

53rd 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
April 14, 2021

Members Present

Wendy Brewster, M.D., Ph.D.
Roger B. Fillingim, Ph.D.
Stacie Geller, Ph.D.
Scott Hultgren, Ph.D.
Reshma Jagsi, M.D., D.Phil.
Sabra Klein, Ph.D.
Ana Langer, M.D.
Louise McCullough, M.D., Ph.D.
Alyson McGregor, M.D.
Amy Paller, M.D.
Judith Regensteiner, Ph.D.
Elena Rios, M.D.
Michelle Robinson, D.M.D.
Yoel Sadovsky, M.D.
Neel Shah, M.D., M.P.P.
Kimberly J. Templeton, M.D.
Susan Wood, Ph.D.

ORWH Leadership Present

Janine Clayton, M.D., FARVO, Director

Samia Noursi, Ph.D., Associate Director for
Science Policy, Planning, and Analysis

NIH and IC Leadership Present

Marie A. Bernard, M.D., Deputy Director,
National Institute on Aging (NIA). Acting Chief
Officer for Scientific Workforce Diversity

Joshua A. Gordon, M.D., Ph.D., Director,
National Institute on Mental Health (NIMH)

Call to Order, Introductions, and Approval of Minutes

Samia Noursi, Ph.D., ACRWH Executive Secretary and ORWH Associate Director, Science Policy, Planning, and Analysis, called the online meeting to order at 9:30 a.m. Dr. Noursi welcomed new ACRWH members Reshma Jagsi, M.D., D.Phil., Yoel Sadovsky, M.D., and Kimberly J. Templeton, M.D. Committee members introduced themselves and approved the minutes of the November 2, 2020 meeting.

The NIH UNITE Initiative to Strengthen Diversity, Equity, and Inclusion

Janine Clayton, M.D., FARVO, NIH Associate Director for Research on Women's Health and ORWH Director, introduced Maria A. Bernard, M.D., Deputy Director, National Institute on Aging (NIA) and Acting Chief Officer for NIH Scientific Workforce Diversity. Dr. Bernard serves as Co-Chair of the UNITE initiative addressing structural racism that launched on February 26, 2021. UNITE reflects principles that emerged from discussions among Institute and Center (IC) Directors, i.e., that NIH must ensure that biomedical research and the administrative system that supports it, is devoid of hostility based on race, sex, and other federally protected characteristics. In this new initiative, NIH is committed to delineating elements that may perpetuate structural racism in biomedical research both within NIH and the extramural community leading to a lack of personnel inclusiveness, equity, and diversity.

At the February 26 launch, five inter-related UNITE workstreams, each supported by a committee of NIH staff members, were identified:

U - Understanding stakeholder experiences through listening and learning: The charge to the U committee is to perform a broad, systematic self-evaluation to delineate elements that perpetuate structural racism and lead to a lack of diversity, equity, and inclusion within the NIH and the external scientific community. This committee is collecting information from ICs on relevant past, current, and planned activities and seeking input on practical and effective ways to improve the racial and ethnic inclusivity and diversity of research-centered environments and workforce via a Request for Information ([NOT-OD-21-066](#)).

N - New research on health disparities/minority health/health equity (HD/MH/HE): The N committee's charge is to address long-standing health disparities and issues related to minority health to advance health equity (HD/MH/HE) in the United States by ensuring NIH-wide transparency, accountability, and sustainability in marshaling resources for HD/MH/HE research. It has launched two FOAs focusing on health disparities/health equity, including one specifically targeting investigators at Minority Serving Institutions (MSIs). Another activity in development is to create an HD/MH/HE Resource Center Dashboard to increase funding transparency by accurately reporting HD/MH/HE research funding.

I - Improving NIH culture and structure for equity, inclusion, and excellence: The charge to the I committee is to change the NIH organizational culture and structure to promote diversity, equity, and inclusion throughout the NIH workforce. Its foundational efforts include providing granular data on the NIH workforce based on position and supervisory status. Next steps include expanding NIH policies to more explicitly acknowledge racial discrimination and establishing a campaign to make NIH staff aware of options for reporting racist actions; expanding recruitment efforts for NIH investigators from underrepresented groups; establishing an anti-racism steering committee; and working with NIH senior leadership to appoint a diversity, equity, and inclusion officer in every IC to track, advance, and coordinate IC-specific diversity, equity, and inclusion efforts.

T - Transparency, communication, and accountability with NIH's internal and external stakeholders: The T committee's charge is to ensure transparency, accountability, and sustainability of all UNITE efforts among NIH internal and external stakeholders. It has launched a webpage on the central NIH portal for anti-racism policies; an external awareness campaign including editorials in scientific journals, mainstream media, and townhall style meetings; and an internal awareness campaign titled "Racism, Discrimination, and Harassment don't work here!" Future plans include diversifying the portraiture around the NIH, and implementing a digital campaign of UNITE: "Together We're Stronger."

E - Extramural research ecosystem - changing policy, culture, and structure to promote workforce diversity gaps: The E committee's charge is to perform a broad systematic evaluation of NIH extramural policies and processes to identify and change practices and structures that perpetuate a lack of inclusivity and diversity within the extramural research ecosystem. This includes developing strategies to address funding disparities and increase applications that would support individuals from underrepresented groups. The E committee will also develop possible programmatic proposals addressing career pathways, institutional culture for academic institutions, NIH processes, and technical assistance and funding for Historically Black Colleges and Universities (HBCUs) and MSIs.

