners are female.

Emily Gericke, Administrative Specialist, ORWH, conducted a live demonstration of the Bench to Bedside course.

Open Discussion

During the open discussion, the following topics were considered:

- Trauma is a cross-cutting theme in the strategic plan for women's health research. One source of trauma is intimate partner violence (IPV) that has not only acute effects but also long-term ones. Exposure to IPV may result in a chronic disabling condition that impacts substance use disorder, depression and other mental health issues, and heart disease in women. It also contributes to maternal morbidity and mortality. IPV should be studied in younger women and transgender populations, among others.
- Members highlighted disadvantages that women experience in U.S. society, in light of the recent Lancet commission on breast cancer and the Dobbs v. Jackson decision. Members posited that their strategies to leverage efforts to combat cancers that are specific to women (e.g., uterine) and others in which the incidence is higher in women (e.g., breast) may be effective in elevating women's rights and societal justice and relationships to health.
- Applying SABV to the study of non-female-specific cancers with a higher prevalence among women is important.
- Considering the huge gaps in knowledge about women's health and limited resources, it is essential to think about the potential end results of each grant application and to evaluate where science is poised to move forward so that funding is allocated to those issues where it can have the greatest impact.
- ORWH should search for opportunities to accelerate the implementation of existing evidence about women's health (e.g., quicker development and deployment of professional training courses) to promote more rapid and widespread clinical implementation of the current knowledge base.
- Translating science works better when researchers engage women and the community as central factors in the discussion.
- Despite the overwhelming needs in women's health research, much more is known about women's health today than when ORWH was founded.
- More research is needed at the biological level to understand the symptoms of menopause and to develop treatments. More research on hormone replacement therapy is also needed.

Closing Statement

Dr. Clayton adjourned the meeting at 4:07 p.m.

Certification

We certify that the contents above are accurate and complete.



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



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

Date 12/15/2022

Date 12/15/2022