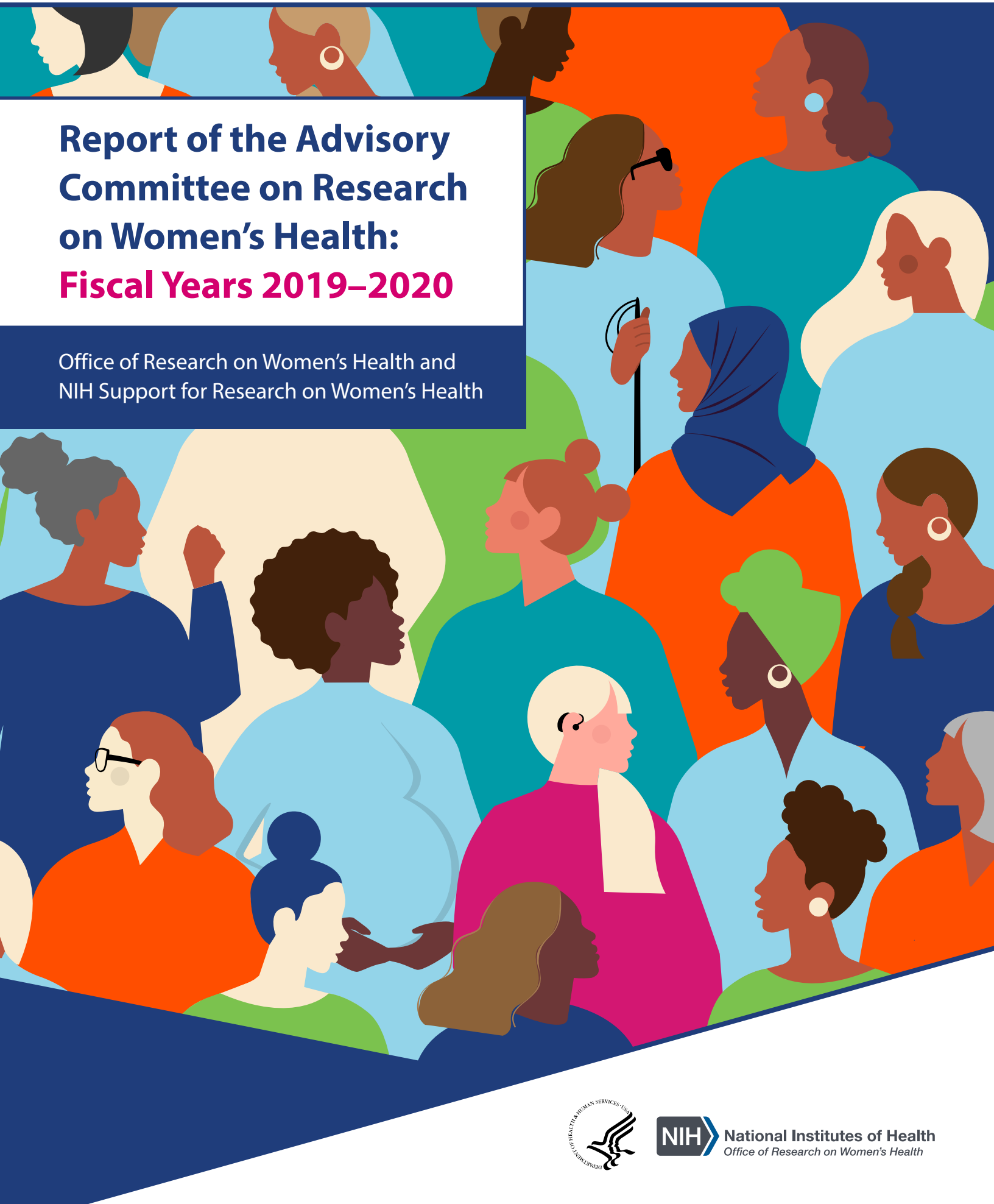
NATIONAL INSTITUTES OF HEALTH

Report of the Advisory Committee on Research on Women's Health: Fiscal Years 2019–2020

Office of Research on Women's Health and
NIH Support for Research on Women's Health



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Letter from the ORWH Director

I am honored to share with you the accomplishments related to the health of women achieved by the National Institutes of Health (NIH) in fiscal years (FYs) 2019 and 2020. This biennial report is issued by the NIH Advisory Committee on Research on Women's Health (ACRWH), whose members play a key role in advising NIH regarding research activities related to women's health. I would like to thank the members of ACRWH for their thoughtful recommendations and tireless work to advance the field. This report summarizes NIH's investments in research on the health of women and the examination of the influence of sex and gender on health and disease, highlights scientific advances made by NIH-supported projects, and describes programs to promote the advancement of women in biomedical careers during the reporting period.

2019 saw a significant expansion of the NIH policy on inclusion in clinical research. The NIH Revitalization Act of 1993 (Public Law 103–43) directed NIH to ensure women and racial and ethnic minorities are appropriately represented in NIH-funded clinical research. In 2016, the 21st Century Cures Act (Public Law 114–255) expanded that mandate with the Inclusion Across the Lifespan policy (Section 2038), which requires NIH-supported research to include people of all ages. Additionally, a provision was made requiring that applicable NIH-defined Phase III clinical trials report results by sex/gender, race, and ethnicity on ClinicalTrials.gov. This addition may lead to new knowledge in the safety and efficacy of new treatments.

We know that women have a longer life expectancy than men, yet women of advanced age have been excluded from many studies in the past because of their age. For the first time, through the Research, Condition, and Disease Categorization's (RCDC) Inclusion Statistics Report webpage, NIH is providing data on the proportion of women enrolled in studies by disease category, continuing the move toward enhancing transparency and accountability in research. Despite there being a mandate for nearly 30 years that women be included in clinical studies and women representing half of study participants in NIH-supported clinical research overall, publications from those studies infrequently report results disaggregated by sex. This indicates that women may not be reaping the benefits of their participation in these studies and that clinicians may have limited evidence upon which to make gender-aware treatment decisions. ORWH is working with journal editors, publishers, and other stakeholders to address these issues. Guidelines have been implemented by these parties to improve sex-specific results reporting. However, these changes have not been made across the board, which means there is more work to be done. NIH is committed to making improvements in this arena to enhance the rigor and relevance of research results and findings for everyone.

Many issues in women's health took on greater significance during FYs 2019 and 2020. Maternal morbidity and mortality (MMM), the COVID-19 pandemic, and the health and health disparities of women in underserved populations rose as top priorities. Though pregnancy is a life-changing event, it should not be a life-ending event for women. Pregnancy can reveal risks for subsequent development of chronic diseases—such as diabetes, hypertension, and cardiovascular disease—yet most pregnancy-related deaths are preventable. In 2019, ORWH issued a call to action on maternal health, and NIH's response has been robust. Multiple NIH Institutes, Centers, and Offices (ICOs) worked together to develop the **I**mplementing a **M**aternal health and **PR**egnancy **O**utcomes **V**ision for **E**veryone (IMPROVE) initiative. Co-led by ORWH, this initiative supports research on how to reduce preventable maternal mortality and improve the health of women before, during, and after childbirth. Though there has been progress, we understand there is a long runway for improvement from both a systemic and a structural standpoint to truly reach health equity in maternal health care. ORWH created an online resource, the NIH MMM Web Portal, to highlight the wide range of NIH efforts from across the ICOs.

Along with MMM, the COVID-19 pandemic posed special challenges for women in FY 2020 and highlighted many issues related to sex and gender, especially secondary effects that have disproportionately impacted women. Frontline health care workers, the majority of whom are women, were at greater risk of SARS-CoV-2 infection. This highlighted potential sex-based issues related to the fit of and thereby the protection afforded by available personal protective equipment (PPE). Women, who also tend to be the primary caregivers of their households, assumed a greater share of unpaid

domestic work as schools closed. Additionally, reports by women of intimate partner violence associated with State-issued stay-at-home orders surged. All these factors contributed to a general decline in the physical and mental health of women in FY 2020. Synchronously, the pandemic had a disproportionate negative impact on women scientists. With increases in family-related responsibilities, many women scientists had to drastically reduce research hours, causing a sharp decline in women authorship in science, technology, engineering, mathematics, and medicine (STEMM) during the pandemic, which could have lasting ramifications for their careers and the demographics of the biomedical workforce.

Both MMM and the COVID-19 pandemic have had outsize effects on the health of women in underserved and vulnerable populations, particularly women of color. In FY 2020, we at ORWH expanded the scope of our funding programs to include COVID-19. ORWH established guiding principles for integrating sex and gender considerations into COVID-19 research in collaboration with the NIH Coordinating Committee on Research on Women's Health (CCRWH). Furthermore, ORWH scientific staff quickly pivoted and augmented the office's signature research programs to include research on sex- and gender-related factors in COVID-19, including for underserved populations.

ORWH has been advancing women in STEMM careers through career development programs, research initiatives, and outreach. We have been energized by the addition of several women Institute and Center (IC) directors at NIH in this reporting period. With 10, we have now reached the highest number of women IC directors that NIH has ever had, in what we are calling the "Power of 10." Additionally, in late FY 2020, NIH welcomed its first woman-of-color institute director, Dr. Rena D'Souza, who now leads the National Institute of Dental and Craniofacial Research. Building on these advancements, NIH will continue to make changes to support women in all career stages.

2020 marked the 30th anniversary of ORWH. Over the past three decades, ORWH has collaborated with ICOs to drive research related to the health of women, set standards for incorporating sex and gender into the entire biomedical research continuum, and provide career support to women's health researchers. This work was featured in a scientific symposium that included excellent presentations from four IC directors, thought-provoking panels and keynotes, and a recognition of this anniversary. ORWH devoted the 2020 volume of *Women's Health in Focus at NIH* to scientific and policy advances and progress. In collaboration with a wide set of stakeholders and partners, ORWH developed and launched a coordinated plan, titled *Advancing Science for the Health of Women: The Trans-NIH Strategic Plan for Women's Health Research*, which NIH is using to guide its efforts through 2023 to address important issues in women's health, including MMM, the impact of COVID-19, and health disparities. As circumstances of FYs 2019 and 2020 showed, ORWH's work remains as important as ever.

In closing, I want to thank the many people who have supported ORWH and its mission of putting science to work for the health of women. Thank you to the countless number of women who have participated in clinical trials. Your courage and willingness to engage in studies has truly helped to advance science for women. Along with the visionary scientists and clinicians, I would like to thank the professional societies, scientific associations, advocacy groups, and Federal agencies that have partnered with ORWH to continue to elevate the issues affecting women. Finally, I deeply appreciate the substantial contributions that ICOs have made to support research on the health of women. Collaborative efforts over 30 years have expanded our understanding of sex- and gender-related influences on health as well as the health of women across the lifespan, and I look forward to continuing our work. We want to ensure all women receive evidence-based care tailored to their own needs, circumstances, and goals, and we are determined to see all women in scientific careers reach their full potential.

Janine A. Clayton, M.D., FARVO
Associate Director for Research on Women's Health
Director, Office of Research on Women's Health
National Institutes of Health
December 2021

PREFACE

Report of the Advisory Committee on Research on Women's Health: Fiscal Years 2019–2020 describes the programs and initiatives undertaken across the National Institutes of Health (NIH) in service of the core mission of the NIH Office of Research on Women's Health (ORWH), which was established in 1990. The mission, outlined in the NIH Revitalization Act of 1993 (Public Law 103–43, Section 486B), is:

- To advise the NIH Director on matters relating to research on women's health;
- To strengthen and enhance research related to diseases, disorders, and conditions that affect women;
- To ensure that research conducted and supported by NIH adequately addresses issues regarding women's health;
- To ensure that women are appropriately represented in biomedical and biobehavioral research studies supported by NIH;
- To develop opportunities for and support recruitment, retention, re-entry, and advancement of women in biomedical careers; and
- To support research on women's health issues.

Over its 30-year history, ORWH has continually sought to carry out its mission by ensuring that NIH-funded research encompasses the health of all women, from head to toe and across the lifespan. It emphasizes the importance of rigorous research that is both transparent and reproducible by prioritizing the need for investigators to consider the influence of sex and gender on health and disease. Therefore, ORWH has expanded its mission statement to include:

- Supporting and advancing rigorous research that is relevant to the health of women; and
- Ensuring that NIH-funded research accounts for sex as a biological variable (SABV).

The members of the NIH Advisory Committee on Research on Women's Health (ACRWH) are pleased to submit this report to the NIH Director through the NIH Associate Director for Research on Women's Health and the Director of ORWH. They have reviewed the report and find that it provides essential information about the research, programs, and other activities of ORWH and all NIH Institutes, Centers, and Offices (ICOs). It describes the breadth and depth of the work undertaken by NIH to achieve its mission in fiscal years (FYs) 2019 and 2020, including:

- NIH-supported research on the health of women and the influence of sex and gender on health and disease. (This research was supported by the Institutes and Centers [ICs] across NIH, as well as by program offices within the Division of Program Coordination, Planning, and Strategic Initiatives [DPCPSI] in the NIH Office of the Director [OD].)[1]
- NIH budget allocations for research on the health of women, submitted by the U.S. Department of Health and Human Services Office of the Assistant Secretary for Financial Resources.
- Advancing implementation of the SABV policy and collaborative efforts across the ICOs through the Trans-NIH SABV Working Group to improve rigor and transparency in NIH-funded research.
- Expanded focus on increasing inclusion of women, underrepresented racial and ethnic groups, children, and older adults in NIH-funded clinical research and efforts to lay the groundwork for applications submitted on or after January 25, 2019, when new requirements became effective based on the Inclusion Across the Lifespan policy.
- The announcement of the first ORWH-led R01 grant that will fund investigator-initiated research across scientific disciplines to understand how sex and gender influence health and disease.
- Continuation of the Specialized Centers of Research Excellence (SCORE) on Sex Differences cooperative agreement program; the administrative supplements for research on sex and gender influences; and the U3 Administrative Supplement

1. ORWH recognizes that the use and understanding of the concepts of "sex" and "gender" continue to evolve. Although this report may use the language "sex/gender" to align with language in previous policies and funding opportunities, it is understood that these terms are distinct and are not interchangeable. When "sex/gender" or "sex and gender" is used in this report, it means "sex, gender, or both."

Program, which funds interdisciplinary research on populations of women that are understudied, underrepresented, and underreported (U3) in biomedical research.

- Meetings of the NIH scientific interest group (SIG) called Sex and Gender in Health and Disease, which fosters interdisciplinary collaboration among NIH scientists who work on or are interested in sex differences research at various points along the research continuum.
- Promotion of career advancement for women in biomedical careers. (The ORWH Director co-chairs the NIH Working Group on Women in Biomedical Careers with the NIH Director. Resources for women in biomedical careers are regularly made available on the ORWH website, at https://orwh.od.nih.gov/career-development-education, and on womeninscience.nih.gov.)
- The Women of Color Research Network, an online forum hosted by ORWH that aims to foster the research careers of women of color.
- Promotion of research on maternal morbidity and mortality (MMM) through the Implementing a Maternal health and PRegnancy Outcomes Vision for Everyone (IMPROVE) research initiative.
- Contributions to the NIH Helping to End Addiction Long-term℠ (HEAL) Initiative to study the impact of prenatal and postnatal exposure to opioids on child brain development in the HEALthy Brain and Child Development (HBCD) Study.
- Support for the *NIH-Wide Strategic Plan for COVID-19 Research* where the goals of the plan intersect with ORWH mission areas, such as the consideration of COVID-19 as it relates to maternal health and pregnancy outcomes and the inclusion of U3 populations in clinical trials.
- Continued support for women in biomedical careers through the Building Interdisciplinary Research Careers in Women's Health (BIRCWH, pronounced like "birch") program, which celebrated its 20th anniversary in 2020. (A mentored career-development program, BIRCWH has supported more than 700 junior faculty through 88 grants to 44 institutions since its inception.)

ORWH has continued to make significant progress with key elements of its mission, including advancing the careers of women in biomedical fields. ORWH has provided resources on mentoring, retention, and career advancement; leadership development; and work–life integration. In addition, investments related to the NIH Working Group on Women in Biomedical Careers–led 2008 request for applications (RFA), titled "Research on Causal Factors and Interventions that Promote and Support the Careers of Women in Biomedical and Behavioral Science and Engineering," are paying dividends, with significant findings contributing to our understanding of how individuals make career choices, how workplaces may inadvertently impede advancement, and the effectiveness of interventions. For example, research found that when workplaces offer flexibility policies, they can provide assistance in work–life integration, but these programs are still underused by employees.

In September 2020, ORWH announced the launch of the NIH Prize for Enhancing Faculty Gender Diversity in Biomedical and Behavioral Science, a prize competition that conceptually originated from the NIH Working Group on Women in Biomedical Careers. This prize will award up to 10 institutions with $50,000 each for acting to effect systemic change to address gender equity and diversity among faculty members in the biomedical and behavioral sciences. More than simply incentivizing gender diversity in academic institutions, the prize is intended to promote replicable, evidence-based approaches for institutions to promote that diversity.

In collaboration with the NIH Working Group on Women in Biomedical Careers and NIH Office of Extramural Research partners, ORWH also led the development of administrative supplement programs to enhance the retention of early-career investigators. Among those supplements released during the reporting period were the *Administrative Supplement for Continuity of Biomedical and Behavioral Research Among First-Time Recipients of NIH Research Project Grant Awards* and the *Administrative Supplements to Promote Research Continuity and Retention of NIH Mentored Career Development (K) Award Recipients and Scholars*. The criteria for both consider life events such as childbirth and were developed to complement other ongoing NIH efforts to enhance the diversity of the biomedical research workforce.

Over the past 2 fiscal years, the Trans-NIH SABV Working Group has continued efforts to implement the SABV policy, supporting rigor and transparency in NIH business practices. With ORWH support, tools and resources were developed. SABV-related information has been disseminated to the ICOs through road shows across NIH, website resources, and grant review guidance. New and updated FAQs were developed for grant applicants. ORWH is continuing to provide support for consideration of SABV across the research continuum through programming, policies, and practices.

Policy

The 21st Century Cures Act (Public Law 114–255),[2] signed into law in 2016, introduced several significant changes in how research is conducted and the way ORWH operates, including increased interaction and collaboration between the ORWH Director and the directors of all the ICs. The 21st Century Cures Act ensures that the ICs' strategic plans have objectives that take women into account and focus on reducing women's health disparities. NIH updated its inclusion policy to include people of all ages, and this became the Inclusion Across the Lifespan policy. Overall, it calls for women, people in underrepresented racial and ethnic groups, and people of all ages to be appropriately represented in NIH-supported clinical research. Participant age at enrollment must now be provided in annual progress reports, and certain Phase III clinical trials must report their results in ClinicalTrials.gov by sex/gender and by race and ethnicity, which reinforces the inclusion and SABV policies.

In line with prior requirements of the 21st Century Cures Act, ICOs were encouraged by the NIH Director to (1) improve research related to the health of sexual and gender minority populations through increased participation in NIH clinical research and reporting, (2) develop valid and reliable methods for research relevant to sexual and gender minority populations, and (3) address methodological challenges. In May 2019, NIH launched the Research, Condition, and Disease Categorization (RCDC) Inclusion Statistics Report. which

2. 21st Century Cures. H.R. 34. 114th Cong. (2016). Retrieved from https://www.congress.gov/114/plaws/publ255/PLAW-114publ255.pdf

publicly reports inclusion data by sex/gender, RCDC category, and IC, helping to demonstrate inclusion of women and other understudied groups in research across an array of diseases and conditions.

In June 2020, ORWH published an article in the *Journal of Women's Health* commenting on the development and implementation of NIH's SABV policy. The article, titled "Sex as a Biological Variable: A 5-Year Progress Report and Call to Action," describes many of the NIH initiatives, programs, research projects, resources, organizations, and funding opportunities designed to enhance SABV policy implementation and promote its ethos throughout the larger biomedical and biobehavioral research community.

In September 2020, the NIH Inclusion Governance Committee, co-chaired by the ORWH Director and the National Institute on Aging's Deputy Director, hosted the virtual "Inclusion Across the Lifespan-II Workshop: Implementation and Future Direction," convening stakeholders from a wide range of backgrounds in clinical study development and execution. It focused on pediatric, older adult, and special populations (e.g., people in underserved racial and ethnic groups, people with disabilities, rural/isolated populations, language-minority individuals, pregnant women, lactating women, people with comorbidities, and sexual and gender minorities). Researchers shared lessons learned on the recruitment and inclusion of these populations in clinical studies and presented evidence-based advice. Topics included inclusion/exclusion criteria; study design and metrics; recruitment, enrollment, and retention; and data analysis and study interpretation. A meeting report is available here.

NIH Inclusion Outreach Toolkit: How to Engage, Recruit, and Retain Women in Clinical Research

Several years ago, ORWH, in collaboration with other entities, developed the NIH Inclusion Outreach Toolkit

to assist principal investigators and their teams in fulfilling their responsibility of including women in clinical research. During the reporting period, ORWH updated this online toolkit to include additional information on NIH policies, case studies, and best practices for recruiting and retaining women in clinical research. Outreach tools such as this can be applied to other populations as well.

Research

Maternal Morbidity and Mortality

During the reporting period, NIH and ORWH supported research on maternal health, including a particular emphasis on maternal morbidity and mortality (MMM), and research on health disparities and methods to improve health outcomes for those from understudied, underrepresented, and underreported populations through a number of administrative supplements, initiatives, and outreach programs. The IMPROVE initiative is an NIH-wide research initiative developed in 2019 by the NIH Task Force on Maternal Mortality, which is led by the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), ORWH, and OD. It is supported by more than two dozen ICOs and has awarded more than $7 million in grants through administrative supplements announced by a notice of special interest (NOSI) that was released in May 2020. Additional administrative supplement funding was made available in April 2020 for the study of maternal and infant morbidity and mortality through a women's health–focused collaboration between ORWH and the National Institute of General Medical Sciences in the Institutional Development Award (IDeA) program. IDeA States are those identified by the program as having historically low levels of NIH funding, and many have higher levels of maternal and infant mortality than the U.S. average. Additional support for research into health disparities, including maternity-related disparities, was made available in December 2019, when ORWH published a NOSI titled *Research on the Health of Women of Understudied, Underrepresented and Underreported (U3) Populations* in collaboration with multiple ICOs.

In May 2020, ORWH collaborated with NICHD and other ICOs in convening a workshop titled "Pregnancy and Maternal Conditions That Increase Risk of Morbidity and Mortality." During this workshop, a leading interdisciplinary team of experts explored why women die from certain conditions—e.g., postpartum hemorrhage, hypertension, cardiovascular disease, and infection—and what can be done to identify patients at risk, as well as what interventions are required to reduce maternal morbidity and mortality.

The SABV Policy

ORWH has led several research initiatives on sex and gender and sex as a biological variable (SABV) during the reporting period. In September 2019, NIH published a funding opportunity announcement (FOA) on sex and gender, *The Intersection of Sex and Gender Influences on Health and Disease*. This research project grant is NIH's first investigator-initiated R01 that encourages researchers across disciplines to examine sex and gender factors and their intersections in health and disease. In 2020, 11 sites in the Specialized Centers of Research Excellence (SCORE) on Sex Differences program were funded, each as a U54 cooperative agreement. These awards were co-funded by ORWH and five IC partners (the National Institute on Aging, the National Institute on Alcohol Abuse and Alcoholism, the National Institute on Drug Abuse, the National Institute of Diabetes and Digestive and Kidney Diseases, and the National Institute on Minority Health and Health Disparities). Each center in the SCORE program supports translational research through three interrelated research projects in scientific areas relevant to the health of women. SCORE pilot research is conducted within the Career Enhancement Core of each center. ORWH also provides administrative supplements for interdisciplinary, transdisciplinary, and multidisciplinary research on sex and gender influences on human health and disease. Funds are awarded for 1 year. The administrative supplements for research on sex/gender differences support research approaches for (1) adding the opposite sex/gender (the addition of animal or human subjects, tissues, or cells of the sex opposite to that used in the parent grant to allow sex/gender-based comparisons); (2) increasing sample size (the addition of more animal or human subjects, tissues, or cells to a sample that already includes both males and females to increase the power of a study to analyze for sex or gender differences); and (3) analyzing existing data (comparative analyses of extant samples/datasets/databases and/or data mining to investigate the role of sex/gender). Preclinical and clinical studies can be supported.

The COVID-19 Response

In response to the COVID-19 pandemic, NIH released the *NIH-Wide Strategic Plan for COVID-19 Research* in July 2020. ORWH collaborated on the project, and many of the goals contained in the plan align with ORWH's mission areas, including:

- NIH's inclusion policies. Inclusion Across the Lifespan and Inclusion of Women and Minorities as Subjects in Clinical Research, in addition to the SABV policy, informed the creation of the strategic plan and further drive NIH's efforts to benefit everyone. Studies to examine biological factors that influence individual susceptibility to infection—such as age, sex, gender, genetics, and environment—are already in progress.
- U3 interdisciplinary research. NIH recognizes the disproportionate impact of COVID-19 on vulnerable and U3 populations and is striving to mitigate its effects by identifying the underlying factors and barriers that contribute to the higher death toll in these communities. Inclusion of these populations in clinical trials for diagnostics and interventions is a critical part of NIH's pandemic response, as is exploring communication strategies and ways to improve access to care and interventions for at-risk populations.
- Maternal health. The COVID-19 strategic plan articulates how NIH will examine and address COVID-19 as it relates to maternal health and pregnancy outcomes. Ongoing and future studies will include consideration of COVID-19 and maternal morbidity, pregnancy-related alterations to the immune system, preterm birth, infant health, prenatal and postnatal care, rate of cesarean section delivery, possible mother-to-fetus transmission, possible mother-to-child transmission at birth, and possible transmission via breastfeeding.

ORWH will continue to advance fulfillment of these goals through co-funding and other efforts. You can read the *NIH-Wide Strategic Plan for COVID-19 Research* and learn more about how the framework aims to mobilize

the biomedical research response to the pandemic at https://covid19.nih.gov/nih-strategic-response-covid-19.

Research Dissemination

ORWH launched numerous avenues to disseminate research results from women's health studies during the reporting period, including many online resources for both biomedical researchers and the public.

The Maternal Morbidity and Mortality Web Portal and Accompanying Resources

In May 2019, ORWH launched the Maternal Morbidity and Mortality (MMM) Web Portal, which provides science-based information on maternal health for scientists, researchers, health advocates, and, most importantly, women who are pregnant, are considering pregnancy, or have recently given birth. The web portal also includes research and funding opportunities related to maternal health for researchers and clinicians. ORWH also produced an informational booklet titled *Maternal Morbidity and Mortality: What Do We Know? How Are We Addressing It?* and an accompanying video. The booklet examines the factors that contribute to MMM and how maternal health can continue to affect women across their lifespan. The booklet also addresses what NIH and other Federal health agencies are doing to combat this issue.

In August 2020, ORWH Associate Director for Science Policy, Planning, and Analysis Samia Noursi, Ph.D.; Bani Saluja, M.P.H.; and Leah Richey, B.S., published an article in the *Journal of Racial and Ethnic Health Disparities*. The article, titled *Using the Ecological Systems Theory to Understand Black/White Disparities in Maternal Morbidity and Mortality in the United States*, examines the root causes of racial disparities in MMM using Urie Bronfenbrenner's ecological systems theory at the individual (microsystem), interpersonal (mesosystem), community (exosystem), and societal (macrosystem) levels of influence. Factors influencing disparities include access to preconception and prenatal care, implicit bias among health care providers, the need for quality improvement among Black-serving hospitals, and policies such as parental leave. The authors also identify interventions likely to reduce disparities, such as improving health professional education, alternate prenatal care providers, and reforming Medicaid policies.

In September 2020, Dr. Noursi and ORWH Director Janine A. Clayton, M.D., published an article with Drs. Jacquelyn Campbell and Phyllis Sharps in *Current Women's Health Reviews* on the data issues that hinder research on the intersection of MMM and intimate partner violence (IPV) in the United States. The article, titled *The Intersection of Maternal Morbidity and Mortality and Intimate Partner Violence in the United States*, describes the lack of review and discussion in research on MMM and IPV despite the prevalence of IPV during pregnancy.

Women's Health News

ORWH launched a new feature of its website in June 2019, called In the Spotlight (ITS). Updated several times a month, ITS provides ORWH with a means of disseminating breaking news and other timely updates on ORWH initiatives, the health of women, biomedical careers, related funding opportunities, and more. ORWH also continued publication of *Women's Health in Focus at NIH*, a quarterly publication launched in March 2018. In Focus provides a more in-depth showcase of the women's health research performed across NIH through feature articles, profiles of women in science, and a Director's Corner section with messages from Dr. Clayton.

New E-Learning Courses

In November 2019, ORWH updated the Career Development & Interprofessional Education section of its website to include an e-learning webpage, which contains the course *Bench to Bedside: Integrating Sex and Gender to Improve Human Health*, a six-module e-learning course developed in conjunction with the Food and Drug Administration Office of Women's Health. This free course offers guidance for researchers on how sex and gender influence health and disease. Two additional free e-learning courses, *Sex as a Biological Variable: A Primer* and *Introduction: Sex- and Gender-Related Differences in Health*, were developed during the reporting period. *Sex as a Biological Variable: A Primer* is a four-module course developed with National Institute of General Medical Sciences and OD support designed to help researchers understand the SABV policy and incorporate it in their research, while *Introduction: Sex- and Gender-Related Differences*

in Health is an introduction to understanding and accounting for sex and gender influences on health and disease and was designed to help individuals and teams incorporate a sex-and-gender perspective in health-related research and clinical care.