Three FOAs and a Notice of Special Interest (NOSI) have been released to support UNITE's goals: 1) [RFA-RM-21-021](#) - Transformative Research to Address Health Disparities and Advance Health Equity (U01 Clinical Trial Allowed); 2) [RFA-RM-21-022](#) - Transformative Research to Address Health Disparities and Advance Health Equity at Minority Serving Institutions (U01 Clinical Trial Allowed); 3) [RFA-MD-21-004](#) -- Understanding and Addressing the Impact of Structural Racism and Discrimination on Minority Health

and Health Disparities (R01 clinical Trial Optional); and 4) [NOT-GM-21-033](#) - Notice of Special Interest (NOSI): Understanding and Addressing the Impact of Structural Racism and Discrimination on Biomedical Career Progression and the Biomedical Research Enterprise. In addition, the BRAIN Initiative released an FOA in which diversity was part of the scoring criteria.

Discussion: ACRWH members suggested programming to get students on a trajectory for biomedical careers at an early age, perhaps as early as preschool and elementary school; including not only institutions in UNITE's outreach, but also professional networks such as the National Hispanic Medical Association, which provides a research network with mentors; and including sex and gender analyses in UNITE's analysis of the demographics of intramural and extramural employees, as women will have had different experiences than men.

ORWH Director's Report

Dr. Noursi introduced Dr. Clayton, who reported on new developments at ORWH, NIH, and elsewhere related to women's health.

New in Sex and Gender: Dr. Clayton noted there is growing attention to Sex as a Biological Variable (SABV) in both popular and scientific media. She cited several examples, including an interview with ORWH Associate Director for Basic and Translational Research Chyren Hunter, Ph.D., about progress in considering SABV on NPR's "Science Friday." She also shared recent unexpected findings about sex differences in the blood brain barrier discovered by Alisa Morss Clyne, Ph.D., Director of the Vascular Kinetics Laboratory at Drexel University College of Engineering. Dr. Clayton reported that *Nature Neuroscience* (2021) published an article calling for a "global shift in science culture" by incorporating SABV as a key factor in producing impactful, high-profile, rigorous science; by scientists holding each other accountable through manuscript peer review; and by journal editors holding authors to standards that include SABV.

Dr. Clayton reviewed ORWH's e-learning resources to educate the biomedical community about sex and gender. These include the six-module "Bench to Bedside: Integrating Sex & Gender to Improve Health" program; the new "Sex as a Biological Variable Primer;" and the "Introduction to the Scientific Basis of Sex and Gender-Related Differences" with facilitator's guide for beginner audiences.

New in COVID-19 and Women's Health: A new study in the *Journal of General Internal Medicine* (2021) reported that Black women have COVID-19 mortality rates almost 4 times higher than that of White men and 3 times higher than Asian men, despite men being at generally higher risk of dying from COVID-19 than women. She also highlighted research published in *The Lancet* (2021) indicating that 75 percent of COVID "long haulers" (those with symptoms six months post-disease onset) were women, and that female COVID survivors were more likely to experience persistent psychological symptoms, including stress, anxiety, and depression.

The pandemic has disproportionately affected women and parents, according to a 2021 analysis in the *Journal of Women's Health*. Faculty members with children younger than 6 worked significantly fewer hours than other parents. For women, this translates into a significant decrease in the number of article submissions in which women are the first/corresponding author, fewer peer review assignments, and attendance at fewer funding panel meetings.

Both the National Academies of Sciences, Engineering, and Medicine (NASEM) and NIH have studied the impact of COVID-19 on scientists. An NIH-supported study by NASEM, “Impacts of COVID-19 on the Careers of Women in Academic Science, Engineering, and Medicine (STEMM),” found that the pandemic negatively affected the well-being of women in academic STEMM fields in the areas of productivity, work-life boundary control, networking and community building, and mental well-being.” In NIH surveys of extramural researchers, 61 percent of lab-based researchers said the pandemic will negatively affect their career trajectories. Among caretakers, the concerns were greatest among those with children 0-5 years old. Over three-quarters (78 percent) of respondents reported lower productivity. Among extramural administrators, 83 percent cited moderate to major impacts on research productivity. Most have implemented monitoring measures, and 1 in 5 have provided or expanded childcare facilities.

NIH has responded to these COVID-19 career disruptions with no-cost extensions for most awards and funded extensions for F and K awards ([NOT-OD-21-052](#)). Other NIH initiatives address barriers to women’s entry to and advancement in biomedical research, i.e., the NIH Challenge Prize; Advancing Gender Inclusive Excellence (AGIE) Coordinating Center; reissuance of the BIRCSW program; and the NIH Common Fund’s Faculty Institutional Recruitment for Sustainable Transformation. NIH also supports childcare costs for [Ruth L. Kirschstein National Research Service Award \(NRSA\) Individual Fellows](#) and requires that NIH-supported scientific conferences include a diversity plan to achieve appropriate representation.