Social Media

ORWH increased outreach related to women's health research advances, inclusion, and women in careers over multiple social media platforms during the reporting period, including on Twitter, LinkedIn, and Facebook. ORWH hosted four Facebook Live Q&A events, addressing topics such as women of color in science, technology, engineering, mathematics, and medicine (STEMM) fields; the importance of mentorship of women of color in science; and women in STEMM leadership roles.

Careers

The ORWH-led BIRCWH program continues its commitment to supporting career development of women's health researchers by connecting junior faculty with senior faculty mentors who share an interest in women's health and sex differences research. That effort included BIRCWH Annual Meetings in FYs 2019 and 2020, which provided mentors, early-career BIRCWH Scholars, and other researchers a chance to meet, present their research, and engage in mentoring and networking. Since its inception in 2000, BIRCWH has provided funding to over 700 BIRCWH Scholars, men and women who conduct interdisciplinary basic, translational, behavioral, clinical, and health services research relevant to women's health.

In Summary

ACRWH would like to express gratitude for the focused attention of NIH leadership and scientific leaders in the ICOs. These leaders have conducted praiseworthy work on behalf of women's health and sex and gender issues over the past 2 years. Their successful strategies have included ICO-sponsored workshops, specific sex- and gender-related FOAs, and working groups focused on women's health research. They have regularly initiated symposia, travel awards, scientific presentations, and journal publications. Efforts by the ICOs have been attracting more women investigators to STEMM fields. Collectively, these accomplishments have demonstrated the importance of conducting research specific to women, taking a sex- and gender-based research approach, sex-based data analysis, and promoting the advancement of women in biomedical careers.

ACRWH also acknowledges the accomplishments of the NIH Coordinating Committee on Research on Women's Health, the Trans-NIH SABV Working Group, the NIH Inclusion Governance Committee, the NIH Working Group on Women in Biomedical Careers (including the Committee on Women of Color in Biomedical Careers, the Committee on Advancing Women in Independent Positions, and the Committee on the NIH Intramural Research Program), and the Sex and Gender in Health and Disease SIG. Their members are dedicated professionals from a range of backgrounds and scientific disciplines who are committed to achievements in women's health and the advancement of women in the sciences. Finally, the many accomplishments of NIH and the broader research community on behalf of women over the past 2 years would not have been possible without the exemplary work of all ORWH staff members.

Although progress has been made, continued work on these efforts will remain necessary for years to come. Expert recommendations made decades ago are still in the process of being fully realized, and the long history of biomedical research's focusing on men as the norm has resulted in wide gaps in our knowledge of women's health that are still being addressed. Although women now represent approximately half of the participants in NIH-supported clinical trials, they remain underrepresented in studies of some diseases. Less than one-third of NIH-supported Phase III clinical trials publish sex-specific results. Inclusion is not enough; only when sex and gender considerations are integrated across the biomedical continuum, results are analyzed for sex differences, and sex-specific results are published in the scientific literature can the benefit of inclusion be fully realized.

Advisory Committee on Research on Women's Health, Fiscal Years 2019–2020

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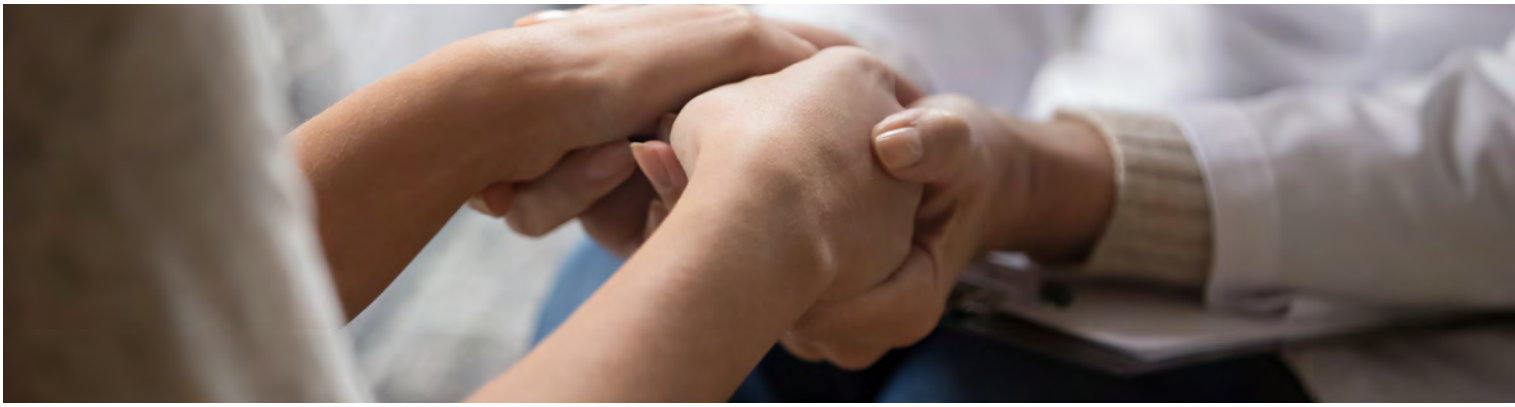

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Organization of the *Report of the Advisory Committee on Research on Women's Health: Fiscal Years 2019–2020*

The FY 2019–2020 report of the Advisory Committee on Research on Women's Health (ACRWH) illustrates how the National Institutes of Health (NIH) has put science to work for the health of women during the reporting period. The sections that follow describe specific NIH Office of Research on Women's Health (ORWH) programs, initiatives, and activities; continuing implementation of the NIH Policy on Sex as a Biological Variable (SABV) across NIH, including updated business practices; research initiatives on the health of women conducted by the NIH Institutes, Centers, and Offices (ICOs); programs that promote the professional development of women in biomedical careers; and recent information on the inclusion of women and minorities as subjects in clinical research. Although this report highlights specific NIH research efforts on women's health, it is not exhaustive. Rather, the projects described convey the breadth and depth of the work undertaken by NIH during the reporting period to improve the health of women.

This report is divided into two major parts. The first part describes ORWH activities and programs, including workforce data on NIH employees and grantees. The second part describes the research and other activities of the individual ICOs.

ORWH Activities and Programs

i. ORWH Background

ii. ORWH Research

iii. NIH Workforce and Grantees

iv. ORWH Biomedical Career Development

v. Monitoring Adherence to the NIH Policy on the Inclusion of Women and Minorities as Subjects in Clinical Research

vi. NIH Budget for Women's Health Research

Section I: ORWH Background describes the historical events leading to the establishment of ORWH and the mission assigned by congressional mandate. Current information is provided on NIH policies that support the ORWH mission, including ongoing SABV policy implementation, the requirements of the 21st Century Cures Act, and updates to NIH inclusion polices.

Section II: ORWH Research provides an overview of the research investments and co-funding dollars used by ORWH to further knowledge on diseases, disorders, and conditions that affect the health of women. It describes the work of specific ORWH programs designed to advance women's health research and increase understanding of the influence of sex and gender on health and disease.

Section III: NIH Workforce and Grantees describes the gender and racial and ethnic demographics of the NIH intramural and extramural workforce, with aggregate data provided by the NIH Office of Equity, Diversity, and Inclusion and the NIH Office of Extramural Research's Division of Statistical Analysis and Reporting. This section highlights the employment, promotion, and leadership status of women scientists in the NIH workforce in relation to their counterparts, with a further assessment of racial and ethnic differences. Also highlighted in this section are the gender-, race-, and ethnicity-based differences in NIH grant applications, awards, and funding amounts.

Section IV: ORWH Biomedical Career Development Activities highlights programs designed to increase the number of women in biomedical careers and the number of researchers focused on women's health concerns. It describes training and mentoring programs and initiatives that facilitate re-entry of women into the biomedical workforce after extended absences.

Section V: Monitoring Adherence to the NIH Policy on the Inclusion of Women and Minorities as Subjects in

Clinical Research describes programs that monitor and foster the inclusion of women and minorities in NIH-funded clinical research. It includes aggregate data on the numbers of women and minorities who participated in this research.

Section VI: NIH Budget for Women's Health Research summarizes NIH funding of women's health research for FY 2019–2020 by disease, condition, or initiative and by sex.

Activities of the NIH Institutes, Centers, and Offices

This section contains reports from the ICOs on the research, publications, and other activities conducted during the reporting period to advance the health of women.

Appendices

The biennial report appendices, starting on page 319 of this report, include:

- **Appendix A.** Coordinating Committee on Research on Women's Health (CCRWH) Roster
- **Appendix B.** Summaries of Research Co-Funded by ORWH
- **Appendix C.** NIH Workforce and Grantees
- **Appendix D.** Members of the NIH Working Group on Women in Biomedical Careers
- **Appendix E.** Aggregate Enrollment Data and Tables
- **Appendix F.** 2021 Biennial Advisory Council Reports Certifying Compliance with NIH Policy on Inclusion Guidelines

I. ORWH Background

The History of the National Institutes of Health Office of Research on Women's Health

The National Institutes of Health (NIH) Office of Research on Women's Health (ORWH) has a long history of highlighting and promoting efforts to improve knowledge about the health of women at NIH through research on women's health, inclusion of women in clinical research, and support for the professional development of women in biomedical careers. The path to the founding of ORWH began in the 1960s and '70s, with the civil rights and women's rights movements. The women's health movement drew attention to the lack of research on how diseases, conditions, and disorders affect women. In response to that, in 1983, then–U.S. Department of Health and Human Services Assistant Secretary for Health Edward N. Brandt Jr., M.D., established the U.S. Public Health Service Task Force on Women's Health Issues. Dr. Brandt appointed Ruth L. Kirschstein, M.D., then–Director of the National Institute of General Medical Sciences, to chair the new task force.

Two years later, the task force published a report, "Women's Health: Report of the Public Health Service Task Force on Women's Health Issues, Volume I," recommending an expansion of women's health research (U.S. Public Health Service, 1985). In response to this report and other concerns raised by women's health advocates, NIH enacted the Inclusion of Women and Minorities in Clinical Research policy. This policy urged researchers applying for NIH funding for studies involving human subjects to include women and others from underrepresented or understudied populations.

In 1990, in response to a request from the Congressional Caucus for Women's Issues, the General Accounting Office (now known as the Government Accountability Office) investigated the implementation of the new inclusion policy and found several issues hindering its uptake. Barriers included poor communication of the new standards, delays in implementation, and a lack of routine analysis by sex or gender in clinical studies (NIH, 1990). The analysis also found that implementation of the policy had little effect overall in increasing the inclusion of women in clinical research.

These findings prompted then–Acting NIH Director William F. Raub, Ph.D., to establish ORWH within the NIH Office of the Director (OD). Dr. Raub appointed Dr. Kirschstein as the first Acting Director of ORWH, where she began to set NIH's women's health research agenda. In 1993, the NIH Revitalization Act (Public Law 103–43) established ORWH in statute, cementing its importance and continued operation in U.S. law. The ORWH Director is mandated by this act to advise the NIH Director and staff on issues related to women's health research, strengthen research on health issues that affect women, ensure that NIH research addresses women's health and includes appropriate representation of women, and develop increased opportunities for women in biomedical careers.

Additionally, the act created two committees to advise the ORWH Director on issues related to women's health research. The Advisory Committee on Research on Women's Health (ACRWH) comprises leading non-Federal experts in many fields and provides the ORWH Director with recommendations from an external perspective. The Coordinating Committee on Research on Women's Health (CCRWH) is a trans-NIH group of Institute, Center, and Office (ICO) directors or their designees who can offer suggestions based on internal knowledge of NIH and its processes.

In 2006, the NIH Reform Act (Public Law 109–482) led to a reorganization of OD. ORWH was placed within the Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI), which focuses on overarching NIH-wide concerns. ORWH's statutory responsibilities were unchanged, but the office's placement in DPCPSI emphasized its role as the focal point for NIH research on the health of women across all ICOs. This interconnection allows ORWH to fully engage with the ICOs and ensure that all science at NIH properly incorporates issues related to women's health. The current ORWH mission statement emphasizes the importance of biomedical research that appropriately includes women and that considers sex and gender, and it highlights the ORWH role in facilitating this research. Additional efforts shepherded by ORWH

include understanding and decreasing health disparities among certain populations of women in various demographics—including age, socioeconomic status, race, and ethnicity—and supporting research and training in interdisciplinary areas.

In 2016, the 21st Century Cures Act (Public Law 114–255) introduced significant changes affecting the conduct of NIH research and communication between ORWH and the NIH Institutes and Centers (ICs). It requires that CCRWH members be either directors or senior-level staff members appointed by the directors. The directors of the national institutes and national centers shall consult at least once annually with the Director of the National Institute on Minority Health and Health Disparities and the Director of the Office of Research on Women's Health regarding objectives of the national institutes and national centers to ensure that future activities by such institutes and centers take into account women and minorities and are focused on reducing health disparities. The strategic plans issued by the individual ICs, required at least every 6 years, must also address women's health and the reduction of women's health disparities. Although the inclusion of women and minorities in NIH-funded clinical research was enacted into law in 1993, the 21st Century Cures Act set forth the Inclusion Across the Lifespan policy,[3] which applies to all grant applications and contract solicitations submitted on or after January 25, 2019. It has expanded NIH's inclusion policy to include individuals of all ages (including children, defined as individuals under the age of 18, and older adults, defined as individuals over 65 years of age). It also states that justifications for exclusion criteria based on age must have valid ethical or scientific reasons, and it requires that participants' ages at enrollment be provided in progress reports. In addition, the 21st Century Cures Act requires that applicable[4] Phase III clinical trials report their results in ClinicalTrials.gov by sex and/or gender and by race and ethnicity. The NIH Inclusion Governance Committee—co-chaired by ORWH Director Janine A. Clayton, M.D., and National Institute on Aging Deputy Director Marie Bernard, M.D.—collaborated with multiple ICOs to organize the virtual Inclusion Across the Lifespan-II Workshop: Implementation and Future Direction (IAL-II), held on September 2, 2020, generating a report summarizing strategies for advancing the inclusion of people of all ages in clinical research. The IAL-II workshop report is available here.

In May 2019, NIH launched the Research, Condition, and Disease Categorization (RCDC) Inclusion Statistics Report on the RCDC website. It publicly reports data about study participants by sex/gender, RCDC category, and IC to help ensure that women are included in research across a wide range of conditions and diseases. Additionally, in December 2019, ORWH updated the NIH Inclusion Outreach Toolkit. An online resource for researchers, the toolkit highlights best practices in recruitment strategies, explains applicable Federal laws and regulations, and serves as a one-stop shop for information on the inclusion of women and underserved racial and ethnic groups in research studies.

May 2019 also saw the launch of the ORWH Maternal Morbidity and Mortality (MMM) Web Portal, which provides information on healthy pregnancy, delivery, and post-pregnancy for scientists, researchers, and the general public. Researchers and clinicians can use the portal to learn about NIH-funded research opportunities and ongoing research related to MMM and to find events, such as workshops and webinars, related to maternal health. The "Information for Women" section of the portal provides reliable, evidence-based information on pregnancy, delivery, and peripartum and postpartum experiences to women who are considering pregnancy, are about to become mothers, or have already had a child.

Trans-NIH Strategic Plan for Women's Health Research and Emerging Strategic Priorities

Guiding Tomorrow's Research on Women's Health

In September 2010, ORWH released a trans-NIH strategic plan for research on women's health, titled *Moving Into the Future with New Dimensions and Strategies: A Vision for 2020 for Women's Health Research* (ORWH, NIH, HHS, 2010a; ORWH, NIH, HHS, 2010b; ORWH, NIH, HHS, 2010c). The research agenda

3. NOT-OD-18-116: NIH Policy and Guidelines on the Inclusion of Individuals Across the Lifespan as Participants in Research Involving Human Subjects (https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-116.html).

4. This requirement does not apply to NIH-defined Phase III trials not considered "applicable" clinical trials under 42 CFR Part 11.

was informed by input from the scientific community and public partnerships, including patient and advocacy groups. This strategic plan comprises three volumes—including an executive summary, reports from regional scientific workshops, and public testimony. The document served as a framework for research investigations galvanized by cutting-edge technologies and emerging scientific concepts to advance women's health research through collaborations among disciplines and across the research spectrum, from basic to clinical to translational (Pinn, Clayton, Begg, & Sass, 2010). In addition to providing a framework for research on the health of women across the ICOs, it guided all ORWH activities, ensuring that resources capitalized on opportunities for advancing scientific research and career objectives for women in biomedical professions.

The research agenda comprised the following cross-cutting goals, each containing several objectives:

- Increase the study of sex differences in basic biomedical and behavioral research.
- Incorporate findings of sex differences in the design of new technologies, medical devices, and therapeutic drugs.
- Actualize personalized prevention, diagnostics, and therapeutics for women and girls.
- Create strategic alliances and partnerships to maximize the domestic and global impact of women's health research.
- Achieve a clearer understanding of women's health issues through strategic communication of research findings to diverse audiences.
- Employ innovative strategies to build a well-trained, diverse, and vigorous women's health research workforce.

On February 25, 2019, ORWH released *Advancing Science for the Health of Women: The Trans-NIH Strategic Plan for Women's Health Research*, which provides a framework to coordinate NIH efforts from 2019 through 2023 to advance the health of women through science. This plan is the result of an ORWH-led NIH-wide effort, and it highlights five strategic goals essential to supporting research efforts and improving the health of women:

- Advancing rigorous research that is relevant to the health of women.
- Developing methods and leveraging data sources to consider sex and gender influences that enhance research for the health of women.
- Enhancing dissemination and implementation of evidence to improve the health of women.
- Promoting training and careers to develop a well-trained, diverse, and robust workforce to advance science for the health of women.
- Improving evaluation of research that is relevant to the health of women.

Read the entire 2019–2023 strategic plan at https://orwh.od.nih.gov/sites/orwh/files/docs/ORWH_Strategic_Plan_2019_508C_0.pdf.

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II. ORWH Research

Introduction: Research Mission

The National Institutes of Health (NIH) Office of Research on Women's Health (ORWH) has a straightforward objective: to put science to work for the health of women. ORWH was the first Public Health Service office dedicated specifically to promoting women's health research within and beyond the NIH scientific community. Since its establishment in 1990, ORWH has pursued this far-reaching mandate on multiple fronts: enhancing and expanding women's health research, ensuring that women and minority groups are included in clinical research, and promoting career advancement for women in biomedical careers.

ORWH is well positioned to drive progress in these areas as part of the Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI) within the NIH Office of the Director. It executes its research mission by implementing the Trans-NIH Strategic Plan for Women's Health Research, chairing the NIH Coordinating Committee on Research on Women's Health, and co-funding research initiatives with other NIH Institutes, Centers, and Offices (ICOs).

ORWH supports and advances rigorous research that is relevant to the health of women in several ways. First, it works with ICOs to design scientific initiatives and co-funds research to strengthen and enhance our knowledge of diseases, disorders, and conditions that predominantly or exclusively affect women. Second, it analyzes the health landscape and NIH research portfolio to ensure the research conducted and supported by NIH adequately addresses issues regarding women's health. Third, it coordinates with ICOs to ensure women and members of underrepresented communities are represented appropriately in biomedical and biobehavioral research studies supported by NIH. ORWH also raises awareness of topics important to women's health by engaging with professional societies around the world, disseminating scientific content, developing instructional materials, and participating in community outreach activities.

Another major goal of ORWH's work is to ensure NIH-funded research accounts for sex as a biological variable (SABV). ORWH leads programs to promote the integration of sex and gender throughout the entire research continuum, from basic to translational to clinical studies. It also develops interdisciplinary initiatives to stimulate research on sex and gender differences across a wide range of biological topics. ORWH creates resources to advise the research community on how to design and implement a sex-aware research program. These efforts all strive to make studies more rigorous, reliable, relevant, and transparent so they can provide knowledge that can ultimately benefit the health of everyone.

ORWH partners with ICOs across NIH to support programs focused on the recruitment, retention, re-entry, and advancement of women in biomedical careers. Its career development initiatives also provide career support to help launch promising researchers in the field of women's health; these collaborations effectively strengthen the diversity of the biomedical workforce. The ORWH Director co-chairs the NIH Working Group on Women in Biomedical Careers, which develops and supports such efforts. Along with other activities, ORWH continues to lead a successful Building Interdisciplinary Research Careers in Women's Health (BIRCWH) program, a mentored career-development program designed to connect junior faculty, known as BIRCWH Scholars, to senior faculty with shared interest in women's health and sex differences research.

ORWH's research mission is reinforced by the 21st Century Cures Act (Public Law 114–255), which was signed into law on December 13, 2016. Notably, the act requires consistent dialogue between ORWH and the ICOs. ICO directors must consult with the ORWH Director annually to discuss how their mission objectives consider the health of women and how they plan to reduce health disparities in populations of women, and each ICO's strategic plan must document these priorities. The Coordinating Committee on Research on Women's Health, established by the NIH Revitalization Act of 1993 (Public Law 103–43), is charged with developing and implementing NIH activities in support of the health of women, and its members must be senior-level ICO staff members or their designees. The 21st Century Cures Act also mandates that applicable Phase III clinical trials report their results by sex and/

or gender and by race and ethnicity in ClinicalTrials.gov, and it expands the NIH inclusion policy to individuals of all ages. Implementation of the requirements set forth in the 21st Century Cures Act will achieve a major milestone in women's health by ensuring the challenges facing women are priorities for NIH and that women of all racial and ethnic backgrounds and of all ages are appropriately represented in federally funded clinical research.

Driving the NIH Research Agenda on the Health of Women

NIH is committed to improving the health outcomes of men and women through support of rigorous science that advances fundamental knowledge about the nature and behavior of living systems. Sex and gender play a role in how health and disease processes differ across individuals. ORWH supports science in partnership with NIH's 27 Institutes, Centers, and Offices (ICOs) to inform the development and testing of preventive and therapeutic interventions to pave the way for better health for women. By expanding the knowledge base on female biology across all levels of research, the scientific field benefits in the following ways: Scientists have more complete data from which to derive insights and interpret their results; published information is more rigorous and transparent; clinicians have a deeper understanding of the influence of sex and gender on disease prevalence, course, treatment, and outcomes; and women and girls can access more accurate guidance on how to monitor and maintain their health. ORWH fulfills this commitment to women's health by focusing on topics that disproportionately or exclusively affect women and by partnering with ICOs to fund research that addresses unmet needs in the women's health research landscape. Successful ORWH research initiatives include the Specialized Centers of Research Excellence (SCORE) on Sex Differences program, the Building Interdisciplinary Research Careers in Women's Health (BIRCWH) program, and the U3 Administrative Supplement Program, which supports interdisciplinary research on populations of women that are understudied, underrepresented, and underreported (U3) in biomedical research. ORWH also provides administrative supplements for research on sex and gender differences and created a unique research program for studies to examine the intersection of sex and gender influences on health and disease (RFA-OD-19-029). This new program builds on prior investments and initiatives related to sex and gender and is NIH's first investigator-initiated, disease-agnostic R01 on sex and gender. It is an important advancement that reaffirms NIH's commitment to the ORWH mission.

In addition to research initiatives in collaboration with ICOs, ORWH develops and disseminates a wide variety of resources highlighting topical issues in women's health.

Increasing Consideration of Sex as a Biological Variable in Preclinical Research

Biomedical research has historically discounted the importance of sex differences, assuming instead that meaningful distinctions between males and females are restricted to reproductive functions. As a result, most studies have focused on male animals, ignored sex as a biological variable, and failed to compare males and females when data from both were available. ORWH and NIH are dedicated to filling the gap in knowledge that remains. Both are working to expand the scope of biomedical research to account for sex as a biological variable and to explore the influence of sex and gender on health and disease.

A major goal outlined in NIH's 2019–2023 strategic plan for women's health research, *Advancing Science for the Health of Women: The Trans-NIH Strategic Plan for Women's Health Research*, is to learn more about basic female biology, physiology, and pathology. Closing the sex gap in knowledge of basic animal and cell model systems is critical to gaining an accurate understanding of biological processes and pathways, and it will be essential to translating information into new therapies that can be tailored to individuals. ORWH is at the forefront of NIH-wide efforts to ensure studies appropriately consider sex as a biological variable (SABV), with the goal of creating a rigorous and transparent scientific enterprise in which experiments are reproducible and beneficial to all (NOT-OD-15-103).

NIH described its intentions for the SABV policy in the notice titled *Consideration of Sex as a Biological Variable in NIH-funded Research* (NOT-OD-15-102):

"NIH expects that sex as a biological variable will be factored into research designs, analyses, and reporting in vertebrate animal and human studies. Strong justification from the scientific literature, preliminary data, or other relevant considerations must be provided for applications proposing to study only one sex." The policy went into effect in January 2016; therefore, grant applications must now describe how they will address SABV, and study sections must assess the adequacy of their plans when they review applications.

ORWH has led the charge in urging greater consideration of SABV in animal and cell studies funded by ICOs, and it continues to support efforts to make its implementation successful. For example, in FY 2013 ORWH began providing administrative supplements for research on sex and gender influences to enhance the rigor and reproducibility of NIH's portfolio by providing funds for investigators to add a sex and gender component to existing research projects.

ORWH has also sought to enhance the impact of the SABV policy through engagement with internal and external stakeholders. ORWH leads the Trans-NIH SABV Working Group, which includes senior representatives from ICOs and provides a forum for ICO staff members to describe their respective ICOs' approaches to SABV. These interactions are instructive because every discipline has unique circumstances, health conditions, and research methodologies to consider, and ICOs are encouraged to integrate sex and gender into their programs as they see fit. The working group disseminates information on new SABV practices to the ICOs, biomedical research community, and public through symposia and online tools, including the ORWH and Office of Extramural Research websites. Moreover, ORWH created and chairs the NIH scientific interest group (SIG) called Sex and Gender in Health and Disease (SGHD), which explores the range of ways SABV applies to different scientific disciplines. The SGHD SIG brings together NIH intramural scientists and extramural scientists from academic and other research institutions to foster interdisciplinary collaborations that develop new ways to investigate the influences of sex and gender on health and disease.

To complement its other efforts to incorporate SABV into the biomedical research enterprise, NIH released a funding opportunity announcement (FOA) in 2019 titled *The Intersection of Sex and Gender Influences on Health and Disease* (RFA-OD-19-029). This FOA is NIH's first investigator-initiated, disease-agnostic R01 on the influences of sex and gender on health and disease. It encourages research across many scientific disciplines, with the stipulation that proposals must include both sex- and gender-related variables and must address at least one of the five objectives from Strategic Goal 1 of the 2019–2023 Trans-NIH Strategic Plan for Women's Health Research (i.e., advance rigorous research that is relevant to the health of women). The first year of this 3-year initiative saw applications from new as well as established investigators that covered a broad spectrum of research disciplines.

In FY 2020, ORWH developed free online courses to educate health science professionals about the myriad ways sex and gender can influence health and disease and to highlight important aspects of the SABV policy:

- Bench to Bedside: Integrating Sex and Gender to Improve Human Health: Developed by ORWH in partnership with the Food and Drug Administration Office of Women's Health, this course explores sex- and gender-related differences in key disease areas: immunology, cardiovascular disease, pulmonary disease, neurology, endocrinology, and mental health. It provides biomedical researchers, clinicians, and students in the health professions with knowledge they can apply when designing and conducting research and/or interpreting evidence for clinical practice.
- Sex as a Biological Variable: A Primer: Developed by ORWH with funding from the National Institute of General Medical Sciences and the NIH Office of the Director, this course includes four modules that will help investigators understand and apply the SABV policy in research design, analyses, and reporting. It addresses basic, preclinical, clinical, and population health studies. ORWH is also currently creating a supplementary video series that will highlight SABV in ongoing ORWH-funded research.
- Introduction: Sex- and Gender-Related Differences in Health: This self-paced introductory training course is aimed at researchers, clinicians, and policymakers. It includes a downloadable slide deck that people may incorporate into their own presentations and a "Facilitator's Guide," which will help individuals and teams initiate dialogue about how—and why—to incorporate a sex-and-gender lens into research and clinical care.

These tools and resources are targeted to the scientific community, including investigators and their trainees; clinicians; editors, publishers, and reviewers; professional associations and scientific societies; and other private and Federal partners. Within NIH, tools and resources are also being developed to evaluate SABV policy implementation in the business practices that support research funding.

The ORWH website includes additional information on women's health research and the SABV policy, and it contains highlights from research symposia, workshops, and seminars; highlights from presentations at national and international meetings and roundtables; and journal editor guidelines.

Specialized Centers of Research Excellence on Sex Differences

The Specialized Centers of Research Excellence (SCORE) on Sex Differences program is a signature program of ORWH. It supports disease-agnostic research on sex differences, with a special focus on interdisciplinary and translational projects. To understand the diversity of health outcomes, scientists must consider the contributions of sex to all biological processes. Knowledge generated from studies that account for sex can be applied to the development of new interventions and medical treatments that will improve women's health. ORWH uses the SCORE program to advance research on sex differences, and it coordinates interactions across SCORE sites by working strategically with NIH Institutes, Centers, and Offices (ICOs) to fund new research.

Each center in the SCORE program serves as a national resource for translational research, at multiple levels of analysis, to identify the role of biological sex differences in the health of women. These NIH-supported Centers of Excellence are vital hubs for research on sex and gender that also provide pilot funding, training, and education. SCORE investigators provide leadership in the development and promotion of standards and policies for the consideration of sex as a biological variable (SABV) and sex differences in biomedical research. They identify the contributions of biological sex to health outcomes and apply this knowledge to the development of the next generation of interventions and medical treatments, leading to improvements in women's health.