NIH and ORWH Update: ORWH welcomed over 500 people to its December 2020 virtual symposium celebrating its 30th anniversary. There is new and diverse health and science leadership at both the White House and the Department of Health and Human Services (HHS). There is a new Office of Nutrition Research within the Office of the Director with responsibility to coordinate implementation of the first “Strategic Plan for NIH Nutrition Research,” organized around a unifying vision of precision nutrition research. There are now ten women IC Directors at NIH including Lindsey A. Criswell, M.D., M.P.H., D.Sc., Director, National Institute of Arthritis and Musculoskeletal and Skin Diseases, and Joni L. Rutter, Ph.D., Acting Director, National Center for Advancing Translational Sciences.

ORWH is working to expand sex disaggregation of research data and design of studies that incorporate sex and gender; communicate the impact of sex and gender influences; and highlight and address the impact on women in STEMM. ORWH is participating on these relevant initiatives: “NIH Wide Strategic Plan for COVID-19 Research,” “Guiding Principles: Sex and Gender influences in COVID-19 and the Health of Women” website, “COVID-19 and Maternal Health” webpage, and the “Diverse Voices: COVID-19, Intersectionality, and the Health of Women” meeting on June 24, 2021. ORWH supports FOAs on sex- & gender-related research on COVID-19, as well as expanded FOAs to add COVID-19 to the scope of Sex and Gender Administrative Supplements; Under-studied, Under-represented and Under-reported Women (U3) Administrative Supplements; and the Sex and Gender R01. ORWH also works to improve the representation of women and underrepresented minorities in clinical trials and research through participation in “[CEAL: NIH Community Engagement Alliance Against COVID-19 Disparities](#)” and in the NASEM “[Overcoming Barriers to Diversifying Clinical Trials](#)” workshop on March 29, 2021.

Scientific Collaborations: Dr. Clayton highlighted the work of investigator Jill Goldstein, Ph.D., Harvard Medical School, who directs an ORWH Specialized Centers of Research Excellence on Sex Differences (SCORE) grant titled “Sex Differences in Major Depression: Impact of Prenatal Stress-Immune and Autonomic Dysregulation.” She also noted the work of current and former ACRWH members on a review article titled “Sex and gender: modifiers of health, disease, and medicine” in *The Lancet* (2020).

ORWH has partnered with the National Institute of Mental Health (NIMH) on "[LinkPositively](#): A Technology-Delivered Peer Navigation and Social Networking Intervention to Improve HIV Care Across the Continuum for Black Women Affected by Interpersonal Violence." Dr. Clayton co-authored a blog, "Research is Changing the Face of HIV for Women and Girls," with the Office of AIDS Research Director.

Dr. Clayton co-chairs the NIH Maternal Morbidity and Mortality Task Force that launched "[Implementing a Maternal health and Pregnancy Outcomes Vision for Everyone](#)" (IMPROVE), an NIH-wide program funding interdisciplinary research in foundational biology, behavioral, and sociocultural science about maternal health. The initiative funded 36 projects (\$7.5 million) last year; 17 ICOs are participating. Mental health, cardiovascular disease, and immunity were identified as important research areas for the initiative. For FY21, two NOSIs are available, one for small business initiatives to develop innovative diagnostic tools for improving maternal outcomes and the other for administrative supplements on maternal health, structural racism and discrimination, and COVID-19.

ORWH is partnering with the National Institute on General Medical Sciences (NIGMS) to expand research on women's health in states that have received an [Institutional Development Award \(IDeA\)](#), i.e., those states that traditionally have had low levels of NIH support and where populations have been disproportionately affected. The research must address at least one goal of the "Trans-NIH Strategic Plan for Women's Health Research;" 15 ICOs are participating in this initiative.

FY20 Research Programs Funding: Dr. Clayton reviewed ORWH's budget history over the years, noting that there has been some modest change. ORWH's FY20 extramural research budget was allocated to the SCORE program (35 percent); BIRCWH program (29 percent); other IC co-funds (18 percent); Sex and Gender Administrative Supplements (6 percent); U3 Administrative Supplements (5 percent); Career Continuity Supplements (4 percent); and the Sex and Gender R01 (3 percent).

The 5th Annual Vivian W. Pinn Symposium will be held virtually on May 11-12, 2021. This year's theme is Integrating Sex and Gender into Biomedical Research as a Path for Better Science and Innovation. ORWH continues to publish the quarterly *Women's Health In Focus at NIH* newsletter and the monthly *The Pulse* email.

COVID-19 and Mental Health

Rebecca DelCarmen-Wiggins, Ph.D., ORWH, introduced Joshua A. Gordon, M.D., Ph.D., Director, NIMH. Dr. Gordon addressed COVID-19's impact on mental health, noting that there is little data to date on this topic that has been disaggregated by sex/gender.

Overview: There have been over 30 million cases of COVID-19 and well over half a million deaths. Mental and substance use disorders are the third leading cause of Disability Adjusted Life Years in the United States and the world. Stressful events such as a pandemic can exacerbate existing mental illnesses and increase the rates of those illnesses and stress in the general population.