The SCORE program is now a cooperative agreement (U54 grant mechanism) that leverages over 15 years of NIH investments in sex differences research. Prior to 2018, ORWH led the Specialized Centers of Research (SCOR) on Sex Differences program (P50 grant mechanism) with support from its ICO partners to fund established scientists across the country. Their basic, translational, and clinical research projects led to seminal discoveries on the role of sex in health. Now, with SCORE being NIH's only center program supporting disease-agnostic research on sex differences, ORWH encourages SCORE investigators to communicate and collaborate with one another, to pursue integrative projects that enlist the expertise of others, and to teach a new generation of scientists how to design and carry out sex-aware research. To implement this vision, each center in the SCORE program has three highly integrated, synergistic research projects and an administrative core. The SCORE U54 sites also have a Career Enhancement Core, which supports pilot research and trains early-career scientists in the study of

sex differences. As NIH-supported Centers of Excellence, the SCORE sites help lead the development of standards for considering sex in biomedical research and serve as important resources to develop and train a new generation of scientists.

In FY 2018, ORWH published a request for applications (RFA) titled *Specialized Centers of Research Excellence (SCORE) on Sex Differences (U54 Clinical Trial Optional)* (RFA-OD-18-004). In that year, ORWH co-funded six grants, totaling $9.25 million, with three ICO partners (the National Institute on Aging [NIA], the National Institute on Drug Abuse, and the National Institute of Diabetes and Digestive and Kidney Diseases [NIDDK]). In FY 2019, ORWH reissued the RFA (RFA-OD-19-013) to support additional centers and co-funded five grants, totaling $8.51 million, with NIA, NIDDK, and the National Institute on Alcohol Abuse and Alcoholism. In FY 2020, NIH invested $17.76 million to support disease-agnostic sex differences research.

Administrative Supplements for Research on Sex and Gender Influences

In 2001, the Institute of Medicine published a report titled *Exploring the Biological Contributions to Human Health: Does Sex Matter?*, which highlighted the fact that women and men are characterized by both sex and gender. In this report, "sex" referred to being male or female based on reproductive organs and biological functions assigned by chromosomal complement. "Gender" referred to socially defined and derived expectations and roles rooted in biology but shaped by the environment and experience. Sex and gender, as defined above, are important considerations in many areas of research, including basic biological, psychological, social, and behavioral studies. Consideration of these variables is critical to the accurate interpretation and validation of research findings that affect various aspects of women's health.

In FY 2013, ORWH initiated an NIH-wide program to catalyze exploratory research on sex and gender differences by providing administrative supplements to existing peer-reviewed NIH-funded grants (PA-13-018). The administrative supplements provided 1-year awards of approximately $100,000 to support research projects that fell within the scope of the original parent grants. The initiative advanced research on sex and gender influences—predating the NIH SABV policy, which was issued in June 2015 (NOT-OD-15-102, NOT-OD-15-103).

The sex and gender administrative supplements program supports three research approaches: (1) adding the opposite sex/gender (the addition of animal or human subjects, tissues, or cells of the sex opposite to that used in the parent grant to allow sex- and gender-based comparisons); (2) increasing sample size (the addition of more animal or human subjects, tissues, or cells to a sample that already includes both males and females to increase the power of a study to analyze for sex or gender differences); and (3) analyzing existing data (comparative analyses of extant samples/datasets/databases and/or data mining to investigate the role of sex and gender).

In FY 2019 (PA-19-165), ORWH awarded 26 of 75 (34.67%) applications, for a total of $3.8 million, across 15 NIH Institutes, Centers, and Offices (ICOs). In FY 2020 (NOT-OD-20-049), ORWH awarded 14 of 30 (46.67%) applications, for a total of $2.01 million, across 10 ICOs. Since the inception of this program in FY 2013, ORWH has invested $38.87 million to support 383 investigators across many ICOs to explore sex and gender influences in preclinical and clinical studies.

Research on the Health of Women in Understudied, Underrepresented, and Underreported (U3) Populations

In 2017, ORWH published a funding opportunity announcement about administrative supplements for exploring health issues at the intersection of co-occurring contextual factors in women from populations that have been understudied and underrepresented in biomedical research and that have often been underreported in surveillance activities, known as U3 populations (PA-17-101). The U3 Administrative Supplement Program supports interdisciplinary, transdisciplinary, and multidisciplinary research focused on interactions between sex/gender and other social factors, including race and ethnicity, socioeconomic status, education, health literacy, and socioecological

contexts that can affect health and illness. Projects funded under this program must include a focus on one or more NIH-designated health disparity populations, which include Blacks/African Americans, Hispanics/Latinos, American Indians/Alaska Natives, Asian Americans, Native Hawaiians and other Pacific Islanders, socioeconomically disadvantaged populations, underserved rural populations, and sexual and gender minorities (SGMs). Projects that include more than one of these populations are encouraged.

ORWH collaborates with NIH Institutes, Centers, and Offices to identify gaps in knowledge on U3 populations of women that would benefit from an interdisciplinary research approach. The U3 funding opportunity announcement was reissued in FYs 2019 and 2020, and the program has expanded since its inception, funding diverse research topics. Projects funded in FY 2019 focused on understanding, addressing, and reducing health disparities related to cardiovascular disease, diabetes, cancer, and mental health; others investigated the impact of novel disease prevention methods, including pre-exposure prophylaxis (PrEP) uptake. In FY 2020, funded projects focused on understanding multiethnic differences in severe maternal mortality and perinatal risk, breast and uterine cancers, and lung health epigenetics.

ORWH published a notice of change in 2020 to inform potential applicants that the program would support research on SARS-CoV-2 and COVID-19. Potential topics of interest included methods to accelerate relevant technologies, practices to implement effective therapeutics and vaccines, and ways to mitigate unequal infection vulnerability and disease severity in populations that experienced health disparities before the pandemic.

In support of the U3 supplement goals, ORWH also created the U3 Women's Health Lecture Series. The dynamic seminars have included presentations on improving chronic disease outcomes through approaches that address social determinants; research gaps and opportunities to meet the health challenges of SGM women; reproductive health care for incarcerated populations; and links between housing instability and HIV/sexually transmitted infection risk. The series continues to stimulate interest and generate dialogue on the complex issues affecting the health of women.

As of the end of the reporting period, 59 supplements had been awarded, for a total investment of $10,737,169; over 80% of NIH Institutes and Centers participated. Research sponsored by the U3 program will advance the science of women's health and increase the availability of responsive multilevel interventions that effectively align with the needs of women from all backgrounds. ORWH will continue to pursue collaborations across NIH to co-fund meritorious and high-impact research designed to promote health equity and account for intersections among social determinants of health.

ORWH R56 Program

The High Priority, Short-Term Project Award (R56; NOT-OD-04-047) was an NIH-wide program that ORWH utilized to fund high-priority research on women's health and sex and gender influences on human health and disease with its NIH Institute, Center, and Office (ICO) partners. Investigators could not apply for R56 grants; rather, participating ICOs applied to ORWH for R56 co-funding to support innovative new or competing renewal applications relevant to women's health that received priority scores just outside their respective funding limits. Investigators who received R56 short-term grant support for 1 to 2 years thus had an opportunity to improve their research proposal to enhance the possibility of funding in the highly competitive peer-review environment.

Three offices within the Division of Program Coordination, Planning, and Strategic Initiatives jointly sponsored the R56 program: ORWH, the Office of Dietary Supplements, and the Office of AIDS Research. This collaboration greatly enhanced the breadth, depth, and range of research topics of mutual interest available to ICOs.

In FY 2019, ORWH supported five applications from four ICOs: the National Cancer Institute (two); the National Heart, Lung, and Blood Institute; the National Institute of Mental Health; and the National Institute of Nursing Research. In FY 2020, ORWH discontinued its participation in the program, in part because of a decline in the number of R56 applications it received as ICOs renewed their focus on funding at-risk investigators as part of NIH's Next Generation Researchers Initiative (NOT-OD-17-101).

R56 Grants (FY 2019)

ORWH awarded $1,177,091 for the following applications:

1. Liu, R. Utilizing microRNA-146a to block triple-negative breast cancer cell colonization. University of Alabama at Birmingham, Birmingham, AL. 1R56CA223077-01A1.
2. Eisenmesser, E.Z. Identifying the missing link in inflammatory signaling. University of Colorado Denver, Denver, CO. 1R56CA230069-01A1.
3. Khalil, R.A. Vascular mechanisms of hypertension-in-pregnancy. Brigham and Women's Hospital, Boston, MA. 1R56HL147889-01.
4. Dale, S.K. Monitoring microaggressions and adversities to generate interventions for change (MMAGIC) for Black women living with HIV. University of Miami, Coral Gables, FL. 1R56MH121194-01.
5. Himes, K.P. Healthy beyond pregnancy: Leveraging behavior economics to improve postpartum care. Magee-Womens Research Institute and Foundation, Pittsburgh, PA. 1R56NR017933-01A1.

Grant # 1R56CA223077-01A1

Title: Utilizing microRNA-146a to Block Triple-Negative Breast Cancer Cell Colonization

Triple-negative breast cancer (TNBC) remains a highly aggressive and fatal subtype of breast cancer, with the highest mortality in young women in underserved racial and ethnic groups. This subtype of breast cancer has the worst prognosis because of limited treatment options and its aggressive and highly metastatic nature. This study focuses on the validation of the lipid nanoparticles' (LNPs) anti-metastasis efficacy and the effect on circulating tumor cells in two syngeneic mouse models and incorporates characterization of the LNPs' toxicity and tissue distribution *in vivo*, using imaging, histopathology, and target gene expression profiling approaches. The data from this study will not only provide a novel therapeutic approach to block tumor metastasis in TNBC but also identify a new molecular mechanism responsible for tumor metastasis and could lead to a first-in-human clinical trial.

Grant # 1R56CA230069-01A1

Title: Identifying the Missing Link in Inflammatory Signaling

The Nobel Prize–winning discoveries of toll-like receptors (TLRs) and interleukin-1 receptors (IL-1Rs) have revolutionized our understanding of inflammation and oncogenesis. Specifically, both receptor families share common intracellular toll/interleukin-1 receptor (TIR) domains that engage adaptor TIR domains in order to initiate signaling; however, no human oligomeric TIR complex has been structurally observed, despite the nearly two decades since the first structural characterization of the TIR domains of TLR1 and TLR2 receptors. This study seeks to uncover the molecular mechanisms that underlie the critical roles of TIR signaling. To understand how TIR domains govern downstream events and ultimately modulate immunity, this study has developed a unique method to recombinantly produce and isolate TIR complexes in order to probe their characteristics at a molecular level. The observation of homodimer and heterodimer formation is suggestive of other signaling mechanisms that also form signaling complexes at the cellular membrane. Utilizing a combination of biochemical, biophysical, and biological studies, the molecular basis of TIR domain interactions that underlie the innate immune response can thus be identified and studied, thereby bridging the initiating events on the outside of the cell with downstream events that drive inflammation. Such studies could provide a basis for pharmacologically blocking TLR interactions through targeting at the molecular level.

Grant # 1R56HL147889-01

Title: Vascular Mechanisms of Hypertension-in-Pregnancy

Preeclampsia is a complication of pregnancy characterized by hypertension and intrauterine growth restriction. Preclinical studies in animals have shown that there is a reduction of uterine perfusion pressure in pregnancy associated with reduced vasodilation, increased vasoconstriction hypertension, and intrauterine growth restriction linked to increases in anti-angiogenic factor sFlt-1 and inflammatory cytokine TNF-α. Also, infusion of sFlt-1 or TNF-α in this model decreases vascular relaxation and increases vasoconstriction, blood pressure, and intrauterine growth restriction. The vascular and uterine targets

and cellular mechanisms, however, are unclear, with limited remedies. Normal pregnancy involves extensive uteroplacental and vascular remodeling, and matrix metalloproteinases (MMPs) and the related a disintegrin and metalloprotease (ADAM) family maintain adequate tissue remodeling. Animal models have also shown that disruption of the vasodilator/vasoconstrictor MMP balance results in inadequate uteroplacental remodeling, decreased vasodilation, increased vasoconstriction, and hypertension seen in pregnancy. This project tests the hypothesis that an imbalance, specifically between vasodilators MMP-2 and MMP-9 and vasoconstrictors MMP-1 and MMP-7, is a major mechanism of inadequate uteroplacental remodeling and the vascular dysfunction characteristic of hypertension in pregnancy. Consequently, correcting MMP imbalance by upregulating vasodilators MMP-2 and MMP-9 or downregulating vasoconstrictors MMP-1 and MMP-7 should improve uteroplacental remodeling, promote vasodilation, and reduce vasoconstriction and hypertension in pregnancy. Findings from this study will provide information on the cellular mechanisms underlying preeclampsia in pregnancy and provide a new approach for the management of preeclampsia.

Grant # 1R56MH121194-01

Title: Monitoring Microaggressions and Adversities to Generate Interventions for Change (MMAGIC) for Black Women Living with HIV

Increasing viral suppression rates among Black women living with HIV (BWLWH) (42% unsuppressed) is necessary to decrease HIV transmission. However, research has not rigorously examined whether microaggressions affect their viral suppression, daily stressors, depression diagnosis, care barriers, or antiretroviral therapy (ART) adherence. Gendered racial microaggressions experienced by BWLWH significantly predict post-traumatic stress disorder symptoms, depression diagnosis, barriers to care, and ART adherence, and those microaggressions contribute uniquely to these outcomes above and beyond race- and HIV-related discrimination and macroaggressions. The longitudinal cohort study among BWLWH examines how microaggressions and other adversities affect HIV viral suppression mediated by mental health symptoms and health behaviors and potentially moderated by resilience factors. The researchers test how recurring trauma and violence experienced both directly and vicariously (e.g., violence against a relative) by BWLWH negatively predicts HIV viral suppression mediated by mental health symptoms and health behaviors. The impact of microaggressions, macroaggressions, and trauma on mental health and HIV-related outcomes is an important scientific and public health issue, particularly for women. Longitudinal data are needed to shed light on how microaggressions and other adversities affect HIV viral suppression among BWLWH as mediated by mental health symptoms/diagnosis (e.g., trauma symptoms, depression) and health behaviors (e.g., adherence to and engagement in care) and potentially moderated/buffered by resilience factors at the individual (e.g., self-efficacy), interpersonal (e.g., social support), and neighborhood (e.g., domestic violence shelters) levels. Findings from this study will advance knowledge in this area, elucidating the pathways through which microaggressions and other adversities affect viral suppression and directly inform interventions.

Grant # 1R56NR017933-01A1

Title: Healthy Beyond Pregnancy: Leveraging Behavior Economics to Improve Postpartum Care

There are profound economic inequalities in a wide range of essential maternal and child health outcomes, ranging from neonatal death to maternal morbidity and mortality. The disparity in rates of postpartum care demonstrates that the current care model does not engage all women and disproportionately fails our most vulnerable mothers and babies. This study's overarching scientific premise is that these inequalities stem from poor postpartum care engagement by economically disadvantaged women. The intervention will improve compliance with the postpartum visit and promote equality in maternal–child health outcomes. Researchers have designed an innovative, scalable, and affordable web-based solution: Healthy Beyond Pregnancy. Healthy Beyond Pregnancy uses proven tenets of behavioral economics to target two critical behavioral change drivers: awareness and willingness. The four cornerstones of this program are (1) combating information overload with a personalized approach to postpartum education and care, (2) overcoming self-control issues by formalizing the postpartum visit with a commitment contract, (3) addressing limited attention and increasing awareness by nudging women in the immediate postpartum period via automated text messaging, and (4) incentivizing completion of the postpartum visit. This study will also conduct

a pilot trial to determine whether Healthy Beyond Pregnancy improves important postpartum health outcomes, including uptake of effective contraception, breastfeeding duration, and linkage of care after cardiometabolic pregnancy complications.

The Intersection of Sex and Gender Influences on Health and Disease (R01 Clinical Trial Optional)

In FY 2019, ORWH released a funding opportunity announcement (FOA) titled *The Intersection of Sex and Gender Influences on Health and Disease* (RFA-OD-19-029). This initiative builds on prior investments in sex and gender research and represents an important milestone as NIH's first investigator-initiated, disease-agnostic R01 on sex and gender.

The FOA solicits research to target gaps in knowledge regarding the influence and intersection of sex and gender on disease conditions to improve understanding of the factors and mechanisms underlying sex differences in health. The announcement solicits (1) research applications that examine sex and gender factors and their intersection in understanding health and disease and (2) research that addresses one of the five objectives from Strategic Goal 1 of the 2019–2023 Trans-NIH Strategic Plan for Women's Health Research. Sex- and gender-based factors are defined below.

- **Sex-based factors:** biological variables defined by characteristics encoded in DNA, such as reproductive organs and other physiological and functional characteristics (see NOT-OD-15-102).
- **Gender-based factors:** social, environmental, cultural, and behavioral factors, including individual gender identity and the choices that influence a person's self-identity and health (Clayton and Tannenbaum, 2016, https://jamanetwork.com/journals/jama/fullarticle/2577142).

Applications submitted in response to this FOA are also encouraged to consider health disparities and life course/lifespan factors influencing sex and gender.

Twelve NIH Institutes, Centers, and Offices (ICOs) are participants on the announcement: the National Center for Complementary and Integrative Health; the National Human Genome Research Institute; the National Heart, Lung, and Blood Institute; the National Institute on Aging; the National Institute on Alcohol Abuse and Alcoholism; the National Institute of Allergy and Infectious Diseases (NIAID); the National Institute on Drug Abuse (NIDA); the National Institute of Dental and Craniofacial Research; the National Institute of Environmental Health Sciences (NIEHS); the National Institute of Mental Health; the National Institute of Nursing Research; and the Sexual and Gender Minority Research Office.

In FY 2019, ORWH received 48 grant applications, of which, following review, eight meritorious applications were funded in FY 2020, totaling $4.1 million; seven of these awards were co-funded by ORWH and two participating ICOs (NIAID and NIEHS) in FY 2020.

In FY 2020, ORWH expanded the R01 program (NOT-OD-20-168) to include research on the influence and intersection of sex and gender factors related to SARS-CoV-2 or COVID-19. Topics of interest include sex- and gender-related risk factors associated with COVID-19 prevalence, prevention, and treatment; with the influence of comorbid conditions; and with health-seeking behaviors, access to health care, and health care systems.

COVID-19

According to the World Health Organization (WHO), on December 31, 2019, China reported a cluster of cases of viral pneumonia in the city of Wuhan, which is the capital of the central Hubei province (https://www.who.int/emergencies/diseases/novel-coronavirus-2019/interactive-timeline#event-0). Soon after, similar cases were reported in other nations, and the spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was declared a pandemic on March 11, 2020. As of the end of FY 2020 (September 30, 2020), more than 34 million people around the world had been infected and 1.015 million people had died; in the U.S., there had been over 7.2 million confirmed cases and 207,090 deaths (https://coronavirus.jhu.edu). The pandemic has disproportionately affected marginalized communities, with Black, Hispanic, and American Indian/Alaska Native populations experiencing the highest rates of COVID-19 infection, hospitalization, and mortality (https://pubmed.ncbi.nlm.nih.gov/32706958).

Sex and gender affect COVID-19 outcomes (https://pubmed.ncbi.nlm.nih.gov/32450906, https://pubmed.ncbi.nlm.nih.gov/32384135), and the NIH Policy on Sex as a Biological Variable (SABV) can guide the process of how to appropriately evaluate risk, disease progression, and outcomes for COVID-19 patients in a way that will inform development of treatments and vaccines. Prior to the pandemic, researchers had identified sex differences in susceptibility and outcomes to pathogenic human coronaviruses, including the severe acute respiratory syndrome coronavirus responsible for the SARS epidemic in 2002 and 2003 (https://pubmed.ncbi.nlm.nih.gov/28373583). Similar observations have been made with COVID-19, with generally worse outcomes in men than in women (https://pubmed.ncbi.nlm.nih.gov/32846427). The causes of sex differences in disease severity and mortality are complex and include differences in host cell vulnerability; interactions with steroid hormones; male predominance of comorbidities (e.g., cardiovascular disease, hypertension, and diabetes); immunity (https://pubmed.ncbi.nlm.nih.gov/32528136); disorders of the brain and heart (https://pubmed.ncbi.nlm.nih.gov/32639554); and other factors (https://pubmed.ncbi.nlm.nih.gov/32846427). Sex differences are also apparent in adaptive immune responses and can inform vaccine development (https://pubmed.ncbi.nlm.nih.gov/30455317). These findings make clear that incorporating sex into research on COVID-19 is essential to understanding the disease and developing effective interventions (https://pubmed.ncbi.nlm.nih.gov/32569293).

The COVID-19 pandemic has had a profound impact on women. Women have more occupational risk for infection because they are the majority of workers in health care, caregiving, child care, and teaching professions, and women of color are the most likely to have been laid off or furloughed since the pandemic began (https://www.bls.gov/news.release/archives/empsit_05082020.htm). Women in science, technology, engineering, mathematics, and medicine (STEMM) fields have experienced disproportionate decreases in productivity and publications because of larger increases in caregiving and other nonpaying responsibilities (https://pubmed.ncbi.nlm.nih.gov/32669671), an effect that could have long-lasting consequences in hiring, tenure, and promotion (https://pubmed.ncbi.nlm.nih.gov/32554503, https://pubmed.ncbi.nlm.nih.gov/32563275).

Other studies have found gender inequities in public health governance and decision-making related to the pandemic. Of 115 COVID-19 expert task forces, 85.2% were mostly composed of men, and only 3.5% had gender parity (https://pubmed.ncbi.nlm.nih.gov/33004348). Numerous studies have demonstrated that diversity benefits science and innovation (https://www.pnas.org/content/114/8/1740); therefore, current research efforts and health policy development stand to improve significantly from renewed focus on gender and racial representation, which could make the pandemic response more inclusive and equitable.

The COVID-19 pandemic has caused upheavals in nearly all aspects of life, and it has taken a toll on biomedical research as well. These disruptions have emphasized the importance of ORWH's mission, of NIH's policies on SABV and inclusion, and of equitable representation in STEMM fields and health policy management. ORWH has supported its mission-critical efforts in several ways, including:

1. Developing ORWH's strategic approach to the COVID-19 response.

   ORWH Director Janine A. Clayton, M.D., emphasizes short- and long-term strategies to successfully navigate the COVID-19 public health emergency.

2. Launching the Women, Science, and the Impact of COVID-19 webpage.

   COVID-19 has exposed gaps in our preparedness and mitigation measures. As a result, ORWH has developed a webpage to disseminate useful resources and information.

3. Expanding the scope of three of ORWH's funding opportunity announcements (FOAs) to include COVID-19-related research (administrative supplements for research on sex and gender influences, U3 administrative supplements, and the sex and gender R01).

4. Participating in many NIH COVID-19-related FOAs.

   ORWH participated in many COVID-19-related FOAs to provide scientific expertise relevant to women's health and promote inclusion of women's health into the scientific scope.

5. Supporting women in STEMM.

   Women in STEMM fields are facing difficulties related to their careers, their research, their families, and their mental and physical health because of the COVID-19 pandemic. Together with the Office of Extramural Research, ORWH has participated in efforts to mitigate the adverse effects of the pandemic on the career trajectories of the workforce, particularly those in their early careers. Continuing efforts by NIH can be found at this website: Coronavirus Disease 2019 (COVID-19): Information for NIH Applicants and Recipients of NIH Funding (https://grants.nih.gov/policy/natural-disasters/corona-virus.htm).

6. Developing guiding principles and an annotated digest and bibliography.

   Guiding Principles: Sex and gender influences in COVID-19 and the health of women (https://go.usa.gov/x7Rns)
   The COVID-19 pandemic underscores the need to systematically consider sex and social determinants of health, including gender, to strengthen our collective capacity to respond equitably to COVID-19 and any threats related to future outbreaks and pandemics. Accounting for sex without also accounting for gender (and other social determinants of health) would limit the development and deployment of effective, equitable diagnostics, treatments, and interventions that are relevant to the entire population.

   The COVID-19 Pandemic: Incorporating a Sex-and-Gender Lens (https://orwh.od.nih.gov/sites/orwh/files/docs/COVID19_AnnotBibliography_508C.pdf)
   ORWH Response to the COVID-19 Pandemic: Incorporating a Sex-and-Gender Lens is a digest and annotated bibliography of relevant publications and provides NIH staff members, researchers, and the extramural community with curated background content, research frames, and resources related to sex and social determinants of health to facilitate alignment of the NIH response with the Trans-NIH Strategic Plan for Women's Health Research. It covers 14 topics: sex differences; gender's role in the COVID-19 pandemic; racial and ethnic disparities; sexual and gender minority populations; intimate partner violence; pregnancy, breastfeeding, and reproductive health; stress, trauma, and resilience; comorbidities and underlying conditions; the workforce; child care and caregiving; rural women; incarcerated populations; people experiencing homelessness or housing instability; and stigma and bias.

7. Participating in various NIH research initiatives and activities, such as Rapid Acceleration of Diagnostics (RADx); the Community Engagement Alliance Against COVID-19 Disparities (CEAL); the NIH Pediatric Research Consortium's (N-PeRC) Maternal Child Health subgroup; the Research, Condition, and Disease Categorization (RCDC) System; and the Trans-NIH Social, Behavioral, and Economic (SBE) Impacts of COVID-19 Working Group.

   RADx
   NIH launched the RADx initiative to stimulate innovation in the development, commercialization, and implementation of technologies for COVID-19 testing. Accurate, fast, easy-to-use, and widely accessible testing is required for the Nation to safely return to normal life. The RADx initiative has four programs: (1) RADx Tech, (2) RADx Underserved Populations (RADx-UP), (3) RADx Radical (RADx-rad), and (4) RADx Advanced Technology Platforms (RADx-ATP). ORWH scientific staff members participated in RADx-UP and RADx-rad programs.

   - **RADx-UP**
     The overarching goal of the RADx-UP program is to improve care and outcomes among underserved and vulnerable populations that are disproportionately affected by the COVID-19 pandemic, including pregnant women. It funds research to examine SARS-CoV-2 infection patterns, programs to increase access to Food and Drug Administration–authorized COVID-19 diagnostic methods, and initiatives to improve care and outcomes for communities that have the highest infection rates and are at the greatest risk of suffering complications from COVID-19.

   - **RADx-rad**
     RADx-rad supports new, nontraditional approaches to addressing current gaps in COVID-19 testing, including rapid

detection devices and home-based testing technologies. The program also supports new or nontraditional applications of existing approaches to making them more usable, accessible, or accurate. These may lead to new ways of identifying SARS-CoV-2, as well as potential future viruses.

CEAL

The CEAL program provides trustworthy information through active community engagement and outreach to the people hardest hit by the COVID-19 pandemic, including African Americans, Hispanics/Latinos, and American Indians/Alaska Natives. Its long-term goal is to build long-lasting partnerships with communities, as well as improving diversity and inclusion in the research response to COVID-19. The program consists of State-based consortia (CEAL teams) in locations with disturbing trends in the numbers of confirmed cases of COVID-19, hospitalizations, and death rates, particularly among medically underserved racial and ethnic groups.

N-PeRC's COVID-19 Maternal Child Health subgroup

N-PeRC's COVID-19 Maternal Child Health subgroup aims to leverage the collective strength of the NIH Institutes, Centers, and Offices to accelerate research and better understand the impact of COVID-19 on pregnant women, lactating women, and child health.

RCDC

NIH uses this computerized reporting system to categorize its funding in medical research at the end of each fiscal year. RCDC provides consistent and transparent information to the public about NIH-funded research, providing a complete list of all NIH-funded projects related to each category. The "Coronavirus/COVID-19" category was added for reporting purposes to keep people informed about how their tax dollars are spent to support medical research.

Trans-NIH Social, Behavioral, and Economic (SBE) Impacts of COVID-19 Working Group

This working group identifies the effects of COVID-19 in health disparity populations and other vulnerable populations. The research proposed has the potential to expand knowledge about the use of digital health assessments and interventions to address the social, behavioral, and economic changes experienced by these populations.

8. Developing an intramural COVID-19 survey, an extramural individual COVID-19 survey, and an extramural institutional COVID-19 survey to query the scientific workforce and academic institutions.

   The activity was to help formulate the questionnaires for all three surveys groups—NIH intramural, NIH extramural, and extramural institutional communities—to understand the impact of COVID-19.

9. Creating the Coordinating Committee on Research on Women's Health COVID-19 Working Group.

   The charge of the working group is to identify and address gaps (sex and gender differences and women's health) in NIH research portfolios related to COVID-19.

10. Publishing blog posts and posting on social media.

    In a blog post, ORWH Associate Director for Science Policy, Planning, and Analysis Samia Noursi, Ph.D., discussed how COVID-19 seems to affect women and men differently (e.g., roughly equal rates of infection, greater mortality in men), as well as how gender roles have resulted in greater pandemic-related effects on women's work lives, finances, and domestic roles. These considerations warrant expanding the study of SABV and the ways the pandemic affects women.

    ORWH has posted COVID-19-related content on various social media platforms. From the beginning stages of the pandemic, ORWH shared Centers for Disease Control and Prevention (CDC) guidance for wearing face coverings, NIH and CDC information on the basic symptoms and what to do if sick, and funding opportunities for COVID-19 research. Additionally, ORWH highlighted data on COVID-19-related deaths; featured research and perspective in an article in volume 3, issue 3 of *Women's Health in Focus at NIH* titled "Will the Coronavirus Pandemic Affect Workplace Gender Equity?"; and promoted the NIH-Wide Strategic Plan for COVID-19 Research.

ORWH-Supported Pain Research Activities

Chronic pain is a debilitating symptom of many chronic diseases, and it disproportionally affects girls and women across the life course. Because addressing pain is so important to the health of women, the co-funding of meritorious pain initiatives is a significant component of the ORWH research portfolio. Common chronic pain conditions include headache, low back pain, fibromyalgia, cancer pain, arthritis, and endometriosis. These conditions often co-occur in an individual, and some may share common mechanisms. Overlapping chronic pain conditions occur more often in women than in men and include migraine, myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), endometriosis, fibromyalgia, inflammatory bowel disease, interstitial cystitis/bladder pain syndrome, temporomandibular joint disorders, and vulvodynia. They can be exacerbated by environmental and/or psychosocial factors. Research has documented differences in the development and persistence of pain conditions across the life course related to age, sex, gender, race, ethnicity, and socioeconomic status. To date, little is known about the long-term safety and effectiveness of pain medications for older adults, especially those with multiple health conditions or dementia. These knowledge gaps limit the effectiveness of pain management in older adults and hamper the ability to provide cost-effective and personalized pain care for the aging population.

During FYs 2019 and 2020, ORWH engaged in several important NIH pain research initiatives. ORWH is a member of the NIH Pain Consortium, a collaboration of 25 NIH Institutes, Centers, and Offices (ICOs) that identify, coordinate, and support pain research initiatives and activities. The consortium funds the Centers of Excellence in Pain Education (CoEPEs), which act as hubs for the development, evaluation, and distribution of pain management curricula resources for schools, including medical, dental, nursing, and pharmacy schools. ORWH was one of the original funders of these centers and continues its support. The CoEPEs website provides links to over 50 modules on pain education and includes additional modules that focus on prescription drug risks related to pain and opioid use.

In addition, ORWH representatives participated in the working group that developed the Federal Pain Research Strategy (FPRS). The FPRS addresses recommendations of the National Academy of Medicine to develop a long-term plan for the Federal research agenda in pain prevention, acute and chronic pain, the transition from acute to chronic pain, and disparities in pain. After the release of the FPRS in October 2017, the recommendations were widely disseminated to ICOs and other Federal agencies for use in their pain-related research agendas. The work of the FPRS continues through the Interagency Pain Research Coordinating Committee (IPRCC) and the National Institute of Neurological Disorders and Stroke (NINDS) Office of Pain Policy and Planning, which oversee development of a long-term strategic plan for those Federal agencies and departments that support pain research.

The National Center for Complementary and Integrative Health leads an interagency partnership, known as the NIH-DOD-VA Pain Management Collaboratory, which was funded in the fall of 2017. It includes ORWH, NINDS, the National Institute on Alcohol Abuse and Alcoholism, the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, the National Institute on Drug Abuse, the National Institute of Nursing Research, the U.S. Department of Defense (DOD), and the U.S. Department of Veterans Affairs (VA). This initiative prioritizes real-world research on nonpharmacological approaches to pain management and related conditions in military and veteran health care delivery organizations. Almost two-thirds of military veterans say they are in pain, and nearly 10% say the pain is severe. ORWH continues to provide co-funding to this collaboratory and participate in the oversight of research progress.

ORWH staff members also participate in the implementation of the National Pain Strategy (NPS). The NPS was developed in response to a request from the Assistant Secretary for Health in the U.S. Department of Health and Human Services, who asked the IPRCC to oversee its creation. Experts from a broad array of public and private organizations explored areas identified in the recommendations—population research, prevention and care, disparities, service delivery and reimbursement, professional education and training, and public awareness and communication. ORWH is currently co-chairing the effort to implement the provider education portion of the NPS, leveraging

the CoEPEs' effort (which included support from ORWH; https://coepes.nih.gov).

ORWH joined several NIH funding opportunity announcements (FOAs) that are part of the Helping to End Addiction Long-term℠ (HEAL) Initiative. Many of these funding opportunities will support research on chronic pain, ranging from basic research on the molecular, genetic, and biobehavioral basis of chronic pain to large-scale clinical studies of treatments. In some cases, wording was added to FOAs to encourage applications that will integrate sex as a biological variable in biomedical research on pain and opioid use disorders. In FY 2019, ORWH contributed $1 million to support the HEALthy Brain and Child Development (HBCD) Study, which is establishing a large cohort of pregnant women from regions of the country significantly affected by the opioid crisis, with plans to study them and their children for at least 10 years. The Adolescent Brain Cognitive Development (ABCD) Study is a longitudinal NIH-supported study of 10,000 children conducted at 21 sites across the U.S. This study aims to increase understanding of environmental, social, and biological factors (such as genetic factors) that affect brain and cognitive development. Sex and gender are ascertained, and data are being routinely disaggregated by sex/gender in the HBCD and ABCD studies. Findings from the ABCD cohort are improving our understanding of childhood brain development, as well as the long-term impact of prenatal and postnatal exposure to opioids and other drugs and environmental toxins. For example, sex differences in preadolescent neurodevelopment were reported by researchers utilizing ABCD data. Specifically, voxel-level analyses revealed that cerebellum and subcortical structures (including the hippocampus, amygdala, pallidum, and putamen) differed in size between girls and boys ages 8 and 9 years, increasing our understanding of sex-specific vulnerability or resilience to psychiatric disorders and sex-linked learning disabilities. Along with several other co-authors, ORWH's Rebecca DelCarmen-Wiggins, Ph.D., published a manuscript to serve as a methodological reference that describes the ABCD Study's use of the baseline neuroimaging processing and subject-level analysis methods. The HBCD Study will also examine maternal health over this critical period. Finally, also as part of the NIH HEAL Initiative, ORWH participates in the National Institute of Diabetes and Digestive and Kidney Diseases–led Hemodialysis Opioid Prescription Effort (HOPE) consortium to reduce hemodialysis pain without an overreliance on opioids. ORWH serves on the Data and Safety Monitoring Board and offers guidance in the development of clinical research protocols used in this trial.

Bladder Health Research

During FYs 2019 and 2020, the Prevention of Lower Urinary Tract Symptoms (PLUS) Research Consortium continued to receive support from ORWH and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). Lower urinary tract symptoms (LUTS) are common in women, resulting in significant but underrecognized effects on quality of life, as well as public health and financial burdens. Stigma around LUTS, along with the belief among many women that these conditions are inevitable, frequently results in unreported and therefore untreated symptoms. Many women adopt unhealthy coping behaviors, such as limiting their physical activity, restricting fluid intake, and isolating themselves socially.

The features that lead to having a "normal bladder"—i.e., healthy bladder function and behaviors that might promote bladder health over a lifetime—have yet to be identified. Additionally, efforts to delineate the causes of LUTS have focused primarily on biological factors, without sufficient consideration of the impact of behavior, the mind, mental functioning, cultural contributors, or social determinants of health. In response, PLUS has adopted the social–ecological model (SEM), which considers interactions between social context and biology across the lifespan and views health behaviors as determined by intrapersonal factors, interpersonal processes and primary groups, institutional factors, community factors, and public policy.

Framing the PLUS Research Consortium goals broadly as "bladder health" allows for the possibility that findings will affect the understanding and, ultimately, the prevention and clinical management of numerous urological conditions, including urinary incontinence, overactive bladder, interstitial cystitis/bladder pain syndrome, and urinary tract infections. The consortium is obtaining information from adolescents and women of various ages through multiple complementary research approaches, including qualitative and quantitative research, to characterize the healthy bladder and identify personal behavior and other

factors associated with normal bladder function. It also is identifying protective factors for long-term bladder health and risk factors for developing lower urinary tract conditions. The long-term goals are to obtain the information necessary to plan future studies (including interventions), to promote bladder health and prevent LUTS in women throughout their lives, and to support institutional and societal policy changes.

In FYs 2019 and 2020, PLUS continued its work to establish a new area of scientific inquiry—promotion of bladder health—with a transdisciplinary process. In planning for a foundational longitudinal cohort study, PLUS investigators created four novel measures (the Bladder Health Scale, the Toileting Environment Questionnaire, the Bowel Function Questionnaire, and the Knowledge, Attitudes, and Beliefs Questionnaire); developed a smartphone app for assessing toileting behaviors and environment "in the moment"; conducted a large focus-group study including English- and Spanish-speaking adult women and adolescent girls; and used existing literature and databases to inform our understanding of bladder health, normal bladder function, and risk and protective factors. Their extensive work has been compiled in the longitudinal cohort study ATTRIBUTES (Assessments Taken over Time: Relationships Influencing Bladder and Urinary Tract Experiences). The adult English and Spanish versions are expected to be launched in the summer of 2021. Validation of the Bladder Health Scale was delayed because recruitment was shut down during the COVID-19 pandemic.

PLUS has developed a robust community engagement infrastructure to support its work and inform recruitment and retention strategies for ATTRIBUTES. PLUS is committed to inclusion of a diverse group of study participants in terms of race, ethnicity, sex, and social determinants of health.

In 2019, ORWH supported three pilot and feasibility supplemental grants, highlighted below, which were selected through the PLUS Research Consortium:

1. Social–Ecological Risk Factors for Lower Urinary Tract Symptoms and Protective Factors for Long-term Bladder Health: Prison PLUS: Environmental and Contextual Risk Factors of LUTS among Justice-Involved Women (Smoyer, Southern Connecticut State University);
2. Environmental and Contextual Determinants of LUTS in Adolescent Girls at School in India (Hegde, ARMMAN, Mumbai, India)
3. Social & Environmental Risk Factors for Young Female Athlete Bladder Health & Lower Urinary Tract Symptoms: The Y-FABuLUTS Study (Bennis, Loyola University Chicago).

PLUS published 15 research articles in FY 2019–2020.

Maternal Health Research

According to the Centers for Disease Control and Prevention, approximately 700 women die each year in the United States from pregnancy-related complications. The high and increasing rate of maternal mortality in the U.S. constitutes a public health crisis that disproportionately affects women of color. Interventions that target known maternal health risk factors, such as hemorrhage and hypertension, have shown that up to 60% of maternal deaths are preventable. In addition, over 50,000 women per year experience severe maternal morbidity and require unexpected short- or long-term health care treatments. Like maternal mortality, severe maternal morbidity is highly preventable. Developing targeted, evidence-based interventions requires untangling a complex web of medical and social factors that contribute to risk, including racial disparities in maternal health care.

To address this urgent crisis, NIH created the NIH Maternal Mortality Task Force (MMTF) in early FY 2020. It is led by the NIH Office of the Director, the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), and ORWH. The MMTF spearheaded the Implementing a Maternal health and PRegnancy Outcomes Vision for Everyone (IMPROVE) initiative to support research that can reduce preventable maternal deaths and improve health for all women before, during, and after delivery.

IMPROVE focuses mainly on the leading causes of maternal mortality in the U.S.—cardiovascular disease, infection, and immunity—but it also considers other health conditions and social factors that play a role, such as mental health disorders, diabetes, obesity, and substance use disorders. It also funds investigations into the causes and indicators of significant pregnancy-related health complications (severe maternal

morbidity), with the ultimate goal of developing interventions that decrease their occurrence. Comprehensive interdisciplinary research that engages communities with high rates of maternal deaths and complications is a high priority. Collectively, the work will help create evidence-based solutions that are tailored to women and their individual circumstances across the country.

In connection with IMPROVE, the National Institute of General Medical Sciences partnered with ORWH and other NIH Institutes, Centers, and Offices (ICOs) to expand women's health research by issuing a notice of special interest (NOSI) titled *Administrative Supplements for Research on Women's Health in the IDeA States* in February 2020 (NOT-GM-20-017). The Institutional Development Award (IDeA) program targets States that historically have had low levels of NIH funding and, incidentally, tend to be among those with the highest rates of maternal and infant mortality. The program is interested in women's health in general but prioritizes maternal and infant morbidity and mortality and expressly encourages collaborations among investigators working in different biological disciplines and on health disparities. In total, 19 applications were funded and given a combined $4.8 million.

In May 2020, the IMPROVE initiative leveraged existing grants and research infrastructure to release another NOSI, *Administrative Supplements for NIH grants to Add or Expand Research Focused on Maternal Mortality* (NOT-OD-20-104). The program had three main goals:

1. Incorporate community partnerships and participation in domestic pregnancy-related and pregnancy-associated morbidity and mortality research to resolve health disparities and attain equity in maternal health.

2. Expand research on the leading causes of pregnancy-related and pregnancy-associated morbidity and mortality in the U.S. to strengthen evidence-based care and prevention strategies and improve outcomes.

3. Develop an integrated understanding of pregnancy-related and pregnancy-associated morbidity and mortality causes, including underlying comorbidities, and mechanisms to identify preventable risk factors and develop effective early interventions.

In September 2020, 36 applicants received awards, for a total of over $7 million. ORWH partnered with the National Library of Medicine to fund a project at Northwestern University to study the "Health for All" program and promote the use of libraries as outreach centers.

ORWH also partnered with the National Institute on Minority Health and Health Disparities (NIMHD) and the National Heart, Lung, and Blood Institute to fund new research examining racial and ethnic disparities in pregnancy-related complications and deaths (RFA-MD-20-008). Projects include original, innovative, and multidisciplinary efforts to advance the understanding, prevention, and reduction of pregnancy-related complications and deaths among disproportionately affected populations. They include women from underserved racial and ethnic groups, those living in underserved rural settings, and women with underprivileged socioeconomic status. In addition to examining factors influencing maternal health disparities, researchers will be among the first to evaluate the effectiveness of a multilevel intervention—at the individual, health care setting, community, and societal levels—to reduce maternal deaths and complications. This effort expands upon NIH's commitment to addressing the rising rates of illness and death from preventable pregnancy-related complications through the IMPROVE initiative, which also addresses disparities in maternal health, with grants to six institutions that are expected to total more than $21 million over 5 years.

ORWH participates in the Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC), a group created by the 21st Century Cures Act to advise the Secretary of the U.S. Department of Health and Human Services (HHS) on gaps in knowledge and research on safe and effective therapies for pregnant women and lactating women (Public Law 114–255, December 2016). The Secretary of HHS delegated authority for PRGLAC to NIH in January 2017, and the NIH Director appointed NICHD to lead the effort. The 21st Century Cures Act delineated categories of PRGLAC membership, including specific Federal agencies, professional societies, nonprofit organizations, and industry; ORWH was a member of the PRGLAC Board. PRGLAC reported to the Secretary of HHS and Congress in September 2018 and published the PRGLAC Report, which included 15 recommendations.

In March 2019, HHS extended PRGLAC's charter term to ask for guidance on implementation of the 15 recommendations. Four working groups were created—Research, Regulatory, Communications, and Discovery—with the ORWH representative co-chairing the Discovery working group. Implementation steps were developed for each recommendation, and common themes among them provided a useful overview of key steps. ORWH worked with other ICOs on clearance of the final implementation plan and its submission to the HHS Secretary in August 2020 (PRGLAC Report Implementation Plan).

ORWH created the Maternal Morbidity and Mortality Web Portal to provide science-based information on pregnancy, delivery, and post-pregnancy for researchers, clinicians, and members of the public. It also created an MMM informational booklet, which details in plain language maternal health issues and efforts being made by NIH and other organizations to reduce risks and improve outcomes.

In FY 2019, ORWH issued a multilevel call to action on maternal health during National Women's Health Week at the 4th Annual NIH Vivian W. Pinn Symposium, "Improving Maternal Health: Behind the Numbers," on May 15, 2019. During the symposium, clinicians and researchers described the current state of the maternal health crisis, research gaps, and potential solutions to address the problem. Speakers provided an overview of federally sponsored programs; proposed approaches to improve women's health before, during, and after pregnancy using a life course perspective; and presented the patient perspective. A proposal to collect information into a single publication for readers to benefit from this multi-partner convening was made at the event. (The result is described below.)

ORWH held a workshop with NICHD, titled "Pregnancy and Maternal Conditions That Increase Risk of Morbidity and Mortality," on May 19–20, 2020. Experts explored why women die from certain conditions (e.g., postpartum hemorrhage, hypertension, cardiovascular disease, and infection), what can be done to identify patients at risk, and what interventions are required to reduce maternal morbidity and mortality.

ORWH collaborated with the National Institute of Nursing Research, NIMHD, the NIH Tribal Health Research Office, and NICHD to convene a workshop, titled "Innovative Models of Care for Reducing Inequities in Maternal Health," on September 29, 2020, which discussed research questions on birth settings in the U.S. Potential research areas included:

- The impact of alternative birth settings and community-based providers on maternal and infant health;
- Defining elements of culturally responsive, patient-centered care that are safe, effective, and respectful;
- Factors important to the success of collaborative care among providers in birth settings;
- Structural barriers that inhibit women from seeking health care during pregnancy;
- Models to address attainment of health literacy for health disparity populations during pregnancy, during delivery, and postpartum; and
- The role of community health workers in enhancing equity, safety, and respect for pregnant women within existing health systems.

The meeting occurred after publication of the National Academies of Sciences, Engineering, and Medicine report titled *Birth Settings in America: Outcomes, Quality, Access, and Choice*.

Finally, during the reporting period, ORWH led the organization of a special issue on maternal morbidity and mortality in the *Journal of Women's Health*. Over 80 authors from 15 ICOs, 4 other HHS agencies, and 17 academic institutions and other organizations contributed 21 articles addressing various aspects of the maternal morbidity and mortality crisis. This special issue helps create the framework for a new research agenda to address the national maternal morbidity and mortality crisis.

ORWH Publications

ORWH produces both regular and single-release, project-specific publications and communications material to disseminate information to internal and external stakeholders, researchers, clinicians, and the public. They include a quarterly publication, monthly newsletters, booklets on topics relevant to women's health issues, and matte releases, which are consumer-facing health messages distributed through news outlets.

Quarterly ORWH Publication: *Women's Health in Focus at NIH*

The inaugural issue of ORWH's quarterly publication, *Women's Health in Focus at NIH*, was released in March 2018. The periodical was designed to showcase women's health research performed across the NIH Institutes, Centers, and Offices (ICOs) and to highlight scientific advances that can improve the health of women. The publication also provides content of interest to women in biomedical careers. It includes feature stories, summaries of journal articles, announcements of recent and upcoming ORWH activities, profiles of prominent women in science, best practices to advance women in science, staff updates, links to helpful resources on the health of women, and ORWH funding opportunities for research on women's health and the influences of sex and gender on health and disease. The Director's Corner section includes messages from ORWH Director Janine A. Clayton, M.D.

In FYs 2019 and 2020, issues of *Women's Health in Focus at NIH* included feature stories on the NIH Policy on Sex as a Biological Variable, ORWH's collaborative approach to supporting women in biomedical careers, and the history and founding of ORWH, with examples of how the office has helped to shape and promote women's health research over 30 years. ORWH's quarterly publication can be viewed at https://orwh.od.nih.gov/about/newsroom/orwh-quarterly-publication.

ORWH Monthly Newsletter: *The Pulse*

The inaugural issue of ORWH's monthly newsletter, *The Pulse*, was in November 2019. The newsletter was designed to be a short, informative piece that provides updates on women's health and health research news between issues of the longer ORWH quarterly publication. Issues of *The Pulse* often begin with a message from ORWH Director Janine A. Clayton, M.D., and contain information on a variety of topics, including:

- ORWH news on important issues in women's health and health research, found in the "In the Spotlight" section;
- Related news updates from other Federal agencies;
- Grant opportunities; and
- Upcoming events.

To view the current and past issues of *The Pulse*, visit https://orwh.od.nih.gov/about/newsroom/pulse.

Informational Polycystic Ovary/Ovarian Syndrome (PCOS) Booklet

On September 13, 2019, ORWH published an informational booklet titled *Polycystic Ovary/Ovarian Syndrome: Underrecognized, Underdiagnosed, and Understudied*. It is a resource for women who are concerned they are at risk for this endocrine disorder, who believe they may have it, or who have already been diagnosed with it. This 13-page booklet is divided into eight short sections that provide information on the definition and symptoms of PCOS, signs and health effects of the disease, and risk factors and preventive measures, as well as information for health care providers and researchers. The informational booklet also describes efforts to address PCOS across many ICOs, including the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, the National Institute of Environmental Health Sciences, and the National Institute of Diabetes and Digestive and Kidney Diseases. The PCOS booklet can be viewed at https://orwh.od.nih.gov/sites/orwh/files/docs/PCOS_Booklet_508.pdf.

Informational Maternal Morbidity and Mortality Booklet

ORWH published Maternal Morbidity and Mortality: What Do We Know? How Are We Addressing It? as a follow-up to the 4th Annual NIH Vivian W. Pinn Symposium, which took place in May 2019. The 12-page informational booklet examines factors that influence maternal morbidity and mortality (MMM), including preconception health and behavioral risk factors, such as smoking and opioid use; preventive steps that women can take to reduce incidence of MMM; and how maternal health affects women across their life course. The booklet also addresses how NIH and other Federal health agencies are addressing MMM. ORWH produced an MMM video to complement the booklet. The video can be viewed on YouTube, at https://www.youtube.com/watch?v=9MJh-oREOU8&feature=emb_title.

Matte Releases (consumer-facing news articles)

ORWH produced two matte releases in FYs 2019 and 2020, which were disseminated to and published by

print and online media outlets such as *The Charlotte Post*, *The Philadelphia Sunday Sun*, the *Los Angeles Times*, and the *Houston Chronicle*.

The 2019 release, "Maternal morbidity and mortality: Your guide to healthy pregnancy," emphasized the severity and urgency of the maternal morbidity and mortality health crisis by noting that approximately 700 women in the U.S. die as a result of pregnancy-related complications every year and that more than 50,000 experience unexpected pregnancy-related health problems. The release offered recommendations on how to reduce the risk of pregnancy complications by maintaining a healthy lifestyle, and it underscored the importance of eating well and exercising regularly, of taking care of one's mental health, and of beginning prenatal care early. As of December 31, 2019, the article had reached an online audience of over 213 million readers through more than 1,000 outlets. The article's print circulation was over 50,000 through three outlets.

The 2020 release, "7 Steps to Manage Stress and Build Resilience," explored how stress affects men and women distinctly and how every individual responds differently to stress. The article outlined steps people can take in their lives to reduce stress and build resilience, including taking time for oneself, trying new routines, staying in touch with family and friends, and seeking help with problems. This article was featured in NIH's *News in Health* and was also picked up by 1,116 news outlets, with a potential reach of 213 million people.

ORWH Website

The ORWH website underwent a significant number of additions, revisions, and updates in FYs 2019 and 2020. The additions include the Maternal Morbidity and Mortality (MMM) Web Portal, the In the Spotlight news section, and multiple e-learning courses. Content syndication was also added, with ORWH making select content available for use across the U.S. Department of Health and Human Services (HHS) and utilizing content from HHS to enhance the MMM Web Portal. Revisions and updates were made to the NIH Inclusion Outreach Toolkit, the Newsroom, the Director's Corner, and the Career Development & Interprofessional Education section.

ORWH Maternal Morbidity and Mortality Web Portal

First posted May 15, 2019

ORWH launched the Maternal Morbidity and Mortality Web Portal, which includes articles, statistics, and links to NIH resources. It is intended to be a resource for staff members at NIH and other Federal agencies, researchers, and members of the public, who can use it to find information on current research supported by NIH; specific funding opportunities, programs, and events; and NIH-funded clinical trials related to maternal health. The portal also contains links to information on maternal health from other Federal agencies.

In the Spotlight

First posted June 14, 2019

A new section of the ORWH website, titled In the Spotlight, was launched on June 14, 2019. It is a vehicle for publishing breaking news relevant to ORWH initiatives, the health of women, women in biomedical careers, funding opportunities, and more. In the Spotlight helps ORWH to communicate with researchers, clinicians, policymakers, stakeholders, and the general public between issues of the ORWH quarterly publication, *Women's Health in Focus at NIH*. New items are posted several times a month, and notices are sent to subscribers when content has been added to the ORWH website.

Updated Inclusion Policies Section

March 2019

ORWH launched a rewritten and redesigned Inclusion Policies webpage, featuring significant updates to pages underneath its umbrella, such as Common Definitions in NIH Inclusion Policies and Including Women and Minorities in Clinical Research Background. The NIH Inclusion Policies webpage now includes detailed policy information, historical documents, and references. Additional information on the Inclusion Across the Lifespan policy can also be found on the webpage.

Updated NIH Inclusion Outreach Toolkit

December 2019

ORWH revised the NIH Inclusion Outreach Toolkit to better help researchers recruit and retain women participants in their clinical studies. Inclusion ensures

the composition of studies' participants reflects the sex, gender, race, ethnicity, and age distributions of the population at large, which is essential to reaching their full potential. The updated version of the toolkit includes information on the history of inclusion at NIH, current policies, case studies and testimonials, regulations, checklists, and seminars. This information can help principal investigators and their research teams fulfill their responsibility to conduct research that serves everyone.

Career Development & Interprofessional Education

November 2019

ORWH launched the Career Development & Interprofessional Education section, which expanded upon the previous Career Development section by adding several educational elements: the E-Learning section, a Videocasts & Webinars page, and the Educational Resources page.

ORWH also added three e-learning courses:

- *Bench to Bedside: Integrating Sex and Gender to Improve Human Health* was added in November 2019. This six-module course was developed in partnership with the Food and Drug Administration Office of Women's Health to explore sex- and gender-related differences in key disease areas: immunology, cardiovascular disease, pulmonary disease, neurology, endocrinology, and mental health.
- *Sex as a Biological Variable: A Primer* was developed during the reporting period and will be added in early FY 2021. This four-module course was designed to help researchers understand the history and rationale of the SABV policy, as well as how to integrate the consideration of sex into all aspects of their studies.
- *Introduction: Sex- and Gender-Related Differences in Health* was also developed during the reporting period and will be added in early FY 2021. The course is designed as an introduction to sex and gender influences on health and disease, with the goal of helping individuals and teams incorporate a sex-and-gender perspective into their research and clinical care.

Updated Newsroom

2019–2020

The ORWH Newsroom serves as a resource hub for mass media articles; ORWH events; media releases and coverage; the ORWH digital media kit; ORWH's monthly newsletter, *The Pulse*; and the ORWH quarterly publication, *In Focus*. During FYs 2019 and 2020, the office added *The Pulse*, media releases and coverage, and the digital media kit section.

Updated Director's Corner

September 14, 2020

ORWH launched a revised version of the Director's Corner, with new content and an updated layout designed to highlight the career accomplishments of ORWH Director Janine A. Clayton, M.D. The Director's Corner still features the Director's Messages section and now includes sections titled Publications, Interviews, Videos, and Awards. The redesign creates a streamlined viewing and fact-finding experience for website visitors.

Content Syndication

May 15, 2019, and May 29, 2020

The HHS Syndication Storefront allows NIH offices and other organizations to syndicate (import) content from many HHS websites directly to their own websites or applications. Offices within the HHS umbrella are also able to export their own website content into the HHS Syndication Storefront for others to import onto their own websites. In May 2019, ORWH imported content from 30 webpages from the Syndication Storefront onto the Maternal Morbidity and Mortality Web Portal's Information for Women webpage. In May 2020, ORWH exported three webpages, adding them to the HHS Syndication Storefront.

Bench to Bedside: Integrating Sex and Gender to Improve Human Health

Bench to Bedside: Integrating Sex and Gender to Improve Human Health was developed in partnership with the Food and Drug Administration Office of Women's Health. Through six interactive modules, this free, self-paced online course gives users a thorough and up-to-date understanding of sex and gender

influences on health and disease so users can apply this knowledge when conducting research or interpreting clinical data. Course material showcases examples from basic science through clinical trials, and it illustrates how to translate knowledge into practice to ensure participants understand the importance of considering the influence of sex and gender throughout the research spectrum and beyond. Modules cover immunology, cardiovascular disease, pulmonary disease, neurology, endocrinology, and mental health.

Sex as a Biological Variable: A Primer

In 2018, with the support from the National Institute of General Medicine Sciences, ORWH began the process of developing an e-learning course to help biomedical researchers understand the NIH Policy on Sex as a Biological Variable (SABV) and how to incorporate it into the design of their research. The free e-learning course will be launched in November 2020 and will be titled *Sex as a Biological Variable: A Primer*. This e-learning course will help biomedical researchers, including academics and students, understand the SABV policy as an important element of rigorous science and how to incorporate SABV practices into the design of research studies, the preparation of grant applications, and the education of the next generation of investigators. The SABV primer will consist of four interactive modules that highlight concepts of the SABV policy:

1. "SABV and the Health of Women and Men" will provide the background and rationale for considering SABV in biomedical research.
2. "SABV and Experimental Design" will review how to consider and collect sex-based data, how the SABV policy relates to experimental research design, and where to find tools such as the SABV Checklist to enhance study design.
3. "SABV and Analyses" will present information on how to characterize and analyze sex-based data, including various statistical approaches to measuring sex differences and influences.
4. "SABV and Research Reporting" will explore the importance of communicating sex-based data as part of the research process, the rationale for communicating and reporting data by sex, the basic elements and available guidelines for reporting on sex and gender in research, and best strategies for sharing information about sex and gender outside the scientific community.

All modules will include knowledge checks and complete reference lists and will include a companion guide for instructors.

Introduction: Sex- and Gender-Related Differences in Health

Understanding the influences of sex and gender on health and accounting for them when designing and delivering treatments are key steps toward improving outcomes for all patients. To enhance our knowledge of these issues, in 2019 ORWH began the development of the free online course titled *Introduction: Sex- and Gender-Related Differences in Health*, which will be released in FY 2021 and include a slide deck and Facilitator's Guide. The course will incorporate current research on sex and gender with updated literature and content from a previous course (*The Science of Sex and Gender in Human Health*, which was developed in partnership with the Food and Drug Administration Office of Women's Health). *Introduction: Sex- and Gender-Related Differences in Health* will showcase appropriate applications of the terms "sex" and "gender" in biomedical research, provide an overview of ethical and regulatory considerations related to sex and gender, and introduce the concepts of a "sex-and-gender lens" and a "multidimensional framework." This resource is valuable for a wide range of individuals and teams seeking to initiate dialogue about how—and why—to incorporate a sex-and-gender lens into health-related research, policy, and clinical care.