What has been learned from NIH-funded research on previous disasters/traumatic events: Most people who are exposed to trauma experience initial symptoms such as increased arousal, nightmares, and increased anxiety; for most, symptoms improve with time. A significant minority, however, may have long-term or chronic experiences with mental illness. Social inequities and health disparities increase trauma exposure, as well as subsequent mental health vulnerability and care. There is no single variable that determines individual outcomes. However, risks for poorer outcomes include the nature

and severity of exposure, especially direct exposure to death or injuries, and the type of trauma; individual differences, including a history of trauma or mental illness; ongoing stressors, including occupational and financial strain; substance use/abuse; being female and/or non-White; and the environment, including having few social supports. These negative effects can be mitigated by approaches that support long-term recovery, such as meeting immediate needs (food and housing insecurity); practicing healthy coping strategies; treating new or worsening illness; and finding ways to help others. Disasters may exacerbate disparities in mental health system reach and access.

COVID-19 and mental health: In August 2020, *Morbidity and Mortality Weekly Report (MMWR)* reported that as many as 40 percent of U.S. adults said in late June that they were struggling with mental health or substance use, including 11 percent who had seriously considered suicide. In younger adults, suicidal ideation was closer to 20 percent. Rates of mental health effects, particularly depression and anxiety, have increased as the pandemic has endured. A sizeable proportion of the 40 percent who reported struggling with mental health/substance use issues in the *MMWR* study received help; 10 percent did not.

Research in Cook County, IL, examined whether the pandemic impacted opioid overdose deaths. An increase in such deaths was recorded during the time when the stay-at-home order was in effect, then returned to the pre-2020 rate when the lockdown was lifted. Suicide deaths remained stable or even decreased in the first half of 2020 when the pandemic was in full force.

For vulnerable populations, there were striking disparities in the prevalence and outcomes of mental illness before the pandemic. Vulnerable populations include women, particularly during pregnancy; people with pre-existing mental health and substance use problems, including youth; health disparities populations; and the health care workforce. For women, the biggest issues were perinatal needs and intimate partner violence (IPV).

Individuals with mental illness, particularly those with schizophrenia and depression, were at increased risk of contracting COVID-19. Those individuals with schizophrenia who contracted COVID-19 were at as much as a three-fold increase of dying than those who did not have schizophrenia. Further, the risks of getting sick were not equally distributed. African Americans with schizophrenia were 2.5 times more likely to get the disease than their white peers.

There is also some evidence that children who were confined to home without school were more likely to experience a greater number of tantrums, have more arguments with adults, and engage in spiteful or disobedient behaviors. Establishing or maintaining family routines can reduce such behaviors, as well as reduce depressive and stress symptoms in their mothers.

African Americans are another vulnerable population. There is evidence from Maryland that suicides increased among African Americans in the early days of the pandemic, while they decreased among Whites. This data has been corroborated by data from Massachusetts and Connecticut. Thus, even if there was no increase in deaths from suicide overall, there may have been increases in populations most directly affected by the pandemic. When lockdowns were lifted, suicide rates among African Americans decreased.

Mental distress varies by ethnicity and gender. In one study from the United Kingdom, distress was greater in Black, Asian, and minority ethnic communities than in White communities, and was dramatically higher in April 2020 than in the preceding two years. Black and Hispanic communities in the

United States show more symptoms of stress and worry than do Whites, particularly due to housing and food instability, as well as loss of jobs.

Among health care workers, especially nurses, doctors, and residents on the front lines of caring for COVID patients, there is a reported increase in psychological symptoms.

Responding to the COVID 19 pandemic: One important response to the pandemic has been the expansion of telehealth, which has been shown to be equally effective as in-person care in mental health. One of the lessons learned from the expansion of telehealth is that it can be used effectively in low-income settings.

NIMH is supporting multiple studies to identify the mental health impact of the COVID-19 pandemic, participating in several FOAs on this topic, and has published NOSIs to support administrative supplements for existing grantees.

Discussion: Dr. Clayton asked Dr. Gordon to comment on the disturbing data about the mortality rate of black women exceeding that of White men that she presented in the Director's Report. Dr. Gordon noted that national data on this trend is not yet available; national survey data indicates increased rates of stressors and symptoms for minority populations. ACRWH members' comments addressed the need to disaggregate data on the mental health of health care workers by sex/gender and race/ethnicity since the majority of frontline workers are women and minorities; the challenges of delivering telehealth to those experiencing IPV; and possible mental health issues when the pandemic ends.

Post-Acute COVID Syndrome: Understanding the Persistent Symptoms of COVID and Their Implications for Women's Health

Rajeev Agarwal, Ph.D., ORWH, introduced David Putrino, PT, Ph.D., Director, Rehabilitation Innovation, Mount Sinai Health System, who addressed issues related to long term consequences of COVID-19. Dr. Putrino distinguished between post-acute sequelae of COVID, i.e., persistent symptoms with an explicable medical cause, and post-acute COVID syndrome (PACS), i.e., persistent medically-unexplained physical symptoms. Of note this terminology differs from the Post Acute Sequelae of COVID-19 (PASC) often used by NIH.

In March 2020, at the start of the pandemic, Mt. Sinai was in crisis from the overwhelming number of COVID patients. Yet they also had to deal with those patients who were too sick to be at home but not sick enough to be in the hospital. Mt. Sinai provided technology-based tools to these patients and checked on them daily. By May 2020, staff noticed that 10 percent of these less severe patients were not getting better. Among the first 200 observed cases in this group, patients were more likely to be female than male with a median age of 43 and a body mass index (BMI) of 24, i.e., previously fit and healthy. Common symptoms in this cohort included fatigue, cognitive issues, feelings of weakness, dizziness, heart palpitations, muscle pain and chest pain. Hypocapnia was almost unanimously a symptom, as well as reduced left ventricular heart dimensions (across the group).