Educational Resources

ORWH strives to ensure scientists and clinicians who conduct research and translate discoveries into clinical practice have a complete understanding of issues related to sex and gender. This includes sex- and gender-related terminology, culturally competent recruitment and engagement strategies, and clinical issues relevant to women. Therefore, ORWH updated its Educational Resources webpage in 2020 to provide a

contemporary repository of carefully vetted resources from the U.S. Department of Health and Human Services (including ORWH and the rest of NIH) and non-Federal organizations, including courses, curricula, case studies, and other materials related to sex and gender education.

Meetings, Conferences, and Workshops

ORWH remains current with the status of specific scientific areas related to its mission—strengthening research related to the health of women, ensuring that women are appropriately represented in biomedical and biobehavioral research supported by NIH, and developing opportunities for the professional advancement of women in biomedical careers. This is accomplished in part through NIH-sponsored meetings, conferences, and workshops, in which scientific experts and other stakeholders in women's health discuss current and emerging clinical and research developments. In some cases, ORWH sponsors events to provide a forum for educating researchers on the association between women's health and specific research topics. A list of meetings, conferences, and workshops sponsored or co-sponsored by ORWH during the reporting period, with a description of the focus of each event, is provided below.

Sleep and the Health of Women

Sponsored by ORWH and the National Heart, Lung, and Blood Institute (NHLBI); October 16–17, 2018

This conference was intended to sound a wake-up call in society about the importance of sleep for the health of women. It showcased a decade of federally funded research advances in understanding health risks, societal burden, and treatment options associated with sleep deficiency and sleep disorders in women. Researchers and the public discussed the state of the science regarding sleep and the health of women, barriers to implementing what is already known, and opportunities to translate scientific findings into practice and routine care. The discussion panels included Federal and public stakeholders, who identified actionable new directions and areas in which research is needed.

View the videocast of day one at https://videocast.nih.gov/summary.asp?Live=28213&bhcp=1.

View the videocast of day two at https://videocast.nih.gov/summary.asp?Live=28217&bhcp=1.

Meeting of the Genome-wide Association Studies (GWAS), Sex, and Chromosomes Think Tank

Sponsored by ORWH; February 27, 2019

This meeting was held to determine the extent to which sex as a biological variable (SABV) was being considered in genome-wide association studies (GWAS). The group identified gaps and opportunities related to SABV in genetic studies. Speaker and moderator Louise McCullough, M.D., Ph.D., Professor and Chair of the Department of Neurology and Chief of the Neurology Service at Memorial Hermann–Texas Medical Center, gave a presentation titled "Setting the Stage: Overview of Major Issues, Identifying the Problems." She also moderated a discussion on developing solutions. Participants included investigators from the National Human Genome Research Institute, the National Center for Advancing Translational Sciences, the National Cancer Institute, the National Institute of Neurological Disorders and Stroke, and the National Heart, Lung, and Blood Institute, as well as from the broader research community. Attendees reported on gap analyses in GWAS and discussed problem-framing, methods and approaches, and next steps, including the creation of a consortium.

Symposium Highlighting Evidence-Based Interventions to Address the Underrepresentation of Women in Science, Engineering, and Medicine

Sponsored by ORWH; the National Academies of Sciences, Engineering, and Medicine (NASEM); the National Science Foundation; and the L'Oréal Foundation; March 11, 2019

This NASEM symposium in Washington, DC, highlighted evidence-based interventions to address the underrepresentation of women in science, technology, engineering, mathematics, and medicine (STEMM). The symposium was part of a new consensus study addressing institutional barriers preventing women from pursuing successful scientific careers and examining policies, practices, and strategies that have opened doors to women's participation and success in STEMM fields. Gender equality for women in biomedical

careers had not advanced appreciably since the most recent major study of this kind. The keynote address was given by U.S. Representative Donna Shalala, Ph.D., of Florida, former Secretary of the U.S. Department of Health and Human Services. She was introduced by Vivian W. Pinn, M.D., the first full-time Director of ORWH. A panel session titled "Beyond Bias" was held, addressing institutional strategies to combat bias; a panel titled "Family-Friendly Policies" discussed tenure, parental leave, and child care provisions; "Recruitment, Retention, and Advancement" covered academic programs and policies for women students and faculty; and "National Programs" focused on scientific agencies and foundations designed to improve women's representation in STEMM. ORWH Director Janine A. Clayton, M.D., participated in the latter panel. The study committee of the NASEM consensus project was chaired by Mae Jemison, M.D., a former NASA astronaut and the first African American woman to travel into space.

A recording of the event can be found at https://livestream.com/accounts/7036396/events/8582184.

Symposium on Promising Practices for Addressing the Underrepresentation of Women in Science, Engineering, and Medicine: Opening Doors

Sponsored by ORWH; the National Academies of Sciences, Engineering, and Medicine (NASEM); the National Science Foundation; and L'Oréal USA; March 19–20, 2020

This symposium shared key findings from a NASEM report focused on addressing the underrepresentation of women in science, engineering, and medicine. It featured presentations by ORWH Director Janine A. Clayton, M.D., and NIH Director Francis S. Collins, M.D., Ph.D., as well as other leaders, on the range of issues addressed in the NASEM study. The symposium highlighted the report's recommendations on how to drive greater equity and diversity in STEMM through systemic change. Panel themes included "Why Do We See Different Patterns of Representation and Advancement in Different Scientific, Engineering, and Medical Disciplines?"; "Effective Institutional Practices for Addressing Gender Disparities, Part I: Educational Interventions, Mentoring, and Role Models"; "Effective Institutional Practices for Addressing Gender Disparities, Part II: Recruitment, Retention, and Advancement"; "Overcoming Common Institutional Barriers to Sustainably Implementing Effective Policies, Practices, and Strategies: The Importance of Leadership and Accountability"; and "Making a Difference: How Some Have Driven Change."

View the videocast at https://www.nationalacademies.org/event/03-19-2020/symposium-on-addressing-the-underrepresentation-of-women-in-stemm.

Organization for the Study of Sex Differences (OSSD) and International Society for Gender Medicine (IGM) Joint Meeting

Sponsored by ORWH, OSSD, and IGM; May 5–8, 2019

This second joint meeting of OSSD and IGM, held in Washington, DC, provided information about the most recent advances in research and policy regarding sex differences in physiology and disease. OSSD is a scientific membership organization that seeks to enhance knowledge of sex and gender differences through interdisciplinary collaborations among scientists and clinicians of diverse backgrounds. IGM coordinates scientific and educational efforts worldwide to promote the science of gender- and sex-specific medicine. Eric Vilain, M.D., Ph.D., of the Children's National Health System gave the inaugural Arthur Arnold Distinguished Lecture, "Hurdling over Sex: Sport, Science, and Equity." Joan Roughgarden, Ph.D., of Stanford University was the OSSD Capstone Speaker. Her presentation was titled "The Gender Binary in Nature, Across Human Cultures, and in the Bible." The IGM Capstone Speaker, Alexandra Kautzky-Willer, M.D., of the Medical University of Vienna, gave a talk titled "Sex and Gender Matter in Diabesity: From Pathophysiology to Prevention and Personalized Therapy."

Advancing Science for the Health of Women: A Symposium by the NIH Office of Research on Women's Health (ORWH) at the Organization for the Study of Sex Differences (OSSD) and International Society for Gender Medicine (IGM) Joint Meeting

Sponsored by ORWH; May 5, 2019

Leadership from ORWH held a symposium at the joint OSSD–IGM meeting on May 5, 2019. The ORWH

staff members described key policies and programs overseen by the office, explaining that its mission includes strengthening research on health conditions that affect women and developing opportunities for women in biomedical careers. Following presentations on the consideration of sex as a biological variable in research, NIH inclusion policies, sex and gender in clinical research, and an ORWH grant program targeting marginalized populations of women, there were opportunities for discussion and questions on the topics presented and other areas of interest to participants.

To foster the development of early-career researchers and investigators who are focused on women's health research, especially sex and gender differences research policy, ORWH established the NIH ORWH Science Policy Scholar Travel Award to OSSD at the end of 2018. This annual award supports the travel of the scholar whose OSSD abstract on women or sex/gender differences policy is accepted for a poster, oral session, or symposium at the annual meeting. Dr. Anna Levinsson, a postdoctoral fellow at Université de Montréal and the Montreal Heart Institute, was the first recipient of this travel award for her presentation titled "Sex Differences in Hypertension: Insights from Pharmacogenomics." Because of the COVID-19 pandemic, the 2020 OSSD meeting did not occur, and no award was presented.

2019 NIH Pain Consortium Symposium: Pain Across the Lifespan

Sponsored by ORWH, the National Center for Complementary and Integrative Health, the National Institute on Aging, the National Institute on Drug Abuse, the Eunice Kennedy Shriver National Institute of Child Health and Human Development, the National Institute of Dental and Craniofacial Research, the National Institute of Neurological Disorders and Stroke, and the National Institute of Nursing Research; May 30–31, 2019

The 2019 NIH Pain Consortium Symposium addressed advances in pain research and featured NIH-supported researchers whose work made important contributions in this field. The keynote address was presented by Anne Case, Ph.D., and Sir Angus Deaton, Ph.D., of Princeton University. It was titled "Pain and Opioids in an Epidemic of Mental and Economic Distress." Three panel sessions focused on different aspects of the meeting's theme: "Pain in Pediatric Populations," "Mid-life Pain and Special Populations," and "Pain Management in Older Adults." A presentation titled "A Patient's Perspective" also was given. A poster session featured early-career investigators, and the researchers with the best abstracts were selected to give oral presentations.

View a videocast of day 1 at https://videocast.nih.gov/watch=32042.

View a videocast of day 2 at https://videocast.nih.gov/summary.asp?Live=33199&bhcp=1.

Pregnancy and Maternal Conditions That Increase Risk of Morbidity and Mortality Workshop

Sponsored by the Eunice Kennedy Shriver National Institute of Child Health and Human Development; ORWH; the National Heart, Lung, and Blood Institute; and the NIH Office of Disease Prevention; May 19–20, 2020

This virtual workshop was part of the actions taken by NIH to respond to a public health crisis that finds women in the U.S. experiencing rates of severe maternal morbidity and maternal mortality that are much higher than those of our peer nations. An interdisciplinary team of experts explored why women die from certain conditions (e.g., postpartum hemorrhage, hypertension, cardiovascular disease, and infection), what can be done to identify patients at risk, and what interventions are required to reduce maternal morbidity and mortality (MMM). Workshop participants identified research gaps targeted at the clinical causes of MMM.

View the videocast of day 1 at https://videocast.nih.gov/summary.asp?live=36359&bhcp=1.

View the videocast of day 2 at https://videocast.nih.gov/summary.asp?live=36363&bhcp=1.

Incorporating a Sex-and-Gender Lens from Bench to Bedside: Neurology Webinar

Sponsored by ORWH and the Food and Drug Administration Office of Women's Health (OWH); September 1, 2020

ORWH, in partnership with OWH, developed the e-learning course *Bench to Bedside: Integrating Sex and Gender to Improve Human Health*. This free online course gives users a thorough understanding of sex and gender influences on health and disease, knowledge

users can apply when conducting research and interpreting evidence for clinical practice. On September 1, 2020, ORWH hosted a webinar to introduce the neurology module of the *Bench to Bedside* course. The virtual event featured guest presenter Farida Sohrabji, Ph.D., of the Texas A&M College of Medicine. Dr. Sohrabji discussed the urgency of considering sex and gender in neurological health and briefly introduced the three conditions covered in the neurology e-learning module: ischemic stroke, Parkinson's disease, and epilepsy. Dr. Sohrabji also shared lessons learned from her career as an educator committed to including sex and gender in graduate and medical education. Her lecture was followed by a moderated Q&A session.

Inclusion Across the Lifespan-II Workshop: Implementation and Future Direction (IAL-II)

Supported by ORWH; the Food and Drug Administration; the National Center for Advancing Translational Sciences; the National Cancer Institute; the National Heart, Lung, and Blood Institute; the National Institute on Aging; the National Institute of Allergy and Infectious Diseases; the Eunice Kennedy Shriver National Institute of Child Health and Human Development; the National Institute of Diabetes and Digestive and Kidney Diseases; the National Institute of Mental Health; the National Institute on Minority Health and Health Disparities; the National Library of Medicine; the NIH Office of Behavioral and Social Sciences Research; the NIH Office of the Director; and the NIH Office of Extramural Research; September 2, 2020

The virtual IAL-II workshop convened individuals from a wide range of backgrounds in clinical study development, execution, and inclusion of pediatric, older adult, and special populations. It represented people from underserved racial and ethnic groups, people with disabilities, rural/isolated populations, language-minority individuals, pregnant women, lactating women, people with comorbidities, sexual and gender minorities, and other groups. Researchers shared lessons learned on the recruitment and inclusion of these populations in clinical studies and presented evidence-based advice. Topics included inclusion and exclusion criteria; study design and metrics; recruitment, enrollment, and retention; and data analysis and study interpretation. A video recording of the event is available at https://videocast.nih.gov/watch=38384.

Recurring Events

Meetings of the Advisory Committee on Research on Women's Health (ACRWH)

46th Meeting of the ACRWH

Sponsored by ORWH; October 23, 2018

This advisory committee meeting featured a report from ORWH Director Janine A. Clayton, M.D., who addressed the rising maternal mortality and declining life expectancy of women in the U.S. and the effects of the opioid crisis on women's health and mortality. She also provided updates on recent and upcoming meetings sponsored by ORWH; scientific publications co-authored by ORWH staff members; and an upcoming National Academies of Sciences, Engineering, and Medicine study commissioned by ORWH on reasons underlying the underrepresentation of women in science, technology, engineering, mathematics, and medicine (STEMM) disciplines at pivotal career stages. A primary focus of the meeting was a preview of a new 5-year NIH strategic plan, *Advancing Science for the Health of Women: The Trans-NIH Strategic Plan for Women's Health Research*. Guest speakers included former Senator Barbara A. Mikulski; former Representative Connie Morella; NIH Principal Deputy Director Lawrence Tabak, D.D.S., Ph.D.; National Institute of Diabetes and Digestive and Kidney Diseases Director Griffin P. Rodgers, M.D.; and Wendy M. Kohrt, Ph.D., Professor of Medicine in the Division of Geriatric Medicine at the University of Colorado Anschutz Medical Campus. View the videocast at https://videocast.nih.gov/summary.asp?live=28194&bhcp=1.

47th Meeting of the ACRWH

Sponsored by ORWH; February 25, 2019

This advisory committee meeting focused specifically on concept clearance for ORWH-co-funded programs to achieve alignment with the goals of *Advancing Science for the Health of Women: The Trans-NIH Strategic Plan for Women's Health Research*. The requests for applications (RFAs) and funding opportunity announcements (FOAs) included the Building Interdisciplinary Research Careers in Women's Health (BIRCWH) program; the Specialized Centers of Research Excellence (SCORE) on Sex Differences; the

U3 Administrative Supplement Program; administrative supplements for research on sex and gender differences; and the new R01 related to sex and gender in health and disease. The committee discussed the purpose and achievements of each program, the strategic plan goals and objectives it met, and the rationale for continued funding. This was followed by questions from those in attendance and continued discussion. In each case, ACRWH members voted to move the concept forward. No videocast is available.

48th Meeting of the ACRWH

Sponsored by ORWH; April 10, 2019

The key presenter at this advisory committee meeting was Nora D. Volkow, M.D., Director of the National Institute on Drug Abuse (NIDA), who addressed the national opioid crisis. Dr. Volkow presented on the Helping to End Addiction Long-term℠ (HEAL) Initiative and NIDA-supported research addressing sex differences in pain and addiction. In April 2018, NIH launched the HEAL Initiative as an aggressive trans-agency effort to speed scientific solutions to the national opioid public health crisis. It focuses on improving opioid addiction treatment and enhancing pain management to prevent addiction and overdose. Dr. Volkow explained that NIDA is addressing addiction in new ways and developing better forms of care to the populations that need it. The advisory committee also heard an update on recent ORWH activities from ORWH Director Janine A. Clayton, M.D. Other meeting topics included the NIH anti-harassment program and the NIH inclusion and sex as a biological variable (SABV) policies. View the videocast at https://videocast.nih.gov/summary.asp?live=31469&bhcp=1.

49th Meeting of the ACRWH

Sponsored by ORWH; October 23, 2019

ORWH Director Janine A. Clayton, M.D., provided updates on ORWH research funding, programs, and activities. Bruce J. Tromberg, Ph.D., Director of the National Institute of Biomedical Imaging and Bioengineering (NIBIB), gave an overview of NIBIB's activities related to the health of women, such as advances in imaging to detect breast cancer. Adrienne Hallett, NIH Associate Director for Legislative Policy and Analysis, provided a legislative update, noting that several important topics were being discussed in Congress, including maternal mortality, health disparities, and sexual harassment. NIH Associate Deputy Director Tara Schwetz, Ph.D., moderated a session highlighting work across Federal agencies in the area of maternal morbidity and mortality. Speakers included Dorothy Fink, M.D., Deputy Assistant Secretary for Women's Health and Director of the Office on Women's Health at the U.S. Department of Health and Human Services; Sarah Foster, M.P.H., of the Centers for Disease Control and Prevention; and Johannie Escarne, M.P.H., of the Health Resources and Services Administration.

Information on the implementation and evaluation of the Trans-NIH Strategic Plan for Women's Health Research was provided by Laura Sharon, M.A. Also, P. Kay Lund, Ph.D., Director of the Division of Biomedical Research Workforce in the NIH Office of Extramural Research, led discussions on proposed concepts for advancing women in biomedical careers. Melissa Ghim, Ph.D., Health Scientist Administrator at ORWH, facilitated discussion of a first-time independent research project grant administrative supplement. Lynn Morin, M.A., Health Scientist Administrator at ORWH, gave a presentation titled "Achieving Gender Diversity: Inclusive and Sustainable Institutional Approaches." Teraya Donaldson, Ph.D., American Association for the Advancement of Science (AAAS) Science and Technology Policy Fellow at ORWH, led discussion of a request for information (RFI) for the NIH Prize for Enhancing Faculty Gender Diversity in Biomedical and Behavioral Science. A videocast of the meeting is available at https://videocast.nih.gov/summary.asp?live=34443&bhcp=1.

50th Meeting of the ACRWH

Sponsored by ORWH; April 21, 2020

The keynote presentation, on the challenges facing women in science and their possible solutions, was given by Marcia McNutt, Ph.D., President of the National Academy of Sciences. ORWH Director Janine A. Clayton, M.D., provided opening comments, with updates on ORWH research funding, programs, and activities. Xenia Tigno, Ph.D., was introduced as ORWH's first Associate Director for Careers. Dr. Tigno and Melissa Ghim, Ph.D., Health Scientist Administrator at ORWH, provided a careers update. A panel on career-oriented programs was titled "Approaches to Institutional Change: Lessons Learned," with remarks by Kenneth Gibbs Jr., Ph.D., Program Director within the Division of Training, Workforce Development, and Diversity at the National

Institute of General Medical Sciences; Jessie A. Dearo, Ph.D., Program Director of the Organizational Change for Gender Equity in STEM Academic Professions (ADVANCE) at the National Science Foundation; and Darla Thompson, Ph.D., Project Director for SEA Change Biomedicine at the American Association for the Advancement of Science. The final presentation, "Changing the Culture to End Sexual Harassment at the NIH," was given by Carrie Wolinetz, Ph.D., NIH Associate Director for Science Policy. The meeting concluded with a lively discussion among committee members. View the videocast at https://videocast.nih.gov/summary.asp?live=35545&bhcp=1.

NIH Vivian W. Pinn Symposia

4th Annual NIH Vivian W. Pinn Symposium: Improving Maternal Health: Behind the Numbers

Sponsored by ORWH; May 15, 2019

The NIH Vivian W. Pinn Symposium (VPS) is the signature event of ORWH and is held every year during National Women's Health Week. With a large number of women having lasting medical complications or dying as a result of difficulties associated with pregnancy, the 2019 VPS focused on maternal morbidity and mortality (MMM). Multiple stakeholders attended and participated in the event, including the Centers for Disease Control and Prevention, the Food and Drug Administration, the U.S. Department of Health and Human Services (HHS) Office on Women's Health, the HHS Office of Adolescent Health, the Health Resources and Services Administration, the Veterans Health Administration, the National Medical Association, and the March of Dimes. The keynote speaker, Lisa M. Hollier, M.D., then–President of the American College of Obstetricians and Gynecologists, addressed the path to better maternal outcomes. The voices of women who died from causes related to pregnancy or childbirth were shared in a story-like presentation titled "The Lost Mothers." Leading clinicians and researchers participated in a panel discussion on framing a research agenda to advance maternal health equity, followed by a Q&A session. A review of current statistics and relevant programs sponsored by the Federal Government, including NIH, was provided by representatives of key Federal agencies with medical research and public health missions. During the Federal agency panel updates, a presentation with collated information on MMM activities from all NIH Institutes and Centers was presented. A key outcome of the VPS included a commitment to summarize a broad set of interdisciplinary perspectives into a single publication to inform future research on maternal health. View the videocast at https://videocast.nih.gov/Summary.asp?File=27545&bhcp=1.

There was no VPS in 2020 because of the COVID-19 pandemic.

Building Interdisciplinary Research Careers in Women's Health (BIRCWH)

BIRCWH: 2018

Sponsored by ORWH; November 28, 2018

The Building Interdisciplinary Research Careers in Women's Health program is a mentored career-development effort that connects junior faculty (i.e., BIRCWH Scholars) with senior faculty who have a shared interest in women's health research and the influences of sex and gender on health and disease. The 2018 Annual BIRCWH Meeting provided a forum for these young investigators, their mentors, and other research scientists to meet, present their research results, and engage in mentoring and networking activities. The Ruth L. Kirschstein Memorial Lectureship was the centerpiece of the 2018 meeting. The lectureship honors the life and achievements of Dr. Kirschstein, who provided direction and leadership to NIH through much of the second half of the 20th century, imparting a lasting effect on public policy, public health, and the training of biomedical researchers. Jeanne-Marie Guise, M.D., M.P.H., delivered the first memorial lecture. She spoke on the value of mentorship in scientific research and stressed multigenerational research and multidirectional mentoring to address the complexity and scope of today's scientific problems. Dr. Guise is Director of the Oregon Institute for Patient-Centered Comparative Effectiveness and Associate Director of the Oregon Evidence-based Practice Centers program at Oregon Health & Science University. She is also a professor of obstetrics and gynecology and a practicing OB-GYN. The meeting also included a panel discussion on creating new curricula to incorporate sex as a biological variable (SABV) concepts into the career development of BIRCWH Scholars. Podium presentations showcased research by four BIRCWH Scholars. A poster session was held, as well as

mentoring opportunities with scientists from several NIH Institutes, Centers, and Offices. A videocast of the meeting can be found at https://videocast.nih.gov/summary.asp?Live=28502&bhcp=1.

BIRCWH: Strategic Career Development: Charting the Course

Sponsored by ORWH; December 11, 2019

The 2019 Annual BIRCWH Meeting provided a forum for the BIRCWH young investigators, their mentors, and other research scientists to meet, present their research results, and engage in mentoring and networking activities. The Ruth L. Kirschstein Memorial Lectureship was titled "Strategic Career Development: Charting the Course," by Judith G. Regensteiner, Ph.D., Professor of Medicine, Judith and Joseph Wagner Chair in Women's Health Research, and Director of the Center for Women's Health Research at the University of Colorado Anschutz Medical Campus. A panel discussion, titled "Next-Generation Data and the Future of Women's Health," followed. The meeting included podium presentations showcasing research from three BIRCWH Scholars, whose presentation topics included sex differences associated with asthma and testosterone, differences in body composition and cardiometabolic health between transgender and cisgender youths, and sex differences in inflammatory response to acute psychological stress and risk of major adverse cardiovascular events. During a poster session, NIH scientists were available to answer questions about the research presented. A videocast of the meeting can be found at https://videocast.nih.gov/summary.asp?Live=34523&bhcp=1.

Women's Health Seminar Series

Women's Health Seminar Series: Improving the Health and Well-being of Young Transgender Women: Intersections of Research, Policy, and Practice

Sponsored by ORWH and the NIH Sexual and Gender Minority Research Office; December 6, 2018

This seminar featured a presentation by Nadia Dowshen, M.D., M.S.H.P., on the health of young transgender women. Dr. Dowshen is the co-founder and Medical Director of the Gender and Sexuality Development Clinic at the Children's Hospital of Philadelphia. A review of her research described HIV-related inequities and other health inequities faced by young transgender women. Dr. Dowshen also discussed how these data have been used to inform policy and develop a successful multidisciplinary model of clinical care for transgender children and adolescents. A videocast is available at https://videocast.nih.gov/Summary.asp?file=27224&bhcp=1.

Sex and Gender in Health and Disease Scientific Interest Group

Sex and Gender in Health and Disease Scientific Interest Group: The Role of Estrogen in Cardioprotection

Sponsored by ORWH; November 20, 2018

This meeting featured Elizabeth Murphy, Ph.D., head of the Cardiac Physiology Section at the National Heart, Lung, and Blood Institute. She spoke on the role of estrogen in cardioprotection. Dr. Murphy's research explores how estrogen affects cardiovascular tissue; lipid profiles, including lowering low-density lipoprotein (LDL) cholesterol; vascular remodeling; blood pressure; and cardioprotection. Although the mechanisms by which estrogen mediates these effects is not fully understood, Dr. Murphy's research suggests that estrogen regulates gene transcription in specific tissues and participates in other signaling pathways. Further study of the complex interactions of estrogen may explain why premenopausal women experience less cardiovascular disease and why older postmenopausal women do not seem to gain a cardioprotective effect from hormone replacement therapy.

Sex and Gender in Health and Disease Scientific Interest Group: The Epidemiology of Gastric Cancer

Sponsored by ORWH; March 19, 2019

Participants discussed sex and gender differences in the carcinogenesis and treatment of gastric cancer, the third-leading cause of cancer deaths worldwide. Maria Constanza Camargo, Ph.D., an Earl Stadtman Tenure-Track Investigator in the Division of Cancer Epidemiology and Genetics at the National Cancer Institute, shared her current research in the Metabolic Epidemiology Branch, where she maintains a robust research program with a multidisciplinary team of international collaborators applying cutting-edge molecular epidemiology to the study of *Helicobacter pylori* and

premalignant and malignant gastric lesions. Her talk was titled "The Epidemiology of Gastric Cancer." Data were provided on recent incidence trends; little-known contributors, such as coinfection with the Epstein–Barr virus; and evidence of the effects of *H. pylori* eradication on gastric cancer risk.

Understudied, Underrepresented, and Underreported (U3) Women Lecture Series (Now the U3 Women's Health Lecture Series)

U3 Women Lecture Series: Reproductive Female Genital Mutilation and Cutting: Challenges, Research Gaps, and Opportunities in a Hidden Population

Sponsored by ORWH and the Eunice Kennedy Shriver National Institute of Child Health and Human Development; February 20, 2019

This webinar featured guest speaker Crista Johnson-Agbakwu, M.D., an obstetrician and gynecologist at Maricopa Integrated Health System and the Founding Director of the Refugee Women's Health Clinic. She addressed research gaps and challenges related to female genital mutilation and cutting (FGM/C), as well as the needs of this population of women. As defined by the World Health Organization, FGM/C comprises all procedures involving partial or total removal of the female external genitalia or other injury to the female genital organs for nonmedical reasons. Performing FGM/C on anyone under the age of 18 is a felony in this country. However, the Centers for Disease Control and Prevention estimates that there has been a marked increase in FGM/C in women and girls who are affected by and at risk for this practice. Dr. Johnson-Agbakwu also is the Director of the Office of Refugee Health at the Southwest Interdisciplinary Research Center at Arizona State University. Her research focuses on strategies to improve sexual and reproductive health outcomes for newly arrived refugee women, particularly those who have undergone female genital cutting, as well as sexual and gender-based violence. This webinar was the first in a series focusing on the effects of sex and gender influences among populations of women that are understudied, underrepresented, and underreported (U3) in biomedical research in the U.S. More information is available at https://orwh.od.nih.gov/about/newsroom/events/women-underrepresented-understudied-and-underreported-u3-populations-webinar.

U3 Women Lecture Series: Developing a Translational Research Program to Improve Quality of Life Among Latina Breast Cancer Survivors

Sponsored by ORWH and the Eunice Kennedy Shriver National Institute of Child Health and Human Development; October 24, 2019

Anna María Nápoles, Ph.D., M.P.H., of the National Institute on Minority Health and Health Disparities presented on the experiences of Latina breast cancer survivors, especially those who primarily speak Spanish, as they experience worse symptoms and quality of life than non-Latina survivors. She described the development of the Transcreation Framework for Community-engaged Behavioral Interventions to Reduce Health Disparities and how it was applied to develop a translational research program to address psychosocial health disparities among Spanish-speaking Latina breast cancer survivors. More information is available at https://orwh.od.nih.gov/about/newsroom/events/orwh-U3-womens-health-seminar.

U3 Women Lecture Series: Reproductive Health Care for Incarcerated Women: Strategies for Promoting Justice Through Research Within an Overlooked Population

Sponsored by ORWH; July 16, 2019

This seminar was presented by Carolyn Sufrin, M.D., Ph.D., a medical anthropologist and an obstetrician-gynecologist specializing in family planning at Johns Hopkins University. She is an Assistant Professor in the Department of Gynecology and Obstetrics at the Johns Hopkins School of Medicine, an Assistant Professor in the Department of Health, Behavior and Society at the Johns Hopkins Bloomberg School of Public Health, and the Associate Director of the Center for Medical Humanities & Social Medicine at Johns Hopkins University. Dr. Sufrin reviewed existing data about reproductive health among incarcerated women and strategies for conducting research attuned to the unique aspects of the carceral setting. She stated that there are over 225,000 women in U.S. prisons and jails. Most are

of reproductive age, and they are disproportionately women of color. Understanding their reproductive health outcomes and health care needs is essential for promoting equity and justice. Yet these issues are overlooked by many, including researchers. Dr. Sufrin has worked extensively on reproductive health issues affecting incarcerated women, from providing clinical care in jail to research, policy, and advocacy. Her work is situated at the intersection of reproductive justice, health care, and mass incarceration, which she examines in her book, *Jailcare: Finding the Safety Net for Women behind Bars*. Dr. Sufrin was a BIRCWH Scholar, during which time she conducted the first prospective study to collect data on pregnancy outcomes in U.S. prisons. For more information, see https://orwh.od.nih.gov/about/newsroom/events/orwh-understudied-underrepresented-and-underreported-women-lecture-series-0.

U3 Women Lecture Series: Mass Incarceration, Housing, and HIV/STI Risk: Focusing Attention on Women

Sponsored by ORWH; September 12, 2019

Kim M. Blankenship, Ph.D., Professor of Sociology at American University, presented on the role played by mass incarceration in women's HIV/sexually transmitted infection (STI) risks. She explained that mass incarceration is a major structure through which racial, class, and gender inequalities are produced and maintained in contemporary U.S. society, affecting access to and provision of housing for women. Dr. Blankenship discussed interview data from an ongoing longitudinal, mixed-methods study of low-income residents in New Haven, Connecticut, half of whom had been released from prison or jail within a year of study enrollment. The data demonstrated the complex ways that women's HIV/STI-related risks can be associated with mass incarceration. Dr. Blankenship is currently conducting NIH-funded research on the intersecting effects of mass incarceration, housing instability, and subsidized housing policies on racial inequities in HIV/AIDS. She is also part of a team of collaborators based at Temple University's Center for Public Health Law Research that is exploring the ways laws are influencing health equity in housing. A recording of the meeting is available at https://www.youtube.com/watch?v=DhqPtjYrA7Q&feature=youtu.be.

U3 Women Lecture Series: Improving Chronic Disease Outcomes Through Approaches that Address Social Determinants of Health

Sponsored by ORWH; July 22, 2020

As part of the U3 program, ORWH hosted an online panel discussion on social determinants of health. Lecturers included Marie Lynn Miranda, Ph.D., of the University of Notre Dame and Leah H. Rubin, Ph.D., M.P.H., of Johns Hopkins University, a former Scholar in the BIRCWH program. A moderated Q&A session followed. Dr. Miranda's lecture, "Assessing Residential Segregation's Role in Shaping Health and Well-Being," characterized national and local population patterns as they pertain to race, educational attainment, health care availability, and other factors correlated with health. She detailed how areas of racial isolation correlate with factors associated with poor health outcomes. Dr. Rubin's lecture, "Social Determinants of Central Nervous System (CNS) Dysfunction in Research and Clinical Practice: A Lesson from HIV," described cognitive problems and mental health issues associated with HIV. Though effective antiretroviral therapy has reduced the higher rates of HIV-related CNS dysfunction seen in the early years of the AIDS epidemic, the problem persists for many patients. For more information, see https://orwh.od.nih.gov/about/newsroom/events/understudied-underrepresented-and-underreported-womens-health-webinar.

NIH Director's Wednesday Afternoon Lecture Series (WALS)

WALS: You Want to Quantify That? The Science and Metrics of Partner Engagement in Research

Sponsored by ORWH; December 18, 2019

Melody Goodman, Ph.D., Associate Dean for Research and Associate Professor of Biostatistics at New York University, gave a lecture as part of the NIH Director's Wednesday Afternoon Lecture Series (WALS), titled "You Want to Quantify That? The Science and Metrics of Partner Engagement in Research." Although stakeholder engagement is a crucial part of participatory public health research, measurement of that engagement in research is varied, inconsistent, and

not methodologically sound. Dr. Goodman is pioneering new, comprehensively validated quantitative measures. Emerging data suggest a valid and reliable measure that can be used to determine levels of research engagement and accurately assess associations between research outcomes and stakeholder engagement. Dr. Goodman described her efforts to understand the social risk factors that contribute to health disparities in urban areas, with the goal of developing culturally competent, region-specific, and evidence-based solutions through collaborative activities with community members, community-based organizations, faith-based organizations, and other community health stakeholders. A link to the videocast of the event is available at https://videocast.nih.gov/watch=35117.

WALS: A Two-Act Play: The Character of Cells and the Role of Biomechanics

Sponsored by ORWH; January 29, 2020

Gilda Barabino, Ph.D., President of Olin College, gave a WALS presentation titled "A Two-Act Play: The Character of Cells and the Role of Biomechanics." Dr. Barabino's research at the City College of New York's Laboratory on Vascular and Orthopedic Tissue Engineering Research focuses on cellular and tissue responses to fluid mechanical forces in the context of vascular disease and orthopedic tissue engineering. She concentrates on the characterization and quantification of mechanical and biochemical cues that influence tissue growth and disease progression. Her lecture addressed her interdisciplinary work, which incorporates biology, materials science, and engineering to develop novel therapeutic strategies to improve the health of individuals with sickle cell disease and diseases associated with damaged cartilage and bone. Her innovative engineering technologies create models that recapitulate the environment within the body to better understand the pathophysiology of disease and the most appropriate strategies for treatment. She also employs complementary animal models to bridge translation of research findings to human clinical practice. A link to the videocast of the event is available at https://videocast.nih.gov/summary.asp?live=35109&bhcp=1.

Facebook Live Q&As

Facebook Live Q&A: Research Spotlight: Women of Color in STEMM

Sponsored by ORWH; February 27, 2019

The first ORWH Facebook Live Q&A featured speaker Sadhana Jackson, M.D., an Assistant Clinical Investigator in the Neuro-Oncology Branch of the National Cancer Institute (NCI). During the Q&A, Dr. Jackson answered questions about her work on the role of sex and gender in health and disease and on the health of women from the perspective of an African American woman working in biomedicine. The event was held in observation of Black History Month to highlight women of color in biomedical careers. Attendees had the opportunity to ask Dr. Jackson questions on the importance of the inclusion of women of color in science, technology, engineering, mathematics, and medicine (STEMM) fields; specific health concerns for African American women; and the personal experiences of Dr. Jackson with cancer and its influence on her approach to research. Dr. Jackson's research interests center on evaluating the blood–brain barrier (BBB) of malignant gliomas to transiently disrupt the BBB by pharmacologic means in an effort to improve chemotherapy delivery. She has experience with the use of brain microdialysis, pharmacokinetic analysis, and utilization of preclinical models to study central nervous system pharmacology. A recording of the meeting is available at https://orwh.od.nih.gov/about/newsroom/events/facebook-live-qa-dr-sadhana-jackson.

Facebook Live Q&A: Women of Color in STEMM

Sponsored by ORWH; August 19, 2019

The host speaker for this Facebook Live session was Faustine Williams, Ph.D., M.P.H., M.S., an Earl Stadtman Tenure-Track Investigator from the National Institute on Minority Health and Health Disparities (NIMHD). Dr. Williams shed light on her personal and professional experiences as a woman of color in the biomedical field, how she began conducting research on cancer disparities, notable achievements and obstacles, and the importance of mentorship. Dr. Williams is an NIH Distinguished Scholar who trained as a transdisciplinary researcher with a focus on cancer prevention and

control and health disparities. She is specifically interested in inter- and intra-health disparities in chronic diseases and finding ways to reduce and/or eliminate health disparities. Dr. Williams' Health Disparities and Geospatial Transdisciplinary Research Lab is housed in the Population and Community Health Sciences Branch of NIMHD's Intramural Research Program. She uses mixed methods—including community-based system dynamics, community-based participatory research, geographic information systems, storytelling, and qualitative approaches—to understand the complex interactions of factors contributing to health disparities. This supports the development and implementation of effective interventions to increase healthy behaviors and outcomes, especially among populations that experience the highest disparities. A video recording of the event can be found at https://orwh.od.nih.gov/about/newsroom/events/facebook-live-qa-dr-faustine-williams.

Facebook Live Q&A: Mentorship and Women of Color in Science

Sponsored by ORWH; March 4, 2020

This Facebook Live panel was moderated by ORWH Health Scientist Administrator Melissa Ghim, Ph.D., who leads career development and workforce diversity programs at ORWH. The panelists discussed their experiences with mentorship, shared effective strategies for finding a good mentor, and provided warning signs that a potential mentor might not be a good fit. They also discussed their experiences as women of color in biomedicine. The participants submitted questions and asked for advice on entering and advancing in biomedical careers. The featured panelists included Yarimar Carrasquillo, Ph.D., Principal Investigator at the Pain and Integrative Neuroscience Branch of the National Center for Complementary and Integrative Health; Sherine El-Toukhy Ph.D., M.A., Earl Stadtman Tenure-Track Investigator and NIH Distinguished Scholar in the Division of Intramural Research at the National Institute on Minority Health and Health Disparities; and Sadhana Jackson, M.D., Pediatric Neuro-oncologist at the National Institute of Neurological Disorders and Stroke. A video recording of the event is available at https://www.facebook.com/NIHORWH/videos/522611478675107.

Facebook Live Q&A: Women in STEMM Leadership Roles

Sponsored by ORWH; August 5, 2020

This Facebook Live panel was hosted by ORWH Director Janine A. Clayton, M.D., and moderated by ORWH Associate Director for Careers Xenia Tigno, Ph.D. The discussion explored the importance of women, particularly women of color, in leadership roles in STEMM fields. The panelists discussed their research, career paths, and the importance of the support of both mentors and institutions. Participants were also able to pose questions to the panelists during a Q&A segment. The featured panelists included Kizzmekia Corbett, Ph.D., a Senior Research Fellow at the NIH Vaccine Research Center and the Scientific Lead on the Coronavirus Vaccines and Immunopathogenesis Team at the National Institute of Allergy and Infectious Diseases; Rosemarie Ramos, Ph.D., M.P.H., a biostatistician with the Defense Health Agency; and Kandice Tanner, Ph.D., a Senior Investigator at the Center for Cancer Research at the National Cancer Institute. A video recording of the event is available at https://orwh.od.nih.gov/about/newsroom/events/facebook-live-qa-women-stemm-leadership-roles-1.

Sex and Gender in Health and Disease Scientific Interest Group

ORWH coordinates the Sex and Gender in Health and Disease (SGHD) scientific interest group (SIG), which explores the influences of sex (a biological variable) and gender (a social construct) on health and disease. The SGHD SIG seeks to learn how sex and gender interact across the lifespan, to promote the dissemination of research, to foster interdisciplinary collaborations among NIH scientists who are interested in sex-based research, and to provide a platform to increase awareness of cross-disciplinary connections in biomedical, social, and behavioral research. In FYs 2019 and 2020, the SGHD SIG featured two presentations, titled "Sex Differences in Cardiovascular Disease" and "The Epidemiology of Gastric Cancer."

III. NIH Workforce and Grantees

Growth and Challenges for Women in the NIH Workforce

The *Report of the Advisory Committee on Research on Women's Health: Fiscal Years 2019–2020* (women's health research biennial report) marks the first time that the report includes information about the sex and racial and ethnic breakdown of the NIH workforce. This women's health research biennial report could therefore serve as a baseline against which to measure future data, identify areas for improving parity and diversity, and track changes in the demographics of the NIH workforce. The fiscal year (FY) 2019 and FY 2020 workforce data presented here are from the NIH Office of Equity, Diversity, and Inclusion (EDI).[5]

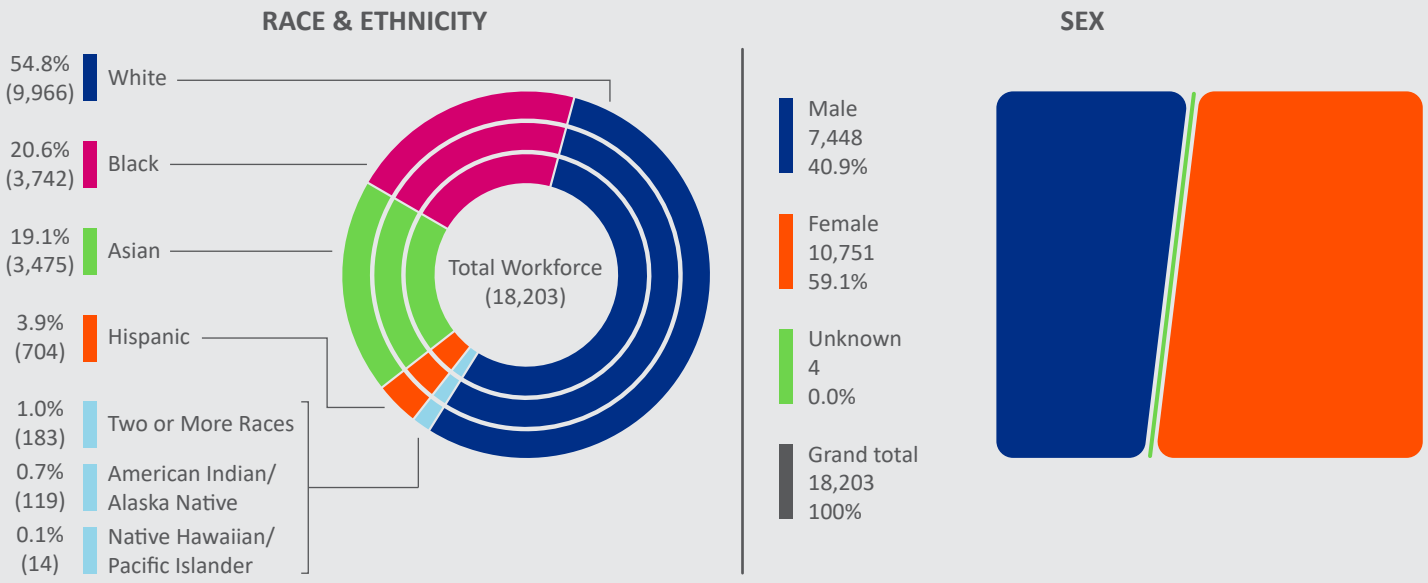
5. Data and definitions provided by the NIH Office of Equity, Diversity, and Inclusion's Data Analytics Branch.

The demographics of the NIH workforce as of the fourth quarter (Q4) of FY 2020 (September 30, 2020) are depicted in Figure 1. There were 18,203 individuals working full time at NIH. The NIH workforce comprised 59.1% females and 40.9% males. It was predominantly White (54.8%), followed by Black (20.6%), Asian (19.1%), and Hispanic (3.9%). Employees who identified as being two or more races, American Indian/Alaska Native, or Native Hawaiian/Pacific Islander races constituted 1.8% of NIH's full-time workforce.

The following sections describe employment, promotion, and leadership status of female NIH employees in relation to those of male NIH employees, with a further assessment of racial and ethnic differences between males and females within the NIH workforce. In this report, comparisons will be made primarily within program type (Extramural, Intramural, and Other[6]) by:

6. Please see Appendix C for the definition of Other Program.

Figure 1. The Race, Ethnicity, and Sex of the NIH Workforce: Quarter 4 (Q4) of FY 2020



Notes: *Please note the overall workforce data only include information on full-time-equivalent employees. Employees classified in the five racial groups or the "Two or More Races" category are all non-Hispanic or Latino. Employees classified as Hispanic or Latino may identify with any combination of the five racial categories. Commissioned Corps (CC), Advisory Council (EI), and ZZ pay plans are excluded.*

Sources: *The data were retrieved from https://www.edi.nih.gov/people/resources/advancing-racial-equity/nih-workforce-profile-fy20q04. The National Institutes of Health (NIH) workforce demographics for the fourth quarter of fiscal year 2020 (Q4 FY 2020) were retrieved from the nVision Human Resources Database on October 23, 2020, with an as-of date of September 30, 2020.*

- The size of the Institute or Center (IC)[7];
- The type of occupation (Scientific or Infrastructure);
- Leadership status;
- Supervisory status and promotions in the past year; and
- The intersections between gender and race and ethnicity.

EDI and the NIH Office of Research on Women's Health (ORWH) analyzed the data. To protect individuals' privacy, the EDI data are presented here as percentages and in aggregate. The data in each area of interest are categorized by sex and, in some cases, by race and ethnicity. No hypothesis testing was performed on the data. All differences discussed are thematically meaningful but may not be statistically significant. A more detailed description of the methodology and definitions appears in Appendix C.

7. Please see Appendix C for IC size classifications.

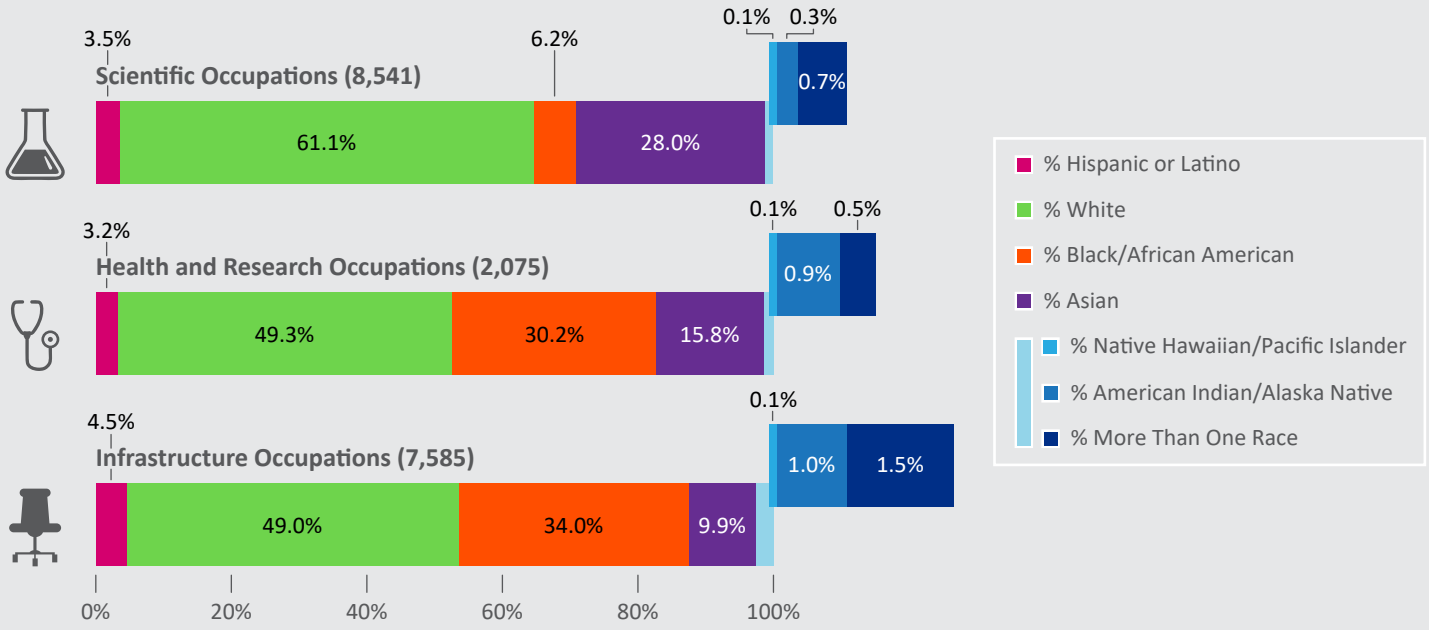
The NIH Workforce by Occupational Categories

The NIH workforce involves three sectors: Scientific occupations, Health and Research occupations, and Infrastructure occupations.

The three sectors are defined as follows:

- Scientific employees directly lead and/or conduct basic or clinical research. They also provide oversight for research, both intramural and extramural. Some examples include, but are not limited to, biologists, health scientist administrators, medical officers, and veterinary staff members. Employees who have a position title containing investigator, scientist, clinician, medical officer, scientific officer, scientific executive, program leader, or policy leader are also classified as Scientific employees.
- Health and Research employees directly support the basic and clinical research conducted at NIH. Many

Figure 2. NIH Workforce Categories by Race and Ethnicity: Q4 of FY 2020



Notes: *The overall workforce data only include information on full-time-equivalent employees. Employees classified in the five racial groups or the "Two or More Races" category are all non-Hispanic or Latino. Employees classified as Hispanic or Latino may identify with any combination of the five racial categories. Commissioned Corps (CC), Advisory Council (EI), and ZZ pay plans are excluded.*

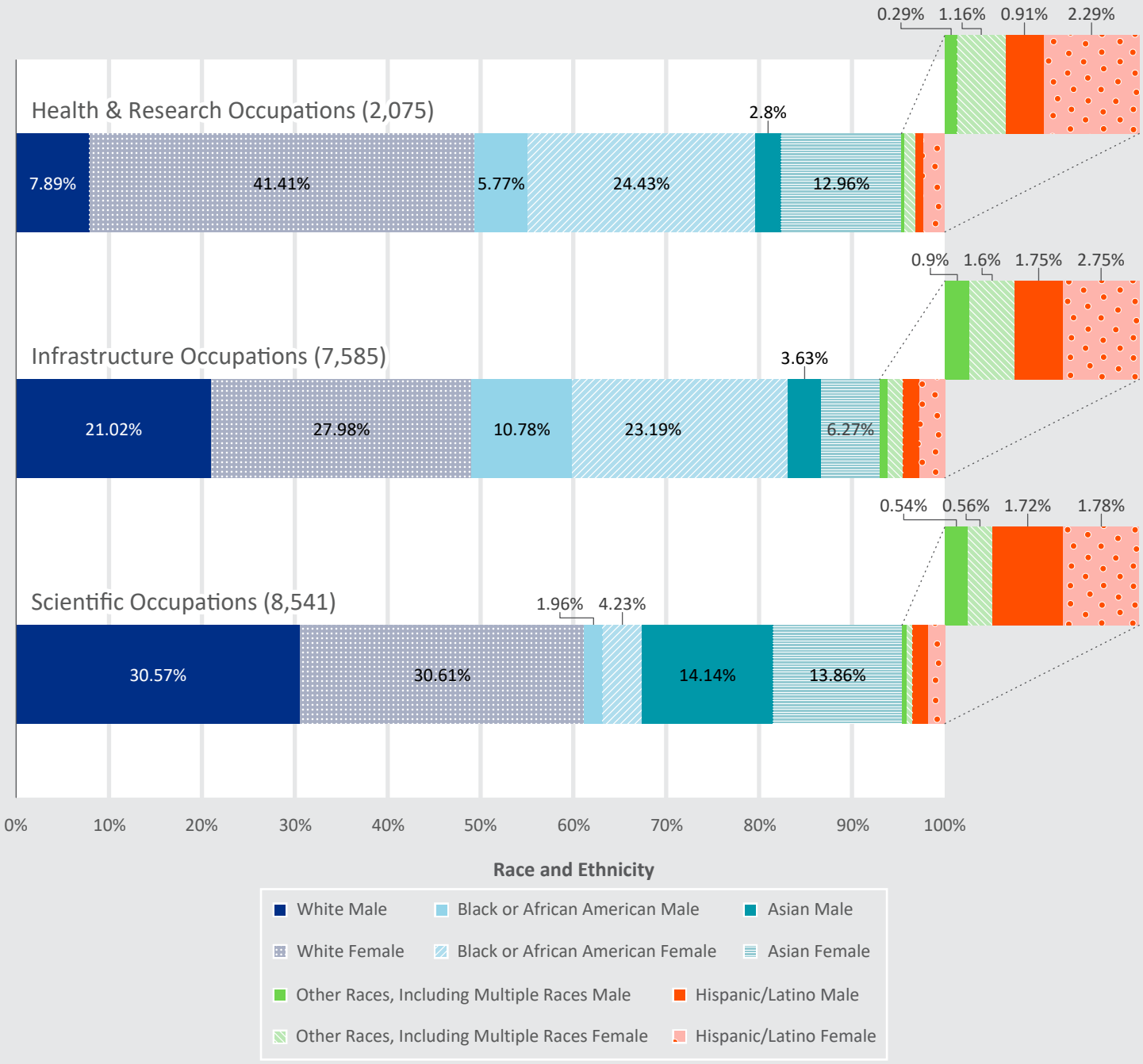
Sources: *The data were retrieved from https://www.edi.nih.gov/people/resources/advancing-racial-equity/nih-workforce-profile-fy20q04. The National Institutes of Health (NIH) workforce demographics for the fourth quarter of fiscal year 2020 (Q4 FY 2020) were retrieved from the nVision Human Resources Database on October 23, 2020, with an as-of date of September 30, 2020.*

of these occupations are allied health professions. Examples of Health and Research occupations include, but are not limited to, nurses, pharmacists, biological lab technicians, and patient care technicians. To protect data confidentiality, most analyses for this report excluded individuals in the Health and Research occupations.

» Infrastructure employees are those in all occupations that are not classified as Scientific or Health and Research. These occupations support the other occupations and include accountants, budget officers, engineers, and other administrative and maintenance staff members.[8]

8. NIH Office of Equity, Diversity, and Inclusion's Data Analytics Branch

Figure 3. NIH Workforce by Race, Ethnicity, Sex, and Occupational Category: Q4 of FY 2020



Source: *Re-graphed from the data produced by the NIH Office of Equity, Diversity, and Inclusion's Data Analytics Branch.*

In Q4 of FY 2020, Scientific occupations constituted 46.9% (n=8,541) of the NIH workforce. Infrastructure occupations made up 41.7% (n=7,585). Health and Research occupations made up the remaining 11.4% (n=2,075).[9] Across all three occupational categories, the majority of the workforce was White. Within the Scientific occupational category, the second-largest racial and ethnic group was Asian, whereas in the Infrastructure occupations and Health and Research occupations, the second-largest racial and ethnic group was Black (Figure 2).

NIH Workforce by Sex, Race, and Occupation: FY 2020

As discussed earlier (Figure 2), White was the predominant race and ethnicity in all categories of occupations. Figure 3 shows that in Scientific occupations, 30.5% were White females and 30.7% were White males; this was followed by 14.2% Asian males, 13.9% Asian females, 4.3% Black females, and 2.0% Black males. Hispanic or Latino females constituted 1.8% of the Scientific workforce, and Hispanic or Latino males made up 1.7% of the Scientific workforce.

For Health and Research occupations, the workforce was composed of 41.4% White females, followed by 24.5% Black females, 12.9% Asian females, 7.9% White males, and 5.8% Black males. Hispanic or Latino females made up 2.3% of Health and Research employees, and Hispanic or Latino males made up 0.9% of that sector.

9. Note: The total workforce was 18,203, but these numbers add up to 18,201 because there are missing data about two employees' occupational category.

The Infrastructure occupations consisted of 28.0% White females, 23.2% Black females, 21.0% White males, 10.8% Black males, 6.3% Asian females, and 3.6% Asian males. Hispanic or Latino females made up 2.7% of Infrastructure employees, and Hispanic males constituted 1.7% of that sector.

Scientific and Infrastructure Occupations Within the NIH Workforce

Workforce by Program, Sex, and Occupational Type

NIH classifies programs into three categories, based on human resources' organizational codes and determined by the functions and structure of an IC. The three program types are:

- "Extramural Program," which includes programs that work with outside researchers;
- "Intramural Program," which includes programs that work with NIH's own research staff members; and
- "Other Program," which refers to administrative units. Individual ICs may vary somewhat in the usage of "Other Program."