To address the health care needs of these patients, Mt. Sinai developed a comprehensive care plan using a multi-disciplinary approach that included breathwork, nutrition, and strengthening conditioning. The approach is novel because the standard rehabilitation regimen would be too intense for these patients. Instead, the providers evaluated symptom attacks and coached patients with ways to avoid specific triggers, such as a hot shower or large meal. The team used a breathwork protocol to

help patients retain carbon dioxide (CO₂) and increase their tolerance for physical reconditioning, which had to begin at a very low intensity level. In the protocol, patients are evaluated initially by a physician, followed by cardiac clearance, referral to breathwork coaching for prehab, referral to additional specialists (e.g., nutritionist) as needed, and finally referral to a physical therapist for autonomic reconditioning.

An initial evaluation comparing 90 patients who underwent this protocol compared to a control group found that those in the physical therapy group improved. Overall disability was reduced, as was pain. The biggest change was a 40 percent reduction in fatigue, compared to the control group where fatigue worsened over time. The “bad news” is that to obtain these changes, 12 weeks of twice-weekly physical therapy is required.

Dr. Putrino concluded by sharing some concerns and key takeaways. One major concern is economic disparities in PACS care, especially for women, minorities, and the disabled. Recovery is a full-time job and those who are juggling work life and family life may not be able to devote the time required for it. Further, insurance generally does not cover the frequency of required physical therapy. There is also a diagnostic concern: Blind reliance on PCR and antibody testing disqualifies some patients because of high false positives in the former and rapid declines in antibody titers and in pro-inflammatory cytokines in the latter. Mt. Sinai instead uses presumptive positive criteria for all patients based on World Health Organization (WHO) guidelines. Key takeaways include the need to manage care in a symptom-centric manner; to learn from the rich literature on conditions similar to PACS; and to respect the patient’s lived experience.

Discussion: ACRWH questions to Dr. Putrino addressed the deployment of Mt. Sinai’s protocols to pregnant women whose symptoms overlap PACS symptom; possible role of the gut/brain relationship in PASC; a request for more information about urinary issues; and a possible relationship between autoantibodies and PASC. Dr. Putrino responded by recommending breathwork for pregnant women with hypocapnia; by noting that nutritionists have not identified any specific microbiome issues; and that urinary issues included some recurrent urinary tract infections, as well as increased frequency and urgency, in about 5 percent of patients, which were successfully treated.

The Committee broke for a virtual group photo and lunch at 12:16 p.m. The meeting resumed at 1 p.m.

NIH Inclusion Update FY19-20

Ching-yi Shieh, Ph.D., ORWH, introduced Dawn Corbett, M.P.H., NIH Inclusion Policy Officer, Office of Extramural Research, who updated ACRWH members on NIH policies regarding inclusion of women, racial and ethnic minorities, and individuals across the lifespan in NIH-funded clinical research; current status of Government Accountability Office (GAO) recommendations related to inclusion of women and minorities; FY2019-FY2020 data on the inclusion of women and minorities in NIH-funded clinical research; and NIH resources related to the inclusion of women, members of racial and ethnic minority groups, and individuals across the lifespan in NIH-funded research.

NIH inclusion policies: Current NIH policy requires that women and minorities be included in all NIH-funded clinical research studies unless there is a compelling rationale for exclusion; that NIH-defined Phase III clinical trials be designed to permit analysis by sex/gender, race and ethnicity and that results of analyses be reported in Clinicaltrials.gov. Applications are further required to include individuals of

all ages in NIH human subjects research unless there are scientific or ethical reasons not to do so; and to submit individual-level data on participant age at enrollment in progress reports.

GAO report: A 2015 GAO report, “Better Oversight Needed to Help Ensure Continued Progress Including Women in Research,” included five recommendations to improve NIH’s implementation of its inclusion policies affecting women. These were: 1. Make IC-level enrollment data readily available through public means. 2. Examine approaches for aggregating more detailed enrollment data at the disease and condition level. 3. Ensure that program officers have a means of recording their monitoring of awardees plans for and progress in conducting analysis of potential sex differences. 4. On a regular basis, systematically collect and analyze summary data regarding awardees’ plans for analysis of potential sex differences. 5. Report on this summary data and analysis in its regular report to Congress on the inclusion of women in research. Each have been accomplished, except the final one which is expected to be completed before the end of the current year.

FY2019-FY2020 data on the inclusion of women and minorities in NIH-funded clinical research: Ms. Corbett provided a detailed summary of FY19-FY20 NIH clinical research inclusion records, reporting on patterns of enrollment by sex/gender, and race and ethnicity in NIH-funded clinical research, including Phase III trials, as recommended in the GAO report. She also referred ACRWH members to the NIH Inclusion Statistics Report where enrollment data by health condition and IC may be found.

Training and resources: Ms. Corbett reviewed online training videos for investigators about how to include diverse populations in NIH studies and how to enter inclusion data in their reports, as well as web-based resources from the Office of Extramural Research (OER) on inclusion and human subjects.

Discussion: ACRWH discussion on NIH inclusion policies began with a focus on resources available to support researchers in attracting more diverse populations to their studies, including OER trainings; resources on the ORWH website, such as the [NIH Inclusion Outreach Toolkit](#); and the CEAL website. Additional discussion addressed the need to engage journal editors and publishers in inclusion conversations. A recommendation was made that NIH should include policy changes that occur due to findings from the research it funds as important outcomes.

Panel: Impact of COVID-19 on Mental Health

Miya Whitaker, Psy.D., ORWH, introduced Panel Moderator John Weisz, Ph.D., ABPP, Professor, Department of Psychology, Harvard University. He introduced each speaker at the beginning of her presentation.

Impacts of COVID-19 on Intimate Partner Violence (IPV) Survivors in the United States

Maya Ragavan, M.D., Assistant Professor of Pediatrics, University of Pittsburgh, addressed supporting IPV survivors during the COVID-19 pandemic. Epidemiological studies have found that IPV increased during the pandemic in the United States; global studies confirm an increase in both its severity and prevalence. However, there has been a gap in knowledge about the experiences, needs, and challenges of IPV survivors, their children, and IPV advocates that have been supporting them during the pandemic. Therefore, Dr. Ragavan and colleagues from Futures without Violence, Children’s Mercy Kansas City, and the American Academy of Pediatrics engaged in a multi-disciplinary study funded by the U.S. Centers for Disease Control and Prevention (CDC) to understand the impact of the COVID-19 pandemic on IPV survivors and their children; to examine how IPV agencies and Child Protective Services have adapted to the COVID-19 pandemic and the impact of the COVID-19 pandemic on front-

line workers at victim services agencies; and to learn about emerging practices happening around the country.

Dr. Ragavan's presentation focused on the experiences of IPV advocates across the nation who participated in 60- minute interviews on Zoom. Findings revealed increased isolation among IPV survivors due to the pandemic, disparities in access to benefits, structural inequities in response to calls for help, and COVID being used as a means to control (e.g., denying access to children). IPV advocates have had to shift strategies, e.g., safety planning changed from helping the survivor exit the situation to finding ways to be safe within the home. Advocates sought ways to balance safety and trauma-informed approaches, and to ensure privacy during virtual visits.

The implications of this study point to continuing to develop cross-sector collaboration to support IPV survivors; including IPV in disaster preparedness and emergency response; and developing technology that allows for safe, confidential, and private communication. There is a need to provide funding and support for IPV agencies serving IPV survivors from marginalized communities, and to prioritize IPV advocates as front-line workers by providing personal protective equipment (PPE) and vaccinations.

Psychotherapies Are Less Effective for Girls Living in Communities with High Sexism

Maggi Price, Ph.D., Assistant Professor, Boston College, shared results from a spatial meta-analysis about the impact of context on treatment efficacy for girls. Dr. Price began by defining structural sexism, i.e., norms, and laws that create and sustain systematic gender inequality in power and resources. Women living in states with high structural sexism are more likely to experience violence (IPV, risk for homicide); physical health problems (chronic health issues, poor physical functioning); and mental health problems (depression, post-traumatic stress disorder [PTSD]).

Dr. Price and her colleagues sought to address the question: Does structural sexism affect psychotherapy efficacy for girls? They employed spatial meta-analysis methodology, i.e., measurement and statistical modeling of community contexts (e.g., prejudicial norms) in relation to intervention efficacy. The first step in the analysis was to measure structural sexism across the U.S. using factor analysis of state-level data of attitudes and norms about women from public datasets. The results categorized states on a 5-point structural sexism scale. This analysis was followed by a meta-analysis of 93 randomized clinical trials with 6,000 youth, mostly girls ages 4-18, across 32 states, i.e., a 2- level random-effects meta-regression. The outcome of interest was effect size; the investigators controlled for median household income.

The main finding of the meta-analysis was that treatment efficacy is significantly lower in states with higher structural sexism, i.e., structural sexism seems to make it harder for girls to benefit from therapy. Thus, psychotherapy studies might consider measuring stigma, as it may mediate treatment efficacy and engagement. Treatment may need to be tailored for stigmatized people (e.g., girls); multi-level interventions that address context are needed.

A Meta-Analysis of Remotely Delivered Youth Psychotherapies

Katherine Venturo-Conerly, Doctoral Student, Clinical Science, Harvard University, reported on a study to investigate the effectiveness of remotely delivered therapy for youth via a literature review to answer two questions: How effective are remote youth psychotherapies overall? What moderates their effectiveness?

Inclusion criteria for the review included randomized clinical trials with study subjects below 18 years-old who were being treated remotely for anxiety, depression, or conduct problems. A total of 43 articles with sufficient information to extract effect sizes at post-treatment were included in the review. The mean age of subjects in these studies was 9.34 years. Just over one-half (51.16 percent) were female and over one-third (37.21 percent) were Caucasian. The mean duration of therapy was 9.4 weeks and involved these modalities: telephone (50.49 percent); computer programs (62.79 percent); email (23.26 percent); pre-recorded videos (44.19 percent); written texts (37.21 percent); and long-form feedback (19.44 percent). Almost six in ten (58.14 percent) included therapeutic provider contact, while 55.81 percent included synchronous (i.e., real-time) provider contact.