In FY 2019, 21.1% of the NIH workforce was employed in the Extramural Program, and 46.8% was in the Intramural Program. The remaining 32% was in the Other Program (Figure 4). Very little change was

Figure 4. NIH Workforce by Program Type: FY 2019 and 2020

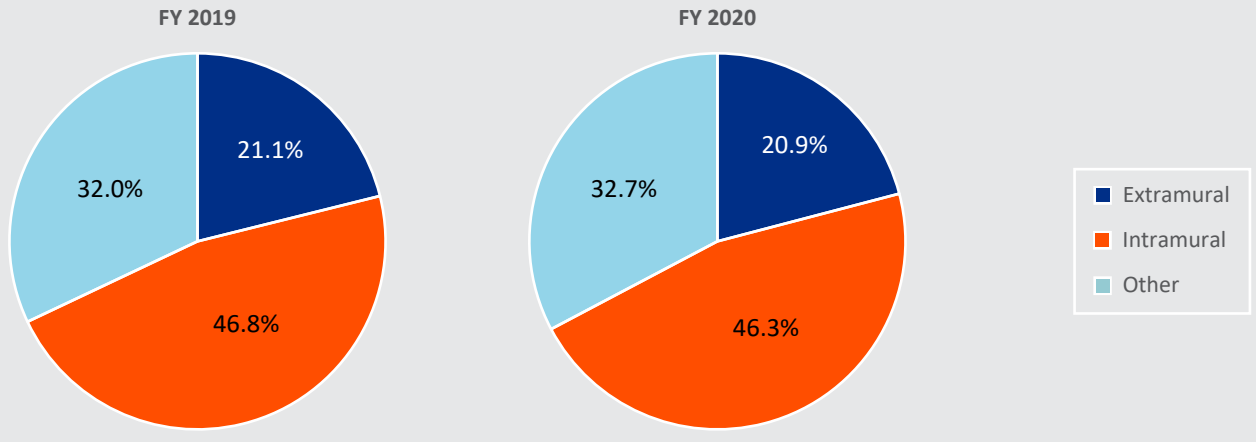
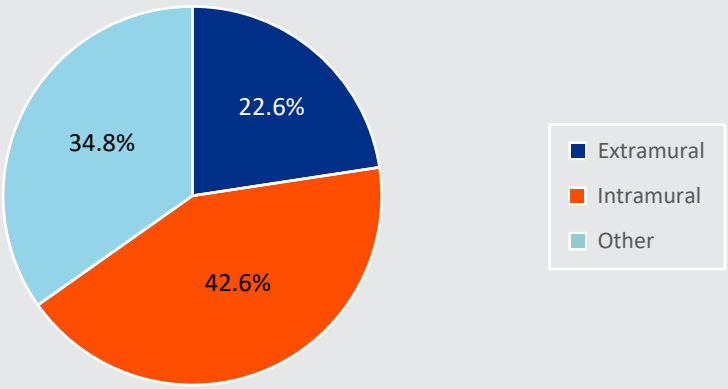


Figure 5. Scientific and Infrastructure Occupations by Program Type: FY 2020



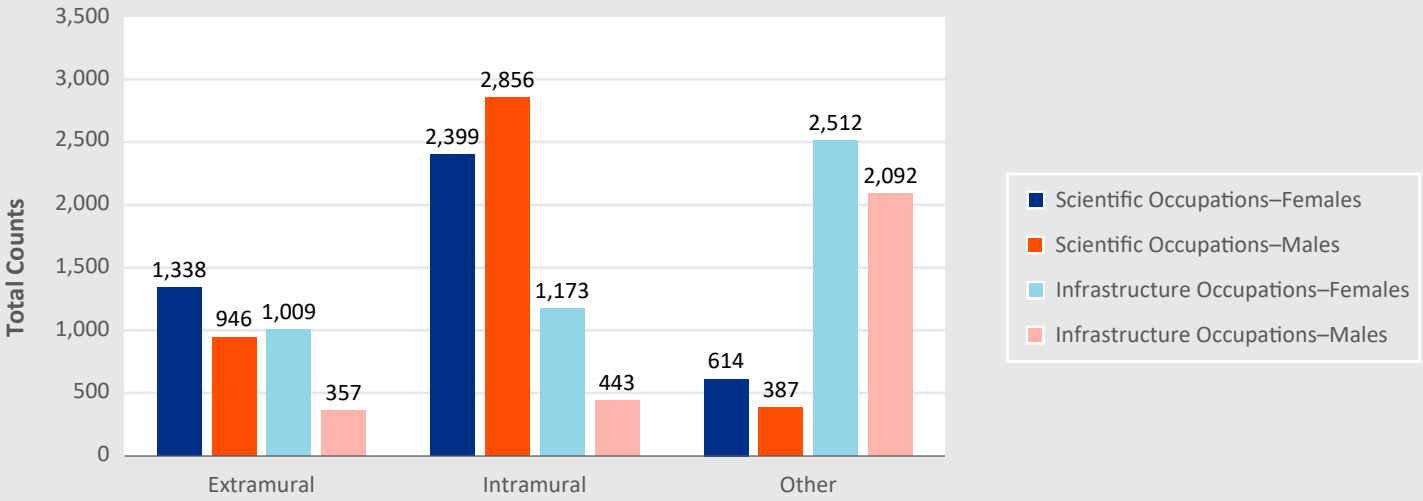
observed in FY 2020, with 20.9% in the Extramural Program, 46.3% in the Intramural Program, and 32.7% in the Other Program. Figure 4 shows the percentages of all three occupational types (Scientific, Infrastructure, and Health and Research) by program types (Extramural, Intramural, and Other).

For the remainder of this report, the analysis will not include data for the Health and Research occupations. Because of small cell counts, the analytical results for that sector do not meet NIH/EDI standards of reliability. Figure 5 shows the proportions of the workforce in the Extramural (n=3,651), Intramural (n=6,872), and Other (n=5,605) programs for only the Scientific occupations (n=8,541) and Infrastructure occupations (n=7,587), the data that form the basis for the remainder of this section.

Across program types (Extramural, Intramural, and Other), the percentages of females and males in the workforce remained fairly constant between FY 2019 and FY 2020 (Figure 6).

In FY 2020, more females than males held Scientific occupations within the Extramural Program (1,338 women versus 946 men, respectively). Females also

Figure 6. FY 2020: Scientific and Infrastructure Workforce by Sex and Program Type



Notes: *Extramural, Intramural, and Other Program types are grouped based on organizational codes. See https://oma.od.nih.gov/DMS/pages/organizational-changes-org-chart-function.aspx.*

Sources: *Data and definitions provided by the NIH Office of Equity, Diversity, and Inclusion's (EDI) Data Analytics Branch.*

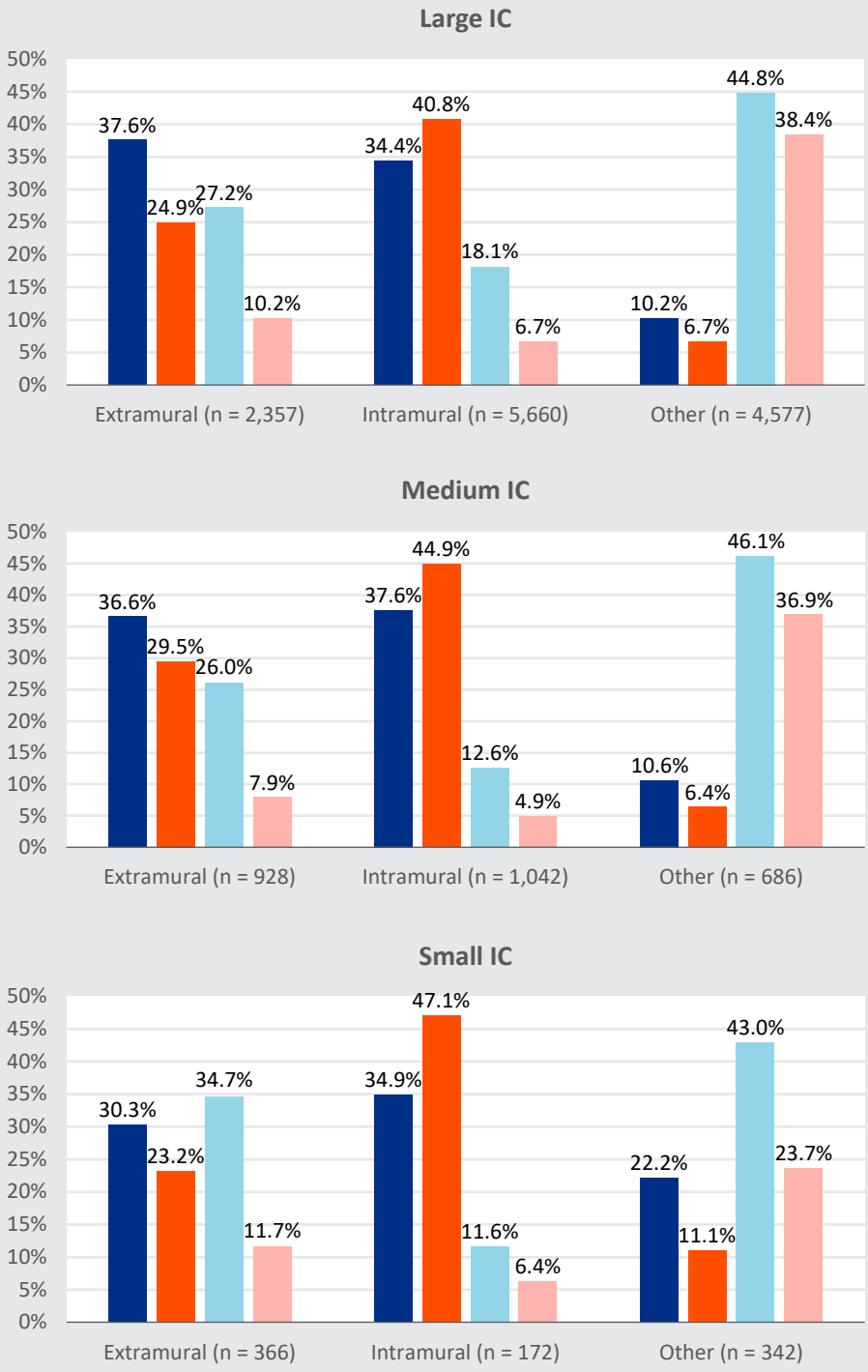
outnumbered males in the Infrastructure category (1,009 versus 357). However, in the Intramural Program, more males (2,856) than females (2,399) occupied Scientific occupations, though in Infrastructure occupations, there were more females (1,173) than males (443). In the Other Program, more females (614) than males (387) held Scientific occupations. The same was true of Infrastructure occupations (2,512 females versus 2,092 males).

Workforce by Program Type, IC Size, and Occupational Category: FY 2020

In FY 2020, marked trends existed in the gender composition of the Extramural, Intramural, and Other programs when it was examined by the size of the IC (Figure 7). IC size is considered large if the IC had 501 employees or more, medium if the IC had 201 to 500 employees, and small if the IC had 200 employees or fewer.

In the Extramural Program, more females than males occupied Scientific and Infrastructure occupations, regardless of the IC size. However, the proportion of Extramural female scientists diminished as the IC size decreased, from 37.6% of Extramural employees in large ICs to 30.3% in small ICs. However, in the Intramural Program, there were more male scientists than female scientists, and the proportion of male scientists

Figure 7. NIH Workforce by Program Type and IC Size: FY 2020



Notes: *Extramural, Intramural, and Other Program types are grouped based on organizational codes. See https://oma.od.nih.gov/DMS/pages/organizational-changes-org-chart-function.aspx.*

Please see Appendix C for IC size specifications.

Sources: *Data and definitions provided by the NIH Office of Equity, Diversity, and Inclusion's (EDI) Data Analytics Branch.*

increased as the IC size decreased. The proportion of male scientists ranged from 40.8% of Intramural employees in large ICs to 47.1% in small ICs.

Yet in the Other Program, females outnumbered males in both the Scientific and the Infrastructure occupations, no matter the size of the IC. Looking more closely, that pattern is the opposite of the situation in the Extramural Program, where instead there were higher proportions of females employed as scientists in the small ICs (22.2%) than there were in large (10.2%) and medium-sized (10.6%) ICs.

Workforce by Race, Ethnicity, Sex, and Program Type

Self-reported data on race, ethnicity, and sex of the FY 2020 workforce indicate wide demographic variations across program types (Figure 8). The following analyses considered combinations of race, ethnicity, and sex among staff from combining two of the sectors of NIH that constitute the majority of the NIH workforce (n=16,128), the Scientific and Infrastructure occupations. Examining the proportion of a particular race, ethnicity, and sex out of the entire Scientific and Infrastructure workforce indicates the predominance of a particular combination within the workforce rather than a programmatic and occupational stratum. Data characterizing the overall NIH workforce indicate the following patterns in the Extramural, Intramural, and Other programs.

The Extramural Program constitutes 22.6% (n=3,651) of the overall Scientific and Infrastructure occupations. In the Extramural setting, White females (5.1%) and White males (3.9%) in Scientific occupations represented the highest percentages of racial and ethnic and sex groups. Black females in Infrastructure occupations (2.7%) and White females in Infrastructure occupations (2.6%) were the next-largest racial, ethnic, and sex groupings. Asian females (1.8%) and Asian males (1.4%) in Scientific jobs had the next-largest proportions in the Extramural Program. Each of the remaining groupings constituted less than 1% of the NIH workforce.

The Intramural Program constitutes 42.6% (n=6,872) of the overall Scientific and Infrastructure occupations. In the Intramural Program, White males (10.8%) and White females (8.6%) employed in Scientific occupations represented the highest percentages among the racial, ethnic, and sex groups. They were followed by Asian males (5.7%) and Asian females (4.8%) in Scientific occupations and then by White females (3.6%), Black females (2.5%), and White males (1.5%) in Infrastructure jobs. Other racial and ethnic and sex combinations in the Intramural Program each represented less than 1% of the NIH workforce.

The Other Program constitutes 34.8% (n=5,605) of the overall Scientific and Infrastructure occupations. In the Other Program, White males (7.2%) and White females (7.0%) in Infrastructure occupations constituted the largest racial, ethnic, and sex groups, followed by Black females (5.7%) and Black males (3.6%) in Infrastructure occupations and then by White females (2.4%) and White males (1.6%) in Scientific jobs. The next-biggest racial, ethnic, and sex groups were Asian females (1.6%) and Asian males (1.2%) in Infrastructure occupations. Hispanic females (0.8%) and Hispanic males (0.6%) in Infrastructure occupations constituted less than 1% of the Scientific and Infrastructure workforce, just like all other racial, ethnic, and sex combinations.

NIH Leadership and Supervisory Roles

Senior Leadership and Supervisory Status by Sex

Close examination of supervisory roles—and leadership positions in general—is a critical part of any workforce analysis. NIH designates the NIH Director, NIH Deputy Directors/Associate Deputy Directors, IC Directors, IC Deputy Directors, Scientific Directors, Clinical Directors, Executive Officers, and Other Executives as senior leadership. NIH excludes Scientific and Clinical Directors serving in acting roles from the designation of senior leadership. Per these designations, in FY 2020, females represented 46.3% of NIH senior leadership—7.5 percentage points lower than males. (Figure not shown.)

NIH considers employees supervisors if they have a human resources supervisory status code of 2, 4, or 5, which also can include Title 42 employees. (Title 42 enables some Federal agencies to hire scientists and other consultants through a streamlined process exempt from many civil service hiring regulations and laws.) In FY 2020, 48.6% of supervisory staff members were females, a 1-percentage-point increase from FY 2019. (Figure not shown.)

Figure 8. NIH Workforce by Program Type and Race and Ethnicity: FY 2020

Notes: *Extramural, Intramural, and Other Program types are grouped based on organizational codes. See https://oma.od.nih.gov/DMS/pages/organizational-changes-org-chart-function.aspx.*

"Other Races, Including Multiple Races" includes American Indians/Alaska Natives, Native Hawaiians/Pacific Islanders, and individuals of two or more races. The ethnic category reflects the Hispanic population, which can be of any race. The coding of racial and ethnic groups is mutually exclusive.

Sources: *Re-graphed from data produced by the NIH Office of Equity, Diversity, and Inclusion's (EDI) Data Analytics Branch.*

Figure 9 illustrates NIH employees' supervisory status by sex, occupational type, and program type for FY 2020.

A greater percentage of females held supervisory functions in the Infrastructure occupations than in the Scientific occupations for both the Extramural (68.9% versus 51.6%) and Intramural (64.8% versus 33.2%) sectors. The Intramural Program employs the smallest percentage of females in supervisory Scientific roles of any program type, with twice as many males (66.8%) as females (33.2%).

Supervisory Status by Sex, Type of Pay Plan/Rank, and Type of Occupation

This section examines FY 2020 NIH workforce data and analyzes supervisory status by sex—with subgroup comparisons for the Scientific and Infrastructure occupations and with additional breakdowns by pay plan and rank. Specifically, the analysis focuses on General Schedule (GS) 12 to 15 employees (note that GS-12 and GS-13 employees do not have supervisory status); physicians, dentists, and veterinarians (occupational series 602, 680, and 701); and Title 42 positions (special consultants, scientists, and clinicians). No meaningful differences existed between FY 2019 and FY 2020 data, so only FY 2020 data are reported.

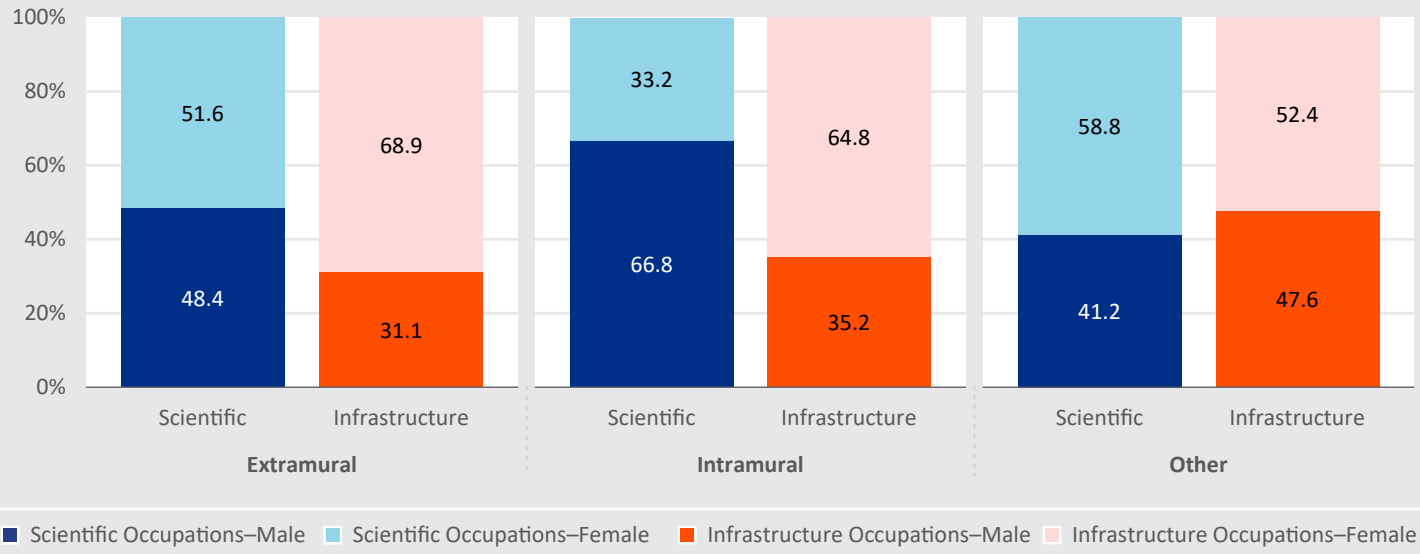
Scientific Occupations

In FY 2020, within Scientific occupations, the majority of GS-14 to GS-15 employees in supervisory roles across all three types of programs were females (51.9% in the Extramural Program; 57.8% in the Intramural Program; and 65.0% in the Other Program); note that only GS-14 and GS-15 employees can have supervisory roles (Figure 10). Likewise, the majority of GS-12 to GS-15 employees in nonsupervisory roles were also females (61.1% in the Extramural Program; 60.1% in the Intramural Program; and 64.3% in the Other Program).

For all program types—Intramural, Extramural, and Other—the majority of Title 42 positions were occupied by males, whether supervisory or nonsupervisory. This is especially true of the Intramural Program, where 71.0% of Title 42 supervisory positions were occupied by males.

Among physicians, dentists, and veterinarians (occupational series 602, 680, and 701), females held more nonsupervisory roles than supervisory roles across all programs. Within these occupations, males and females with supervisory status had almost equal representation in the Extramural Program, but males outnumbered females nearly 3-to-1 in the Intramural

Figure 9. Employees with Supervisory Status by Sex, Program Type, and Occupational Type: FY 2020



Notes: *Supervisory status is determined by the supervisory status codes of 2 (Supervisor or Manager – GSSG), 4 (Supervisor – CSRA), and 5 (Management Official – CSRA). "Supervisory Status" includes Title 42 employees. See https://dw.opm.gov/datastandards/referenceData/1578/current?index=S.*

Extramural, Intramural, and Other program types are grouped based on organizational codes. See https://oma.od.nih.gov/DMS/pages/organizational-changes-org-chart-function.aspx.

Sources: *Data and definitions provided by the NIH Office of Equity, Diversity, and Inclusion's (EDI) Data Analytics Branch.*

Figure 10. Comparison of Employees with Supervisory and Nonsupervisory Status in Scientific Occupations by Sex and Program Type: FY 2020

Notes: *Supervisory status is determined by the supervisory status codes of 2 (Supervisor or Manager – GSSG), 4 (Supervisor – CSRA), and 5 (Management Official – CSRA). "Supervisory Status" includes T42 employees. See https://dw.opm.gov/datastandards/referenceData/1578/current?index=S.*

The "Physicians/Dentists/Veterinarians" category includes the following occupation codes: 602-Physician Series, 680-Dentistry Series, and 701-Veterinary Health Science Series.

**GS-12 and GS-13 do not have supervisory status.*

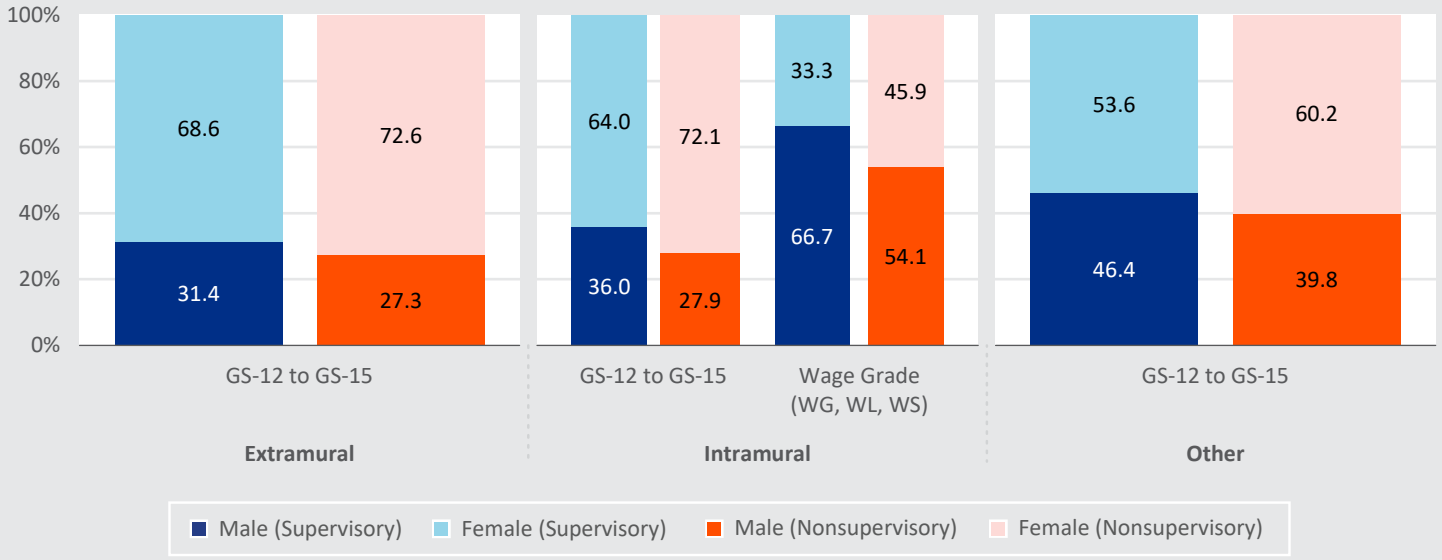
Source: *Data and definitions provided by the NIH Office of Equity, Diversity, and Inclusion's (EDI) Data Analytics Branch.*

Program (73.8% versus 26.2%) and nearly 2-to-1 in the Other Program (64.9% versus 35.1%).

Infrastructure Occupations

Overall, there was a higher proportion of females than males in GS-12–GS-15-level positions in Infrastructure occupations, whether in the Extramural, Intramural, or Other Program (Figure 11). This is true for both supervisory and nonsupervisory positions. For example, within the Extramural Program, females held 72.6% of the nonsupervisory roles and 68.6% of the supervisory roles. For employees in the Intramural Program in GS-12 to GS-15 positions, 72.1% of nonsupervisory roles were held by females and 64.0% of supervisory positions. In the Other Program, females held 60.2% of the nonsupervisory positions and 53.6% of the supervisory positions. Only among the Federal Wage System employees in the Intramural Program was

Figure 11. Comparison of Employees with Supervisory and Nonsupervisory Status in Infrastructure Occupations by Sex and Program Type: FY 2020



Notes: *Supervisory status is determined by the supervisory status codes of 2 (Supervisor or Manager – GSSG), 4 (Supervisor – CSRA), and 5 (Management Official – CSRA). "Supervisory Status" includes T42 employees. See https://dw.opm.gov/datastandards/referenceData/1578/current?index=S.*

GS-12 and GS-13 employees do not have supervisory status.

Source: *Data and definitions provided by the NIH Office of Equity, Diversity, and Inclusion's (EDI) Data Analytics Branch.*

there a greater proportion of males than females in both supervisory and nonsupervisory Infrastructure occupations.

Promotions (GS-Track Employees and Permanent Promotions Only)

Promotions by Occupational Type, Program Type, and Sex

In both FY 2019 and FY 2020, more females than males received a promotion. Females in both Scientific and Infrastructure occupations across all program types obtained at least 58.7% of promotions during FY 2020 (Figure 12).[10] However, the percentages of females promoted in Scientific occupations were lower than those in Infrastructure occupations within the Extramural (66.7% versus 83.0%) and the Intramural (58.7% versus 82.3%) programs. In the Other Program, females represented a higher proportion of those promoted in both the Scientific occupations and the Infrastructure occupations for both years (78.9% versus 63.2%).

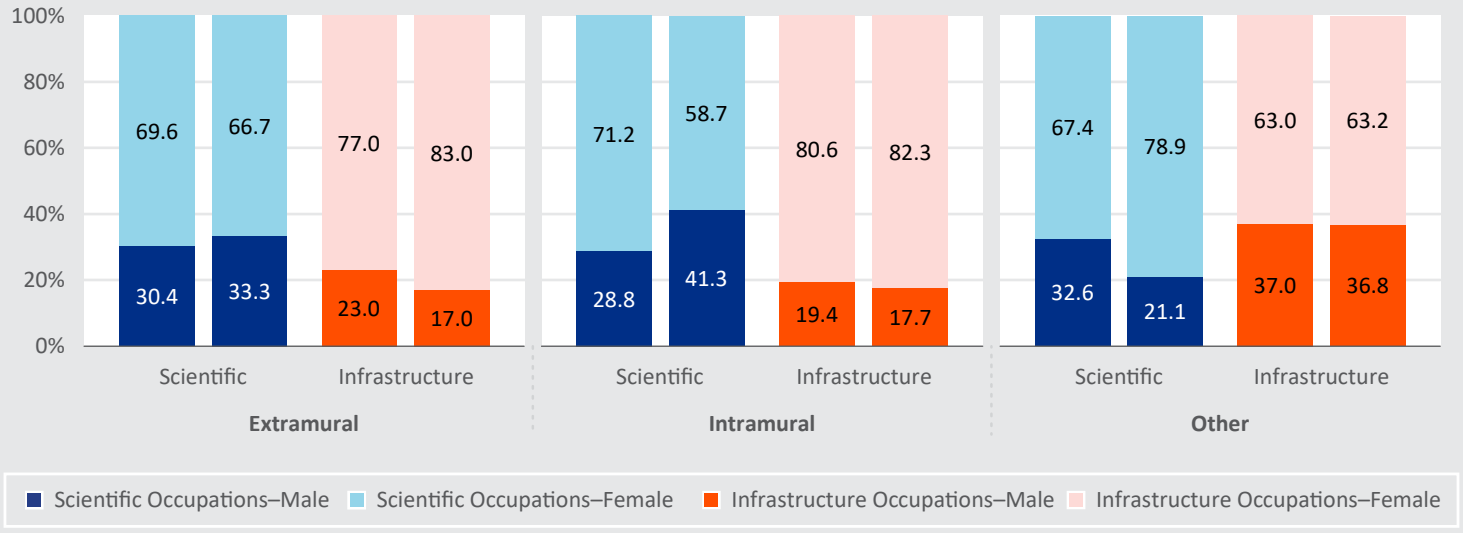
Differences in Promotions by Occupational Type, Program Type, and Sex Between FY 2019 and FY 2020

Between FY 2019 and FY 2020, the promotion rates of females who were employed in Scientific occupations fell slightly for both the Extramural and the Intramural programs. In the Extramural Program, the rate fell by about 3 percentage points, from 69.6% to 66.7%. In the Intramural Program, the proportion fell by more than 12 percentage points, from 71.2% to 58.7%. However, between FY 2019 and FY 2020, promotion rates of female scientists in the Other Program increased by 11.5 percentage points, from 67.4% to 78.9%.

Conversely, for females employed in the Infrastructure occupations, promotion rates among females increased by 6 percentage points in the Extramural Program, from 77.0% to 83.0%, and by about 2 percentage points in the Intramural Program, from 80.6% to 82.3%. The promotion rates remained almost the same in the Other Program.

10. This report defines "promotion" as a change of status, through continuous employment, from one General Schedule (GS) grade to a higher GS grade. Note that promotions in this context did not include tenure-track promotions or conversions from GS to RF. In addition, obtaining a quality step increase was not considered a promotion.

Figure 12. Promoted Individuals by Occupational Type, Program Type, and Sex: FYs 2019 and 2020



Notes: *Promotion data include GS employees and permanent promotions only.*

Source: *Data and definitions provided by the NIH Office of Equity, Diversity, and Inclusion's (EDI) Data Analytics Branch.*

Senior Leadership and Supervisory Employees by Race, Ethnicity, and Sex

White employees held 81.6% of NIH senior leadership positions in FY 2020. Black (10.2%), Asian (6.1%), and Hispanic (2.0%) employees made up the remaining 18.4% of NIH senior leaders. Among personnel with supervisory status, most notably, White employees held 69.8% of the positions, and Asian employees held 13.6%[11] (Figure 13).

Senior and Supervisory Leadership by Sex, Race, and Ethnicity

In FY 2020, most NIH senior leaders and those in supervisory leadership positions were White (Figure

11. The proportions of the different racial and ethnic combinations within senior leadership or personnel with supervisory status did not shift from FY 2019 to FY 2020; therefore, only the FY 2020 results are reported within the overall percentages.