The study found that remote therapies work almost as well as in-person therapies immediately following the conclusion of treatment, and even better at later follow-up. Significant moderators of success included therapeutic provider contact, synchronous provider contact, telephone contact, skill building provider contact, and discussing implementation difficulties with providers. Limitations of the study include difficulties disentangling potential confounds among variables; limited number of studies using video chat, instant messaging, and text messaging; and the rapidly evolving nature of technology-based communication.

Using Mixed Methods to Identify the Primary Mental Health Problems and Needs of Children, Adolescents, and Their Caregivers During the Coronavirus Pandemic

Olivia Fitzpatrick, Doctoral Student, Clinical Science, Harvard University, described research to address the question: Are existing interventions equipped to address the mental health needs of families during this time? In the study, investigators collected idiographic data from caregivers of children ages 1-19 to capture what they judged to be the most prominent mental health problems and needs of their families during the COVID crisis. Research participants, primarily female (81 percent) and mostly White (72 percent), were asked to identify one of their children with the greatest emotional and/or behavioral difficulties and answer several questions with this child in mind. Quantitative measures used in the study included the Behavior and Feelings Survey; GAD-7; PHQ-8; current living situation; and effects of COVID. Qualitative measures addressed the top problems and needs.

Caregiver and youth mental health symptoms, on average, fell within the clinical range, highlighting what appears to be heightened mental health difficulties among this general population sample. Quantitative analyses revealed that child and adolescent mental health symptoms were associated with number of children in the home, and both caregiver and child/adolescent symptoms were more pronounced in regions with more lenient COVID restrictions. Through idiographic responses, caregivers reported a substantial need for mental health services among themselves and their children, and a range of mental health problems that may be important pandemic-specific intervention targets.

Q&A: A question was raised about the validity of information collected from an IPV advocate compared to that collected directly from the IPV survivor. Dr. Ragavan said that the IPV advocate interviews provided a good perspective about their clients, noting that it only reflected the experiences of clients who reached out to services; the researchers decided not to interview survivors during the pandemic because of safety concerns that might arise with Zoom interviews at home.

Evaluation and Concept Clearance: ORWH Sex and Gender Administrative Supplement Program

Dr. Noursi introduced Rajeev K. Agarwal, Ph.D., Senior Research Program Officer, ORWH, who presented evaluation findings on ORWH's Sex and Gender Administration Supplement (SAGE) program, as well as a concept clearance for its re-issuance.

Overview: In FY 2013, ORWH initiated a trans-NIH program to catalyze exploratory research on sex/gender differences by providing administrative supplements to ongoing peer-reviewed NIH-funded grants. The objectives of SAGE are 1) To support research highlighting the impact of sex/gender influences in human health and illness, including basic, preclinical, clinical, translational, and behavioral studies, e.g., adding the opposite sex/gender, increasing sample size, or analyzing existing data by sex/gender; and 2) To stimulate investigators to addresses goals outlined in the "NIH Strategic Plan for Women's Health": Goal 1 - Increase sex differences research in basic science studies; Goal 2 - Incorporate findings of sex/gender in the design and development of new technologies, medical devices, and therapeutic drugs; and Goal 3 - Actualize personalized prevention, diagnostics, and therapeutics for girls and women.

Evaluation of SAGE: ORWH adopted a multi-factorial approach to assess the effectiveness of SAGE, including demographic information of the applicants and awardees; bibliometric data of supplement awardees; a survey of the supplement awardees; subsequent grant applications; and a workshop of supported investigators at the Sex As a Biological Variable Workshop on October 26-27, 2017. The analysis revealed that ORWH funded supplements at 22 ICOs between 2013-2018 with a total investment (2013 – 2020) of \$38.87 million. The evaluation found that SAGE supplements supported researchers to add the opposite sex/gender to their research, increase sample size, and analyze existing data. They also stimulated investigators to address sex differences in basic and clinical research, as well as sex/gender in research approaches and methodologies. Finally, the evaluation established that outcomes warranted the continuation of the program with some modifications: Over three-quarters (76 percent) of investigators said the SAGE award motivated them to seek additional funding related to sex/gender and almost 60 percent submitted subsequent applications using data from their SAGE award. Strategic Plan Implementation Evaluation (SPIE) data analyses of FY 2016 identified a number of SPIE objectives that represented gaps in ORWH's portfolio. The 2017 (PA-17-078) and 2018 (PA-18-658) FOAs were modified accordingly. In FY 2017, a new FOA (PA-17-101) was issued for SPIE 3.9 (health disparities) to target underrepresented women (the U3 program). So far, ORWH has funded 59 applicants and has invested more than \$10 million in the U3 program.

Proposed Concept: Since the SAGE program has accomplished its intended objectives and beyond, there is an opportunity to address other gaps in the consideration of sex/gender in biomedical research, especially those related to sex/gender influences on the COVID-19 pandemic as reflected in "Guiding Principles: Sex and Gender Influences in COVID-19 and the Health of Women," which was developed by ORWH in collaboration with the Coordinating Committee for Research on Women's Health (CCRWH) COVID-19 working group members. Thus, ORWH is proposing a concept to encompass "COVID-19 and the Health of Women" which would create a new FOA to support studies on the SARS-CoV-2 virus or COVID-19 disease in alignment with efforts across NIH to develop and implement effective therapeutics and vaccines and to accelerate research on technologies to validate and improve programs that will overcome barriers and increase uptake of effective therapeutics and vaccines at the point of care. FOA research topics of interest could include, but are not limited to: Sex and gender influences in the development and administration of effective therapeutics and vaccines;

investigations of sex and gender differences in access to care (e.g., admission, diagnosis, and treatment) of COVID-19 affected individuals; investigation of sex and gender influences on the outcome of patient interactions with health care providers; and the impact of sex and gender on mortality due to co-morbid conditions.

Discussion: ACRWH discussion clarified that the new FOA is an opportunity to adjust resources to address the pandemic, a current research priority. There was also discussion about the scope of the research goals, given that the pandemic will end at some point, with some members supporting a broader scope (e.g., the impact of infectious diseases generally on women’s health or the impact of COVID on the future health of women) and others endorsing a COVID-specific focus. Other suggestions included adding the pandemic’s impact on health care providers and on pregnant women as topics of interest. A Small Business Innovation Research (SBIR) component could be included if ACRWH members think it is important. Finally, there was a comment that the percentage of women in the workforce is the lowest it has been in 20-30 years; that will have an impact on health insurance coverage and on women’s health.

Vote: Dr. Noursi requested a vote to approve the concept “COVID 19 and the Health of Women.” The concept was approved with 13 in favor, 0 opposed.

Member Vote: Creating an ACRWH Working Group for the Consensus Conference

Dr. Noursi discussed the creation of an ACRWH Working Group for the Women’s Health Consensus Conference, consistent with NIH’s overall charge to members of the Advisory Committee.

Background: Congress believes that more focus on research related to obstetrics and gynecology is required to address rising maternal morbidity and mortality rates; rising rates of chronic debilitating conditions in women; and stagnant cervical cancer survival rates. Therefore, Congress has encouraged NIH to convene a Consensus Conference to evaluate research currently underway related to women’s health with relevant stakeholders. It has also directed NIH to provide an update in the Fiscal Year 2022 Congressional Justification of Appropriations (CJ) that identifies priority areas for additional study to advance women’s health research, including reproductive sciences.

In response, NIH—with ORWH in the lead and in collaboration with the ICOs, the NIH Coordinating Committee on Women’s Health, the ACRWH Working Group, and public stakeholders—will convene a Women’s Health Consensus Conference (WHCC), including women’s health researchers, ICO representatives, and public stakeholders. The Fall 2021 ACRWH meeting will serve as the consensus forum focused on assessing the current state of NIH-supported women’s health research, including an overall assessment of research on the health of women and a focused assessment of the research requested. ORWH will work with the ACRWH to prepare a report identifying priority areas for additional study.

The “Asks”: ORWH is asking ACRWH members to provide leadership and expertise for the ACRWH Working Group. Specifically, the “asks” include seeking input from experts in women’s health research and the function and structure of the NIH enterprise; seeking input from public and relevant stakeholders, perhaps through a Request for Information (RFI); reviewing women’s health research portfolio assessments; planning the WHCC by identifying priority topics and moderating sessions; and contributing to the WHCC report. It is anticipated that there will be three Working Group meetings in

May, June, and July, with a special ACRWH meeting on September 1, 2021 and WHCC/ACRWH meeting on October 20-21, 2021.

Discussion: Discussion clarified that ORWH is seeking a sub-set of ACRWH members who can dedicate the needed time to participate on the ACRWH/WHCC Working Group. ACRWH members who are not on the Working Group can respond to the Group’s findings, but there is an opportunity to directly contribute to the process through the Working Group. The scale and scope of the Consensus Conference will be informed by the Working Group and the portfolio assessments; all three topics requested by Congress must be addressed. By “consensus,” Congress means input from broad public and scientific communities within and outside NIH, not NIH’s historical consensus format. Whether the Conference is virtual or in-person is still to be decided. Drs. Langer and Geller indicated their willingness to serve on the Working Group.

Note: Dr. Noursi called for a motion to approve the creation of an ACRWH Working Group for the Consensus Conference. The motion was unanimously approved with 16 votes.

Open Discussion

The open discussion focused on the need to clarify language and nomenclature around sex/gender in biomedical research; strategies to incentivize use of ORWH resources by researchers; strategies to engage journal editors and publishers in requiring authors to present data disaggregated by sex/gender and race/ethnicity; the need to tease out the impact of sex/gender vs. job role in considering the impact of COVID-19 on front line health care workers; and suggestions for future meetings. The latter included allowing more time for discussion; providing a greater focus on adolescent girls; and planning presentations on the translation of research into patient care and health disparities within the LGBTQ community.

Closing Remarks

Dr. Clayton welcomed Sarah Temkin, M.D., who has joined ORWH as Associate Director of Clinical Research. She also reviewed upcoming ORWH events, including the 5th Annual Vivian W. Pinn Symposium (virtual) on May 11-12; Diverse Voices: COVID-19, Intersectionality, and the Health of Women (virtual) on June 24; the 54th ACRWH Meeting/Consensus Conference on October 20-21; and the BIRCWH Annual Meeting on November 1. She acknowledged ORWH’s collective efforts to support the ACRWH meeting and adjourned the meeting at 4:27 p.m.

Certification

We certify that the contents above are accurate and complete.

Janine A.
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Samia D. Noursi

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Advisory Committee on Research on Women’s Health

Date _____

Date June 3, 2021