Figure 13. Race and Ethnicity of Senior Leadership and Supervisory Employees: FY 2020

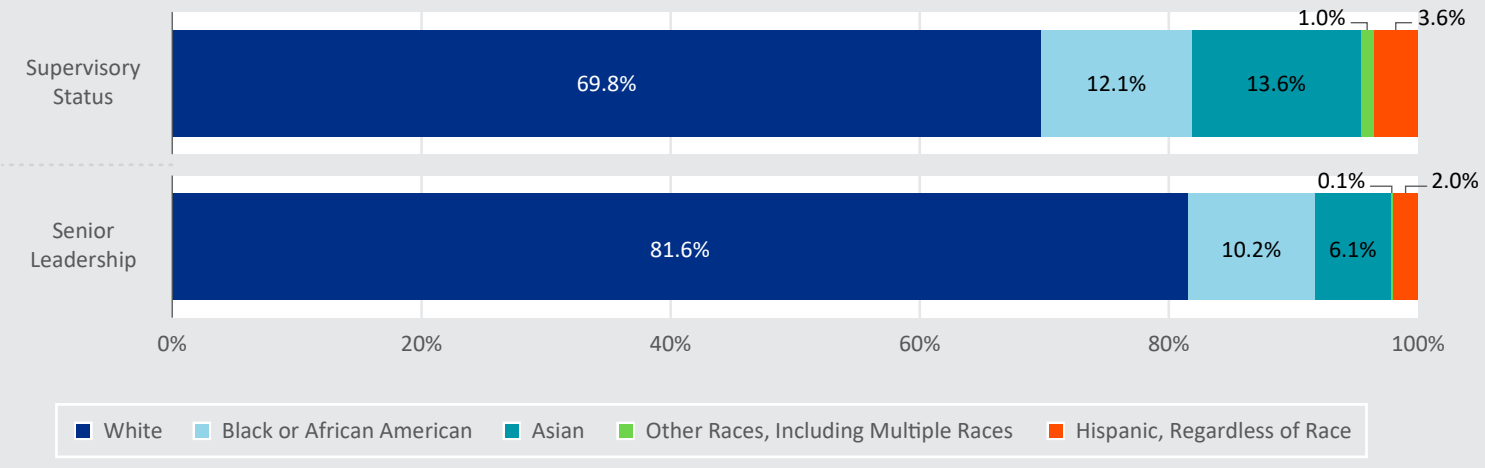
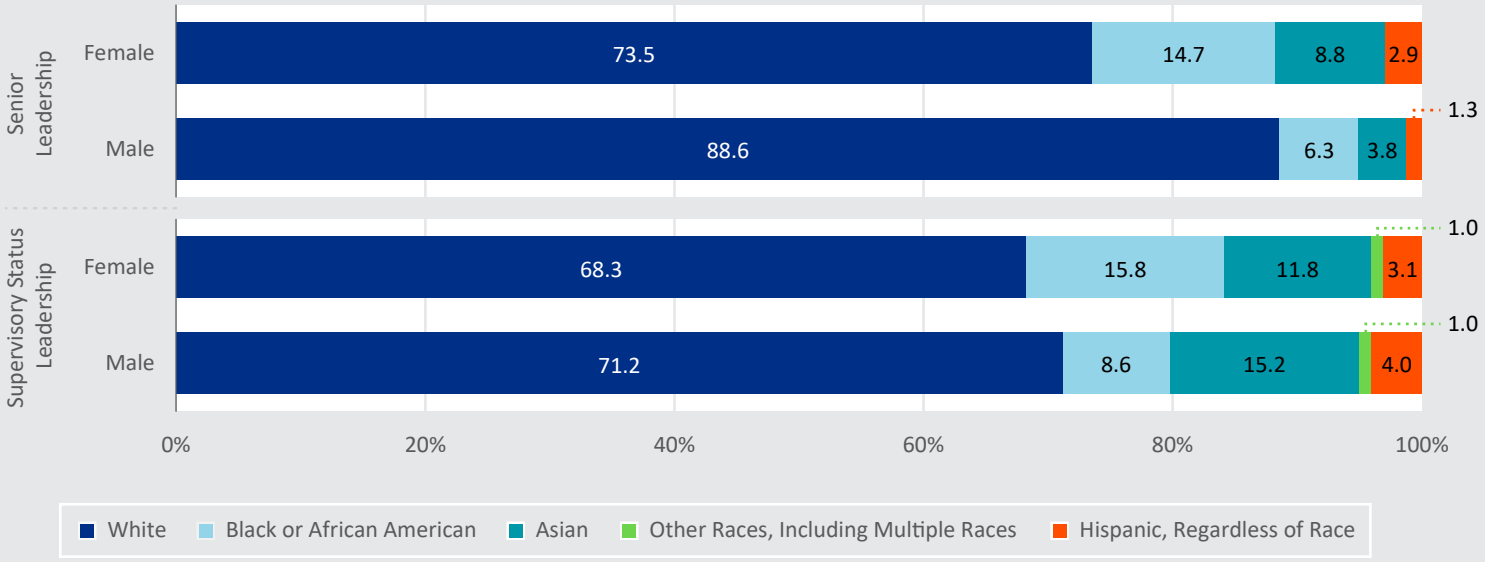


Figure 14. Race, Ethnicity, and Sex of NIH Senior and Supervisory Leadership: FY 2020



Notes: *Senior leadership includes the NIH Director, NIH Deputy Directors/Associate Deputy Directors, IC Directors, IC Deputy Directors, Scientific Directors, Clinical Directors, Executive Officers, and Other Executives (SL, ES). Scientific and Clinical Directors serving in acting roles were not counted under senior leadership. Senior leaders who were in the Commissioned Corps were excluded because of the lack of complete demographic data from Commissioned Corps employees.*

Supervisory status is determined by the supervisory status codes of 2 (Supervisor or Manager – GSSG), 4 (Supervisor – CSRA), and 5 (Management Official – CSRA). "Supervisory Status" includes T42 employees. See https://dw.opm.gov/datastandards/referenceData/1578/current?index=S.

The sample of supervisory leaders here only includes those with the following pay plans: AD, GS, GP, GM, GR, RS, RF, RG, and RS. See the U.S. Office of Personnel Management's Data Standards guide for more information about these pay plans: https://dw.opm.gov/datastandards/referenceData/1497/current?category=&q=pay+plan.

This sample of supervisory leaders also excludes those in the senior leader group defined above. "Other Races, Including Multiple Races" includes American Indians/Alaska Natives, Native Hawaiians/Pacific Islanders, and individuals of two or more races. The ethnic category reflects the Hispanic population, which can be of any race. Coding of racial and ethnic groups is mutually exclusive.

Source: *Data and definitions provided by the NIH Office of Equity, Diversity, and Inclusion's (EDI) Data Analytics Branch.*

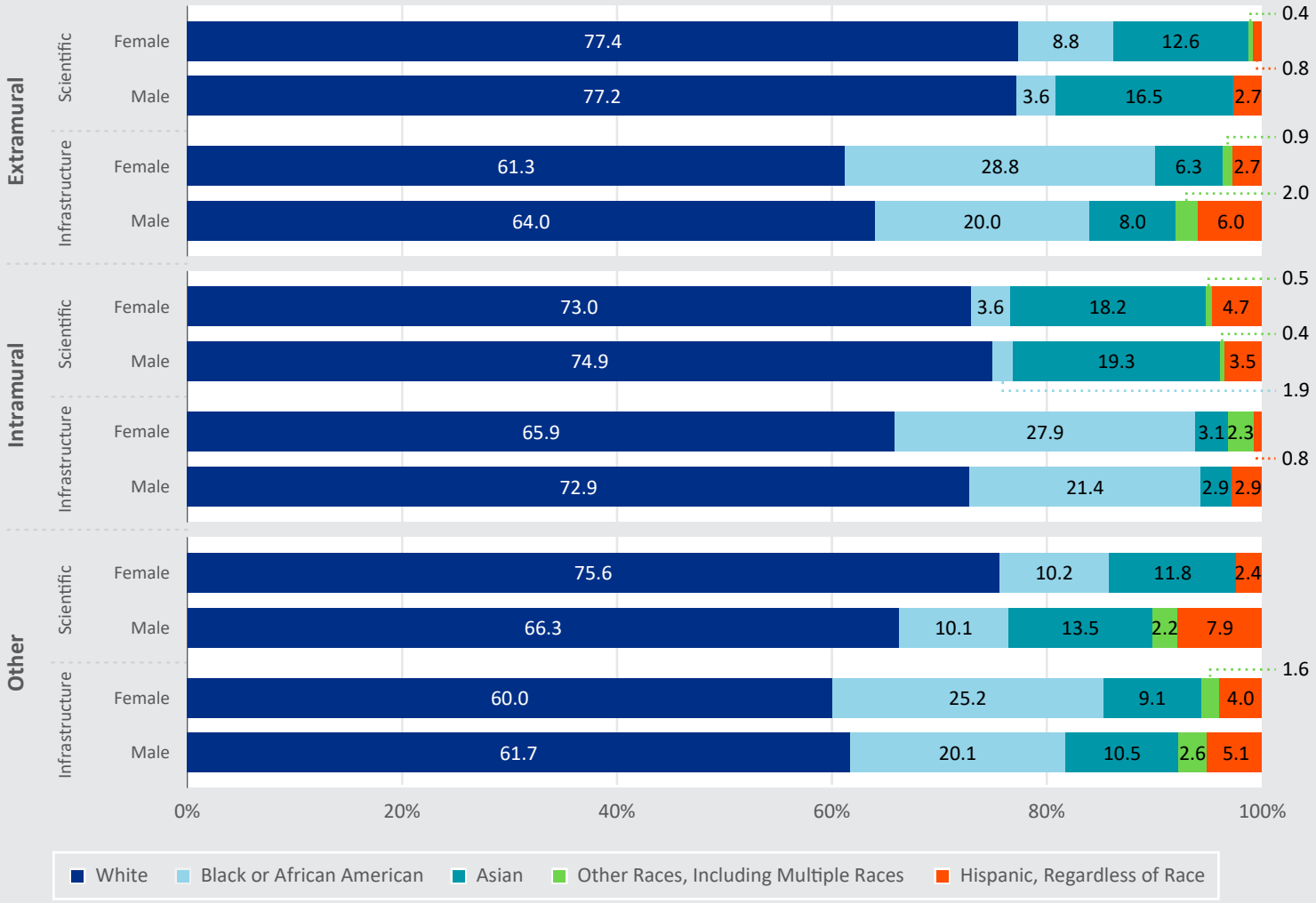
14). Male and female senior leaders and supervisors, however, had different racial and ethnic makeups. Among females, senior leadership was 73.5% White, 14.7% Black, 8.8% Asian, and 2.9% Hispanic. Among males, senior leadership was 88.6% White, 6.3% Black, 3.8% Asian, and 1.3% Hispanic. Female supervisors were 68.3% White, 15.8% Black, 11.8% Asian, and 3.1% Hispanic. Male supervisors, on the other hand, were 71.2% White, 15.2% Asian, 8.6% Black, and 4.0% Hispanic.

Supervisory Status by Occupation and Program Type, Sex, Race, and Ethnicity

Figure 15 illustrates supervisory status by sex, race, and ethnicity, with extended analysis by occupation and program types in FY 2020. Within Scientific occupations, Black males constituted a smaller proportion among their sex than Black females did among their sex in both Extramural (3.6% and 8.8%, respectively) and Intramural (1.9% and 3.6%, respectively) programs. Conversely, the proportion of males with supervisory status who were Asian was higher than the proportion of females with supervisory status who were Asian (16.5% and 12.6%, respectively).

In the Infrastructure occupations across all program types, noticeably higher percentages of female supervisors were Black (28.8% in Extramural, 27.9% in Intramural, and 25.2% in Other) than male supervisors who were Black (20.0%, 21.4%, and 20.1%, respectively) in FY 2020. Greater parity existed between White and Asian males and females in supervisory Infrastructure occupations.

Figure 15. Race and Ethnicity of Employees with Supervisory Status by Sex, Occupational Type, and Program Type: FY 2020



Notes: *Supervisory status is determined by the supervisory status codes of 2 (Supervisor or Manager – GSSG), 4 (Supervisor – CSRA), and 5 (Management Official – CSRA). "Supervisory Status" includes T42 employees. See https://dw.opm.gov/datastandards/referenceData/1578/current?index=S.*

"Other Races, Including Multiple Races" includes American Indians/Alaska Natives, Native Hawaiians/Pacific Islanders, and individuals of two or more races. The ethnic category reflects the Hispanic population, which can be of any race. Coding of racial and ethnic groups is mutually exclusive.

Extramural, Intramural, and Other program types are grouped based on organizational codes. See https://oma.od.nih.gov/DMS/pages/organizational-changes-org-chart-function.aspx.

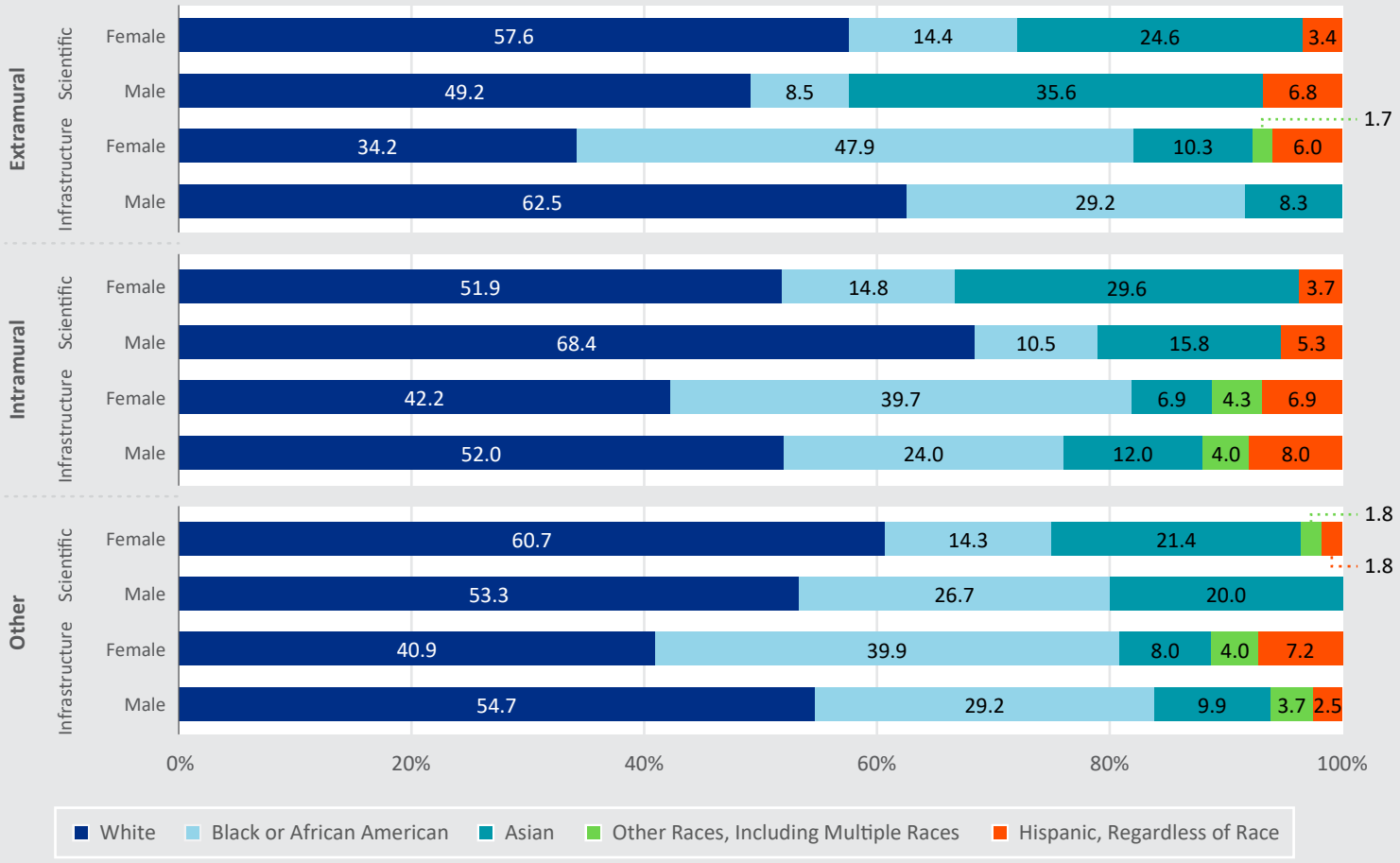
Source: *Data and definitions provided by the NIH Office of Equity, Diversity, and Inclusion's (EDI) Data Analytics Branch.*

Promotions by Occupational Type, Program Type, Sex, and Race and Ethnicity in FY 2020

The racial and ethnic breakdowns by sex for promotions in FY 2020 are presented in Figure 16.

Among those who received promotions in FY 2020, females in Scientific occupations across all three program types were predominantly White—57.6% in the Extramural Program, 51.9% in the Intramural Program, and 60.7% in the Other Program. The same trend can be seen in males who received promotions in Scientific occupations across the program types. In the Extramural sector, White males constituted 49.2% of male scientists promoted—i.e., a greater percentage than that of any other racial and ethnic group. In the Intramural Program, 68.4% of male scientists who were promoted were White, and in the Other Program, 53.3% of male scientists who were promoted were White.

Figure 16. Race and Ethnicity of Promoted Individuals by Sex, Occupational Type, and Program Type: FY 2020



Notes: *Promotion data include GS employees and permanent promotions only.*

"Other Races, Including Multiple Races" includes American Indians/Alaska Natives, Native Hawaiians/Pacific Islanders, and individuals of two or more races. The ethnic category reflects the Hispanic population, which can be of any race. The coding of racial and ethnic groups is mutually exclusive.

Source: *Data and definitions provided by the NIH Office of Equity, Diversity, and Inclusion's (EDI) Data Analytics Branch.*

In the Extramural Infrastructure positions, the proportion of White females who were promoted was 34.2%. In the Intramural and the Other programs, White females dominated the proportions of females promoted—42.2% and 40.9%, respectively. Among males working in Infrastructure occupations who received promotions, the majority were White; in the Extramural Program, it was 62.5%. In the Intramural Program, White males made up 52.0% of the males who were promoted in Infrastructure positions, and in the Other Program, the proportion was 54.7%.

In the Extramural Program, the proportion of males promoted in Scientific positions who were Asian (35.6%) was higher than that for Asian females (24.6%). This was not the case for both the Intramural and the Other programs, where the proportions of females promoted in Scientific occupations who were Asian (29.6% and 21.4%, respectively) were higher than the proportions of males promoted in Scientific occupations who were Asian (15.8% for Intramural, 20.0% for Other).

Regarding promotions in Scientific positions in the Extramural and Intramural programs, the percentages of males and females who were Black were lower than the percentages of Whites and Asians. The proportion of females promoted in Scientific positions who were Black was 14.4% in the Extramural Program, and it was 14.8% in the Intramural Program. The proportion of males promoted in Scientific positions who were Black was 8.5% in the Extramural Program, and it was 10.5% in the Intramural Program. In the Other Program, the

proportion of females promoted in Scientific positions who were Black was 14.3%, and it was 26.7% for Black males.

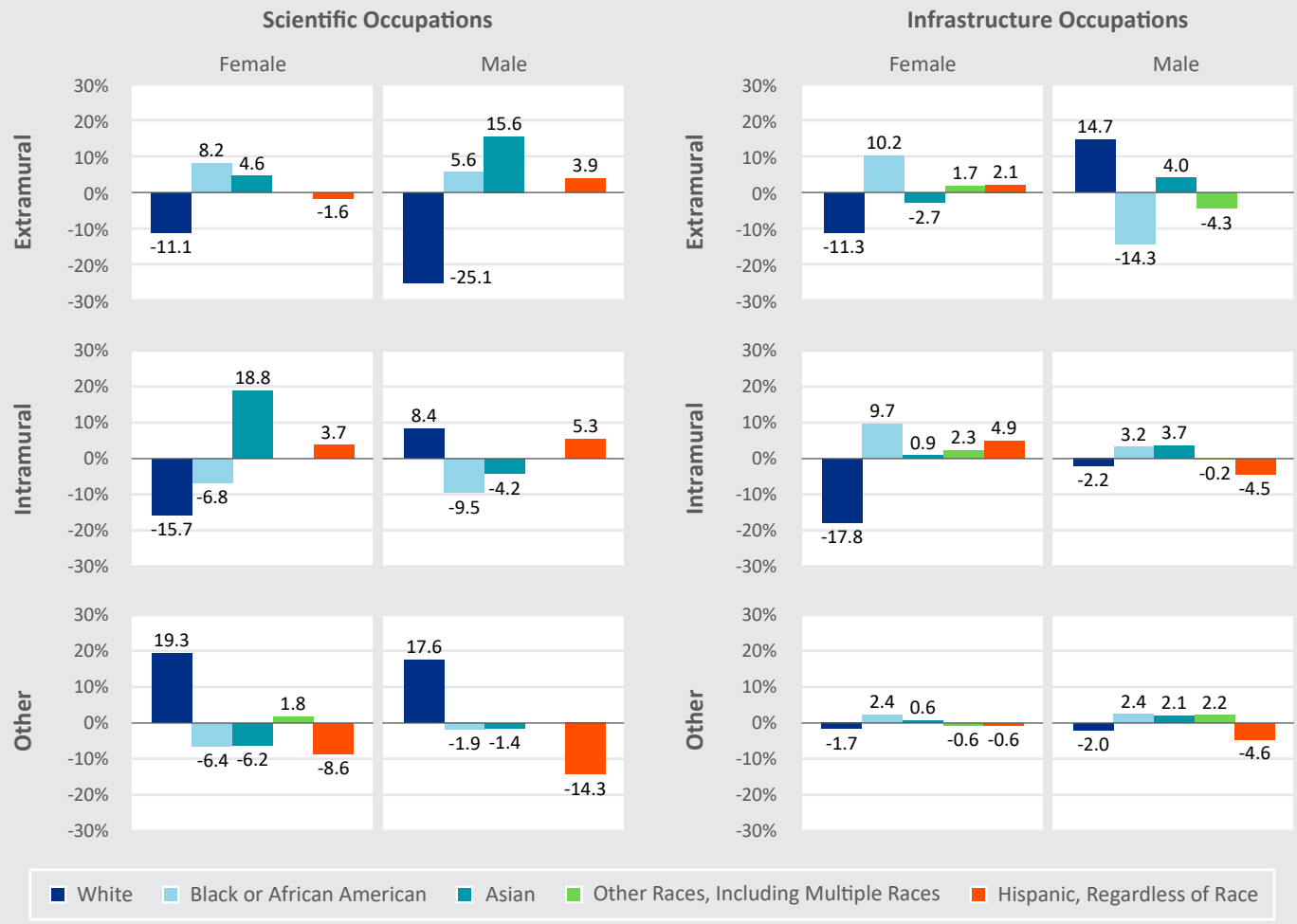
Among females in Infrastructure occupations who received promotions in the Extramural Program, 47.9% were Black, constituting the largest racial group among females who were promoted in these occupations. The proportion of females promoted in Infrastructure positions who were Black was 39.7% in the Intramural Program, and it was 39.9% in the Other Program. Among males who were promoted in Infrastructure positions, Black males constituted 29.2% in the Extramural Program, 24.0% in the Intramural Program, and 29.2% in the Other Program.

Furthermore, the percentages of promoted females who were Hispanic were lower than those of promoted males who were Hispanic in the Extramural (3.4% versus 6.8%) and Intramural programs (3.7% versus 5.3%).

Changes in Promotions by Occupational Type, Program Type, Sex, and Race and Ethnicity Between FY 2019 and FY 2020

Substantial changes in promotion status among males and females of different racial and ethnic groups occurred between FY 2019 and FY 2020 (Figure 17). In the Extramural Program, both White females and White males in Scientific occupations had lower percentages of promotions in FY 2020 than in FY 2019, decreasing

Figure 17. Percentage-Point Change in Race, Ethnicity, and Sex of Promotees by Occupational Type and Program Type: FY 2019 to FY 2020



Notes: *Promotion data include GS employees and permanent promotions only.*

"Other Races, Including Multiple Races" includes American Indians/Alaska Natives, Native Hawaiians/Pacific Islanders, and individuals of two or more races. The ethnic category reflects the Hispanic population, which can be of any race. Coding of racial and ethnic groups is mutually exclusive.

Source: *Data and definitions provided by the NIH Office of Equity, Diversity, and Inclusion's (EDI) Data Analytics Branch.*

by 11.1 and 25.1 points, respectively. All other non-White racial–sex group combinations experienced increases in their proportions of promotions between the two years except for Hispanic females in Scientific occupations, whose proportion of promotions declined by 1.5 percentage points. For those employed in Infrastructure occupations in the Extramural Program, the percentage of promoted females who were White declined by 11.3 points, but the percentage of promoted males who were White increased by 14.7 points. In contrast, the share of promotions for Black females increased by 10.2 percentage points, and the share of promotions for Black males declined by 14.3 percentage points.

In the Intramural Program, the percentage of promoted females who were of Asian descent increased by 18.8 points. In contrast, the percentage of promoted males who were Asian declined by 4.2 points. Although there were increases in the percentages of promoted employees who were Hispanic in Intramural Scientific occupations, the magnitude was higher for males (5.3 points) than for females (3.7 points).

There were increases in the percentages of promoted employees who were White for both males (17.6 points) and females (19.3 points) working in Scientific occupations in the Other Program. Conversely, among people working in Scientific occupations, the percentage of promoted males who were Hispanic decreased by

14.3 points, and the percentage of promoted females who were Hispanic decreased by 8.6 points. Regardless of sex, race, and ethnicity, the distribution of race and ethnicity for promotions in Infrastructure occupations in the Other Program remained relatively stable between FY 2019 and FY 2020, varying from an increase of 2.4 percentage points for Black females and Black males to a decrease of 4.6 percentage points for Hispanic males.

Conclusions

Presented in this section was how NIH employees in select roles, programs, and occupations differed by the various intersections of sex, race, and ethnicity in FY 2020 and, when comparisons were meaningful, in FY 2019. The data suggest key areas where the roles of females, particularly those coming from underrepresented racial and ethnic groups, could be expanded.

In FY 2020, females held the majority of Scientific and Infrastructure positions across ICs of all sizes and all program types—except for Intramural programs, where males held the majority of Scientific jobs. This occupational pattern was consistent for the sex breakdown of those in supervisory roles. Further review of supervisory roles revealed that higher percentages of females occupied supervisory roles in Infrastructure occupations than in Scientific occupations in both Extramural and Intramural programs. Further, a gap of 7.5 percentage points between females and males remained in senior leadership positions at NIH.

The percentage of individuals receiving promotions in Infrastructure occupations who were female was higher than that of those receiving promotions who were female in Scientific occupations, for both the Intramural and the Extramural programs, although the opposite was seen in the Other Program. The percentage of people promoted in Scientific occupations who were female fell by 2.9 points in the Extramural Program (from 69.6% in FY 2019 to 66.7% in FY 2020), and the percentage of people promoted in Scientific occupations who were female decreased by 12.5 points in the Intramural Program (from 71.2% in FY 2019 to 58.7% in FY 2020). The percentage of people receiving promotions who were female increased in Infrastructure occupations by 6.0 points in the Extramural Program (from 77.0% in FY 2019 to 83.0% in FY 2020) and by 1.7 points in the Intramural Program (from 80.6% in FY 2019 to 82.3% in FY 2020). White females and males received the plurality of promotions in Scientific occupations in FY 2020 across program types. The rates of promotion changed from FY 2019 to FY 2020 across the racial and ethnic groups, with no consistent pattern by program or occupational type.

This analysis indicates that NIH could achieve greater sex and racial and ethnic parity by increasing the number and percentage of females within its workforce, particularly at the supervisory and senior leadership levels, in all program types and for women of underrepresented racial and ethnic groups in Scientific occupations. As the COVID-19 pandemic has demonstrated, flexible family-friendly policies can help to address sex and gender disparities in NIH's workforce. In addition to existing policies, paid parental leave for employees and contractors; expanded access to child care and potentially senior care; and maximizing flexible or telework scheduling for eligible employees could be future workforce-related areas to explore. Additionally, programs such as mentorship programs or circles, targeted leadership training courses, diversity training, and other programs could help to increase the number and percentage of females, especially those coming from underrepresented groups, in supervisory positions and leadership roles in Scientific occupations.

NIH Grant Funding and Success Rates: Differences by Sex and/or Gender from Fiscal Years 2016 to 2020

Introduction

The *Report of the Advisory Committee on Research on Women's Health* (women's health research biennial report) for fiscal years (FYs) 2019–2020 includes, for the first time, information about the sex and/or gender, race, and ethnicity[12] of NIH grantees and will serve as a baseline for future reports. The grant data from FY 2016 to FY 2020 presented in this section were compiled and analyzed by the Division of Statistical Analysis and Reporting (DSAR) within the NIH Office of Extramural Research's Office of Research Reporting and Analysis[13] and detail sex- and/or gender-, race-, and ethnicity-based differences in applications, awards, and funding in the following areas:

1. type of grant mechanism: R01-equivalent grants versus all research project grants (RPGs);
2. career stage of the principal investigator (PI): early-stage investigator (ESI) versus established investigator, as well as the type of training and career development grants received; and
3. grant application type: new application (Type 1) versus renewal application (Type 2).

The data provided by DSAR are presented as aggregates to protect individuals' privacy. The report summarizes analytical findings by sex and/or gender and, in some cases, by race and ethnicity. No hypothesis testing was performed on the data, and all differences discussed are thematically meaningful but may not be statistically significant. More detailed methodology and definitions can be found in Appendix C.

12. Sex, race, and ethnicity are all self-reported.
13. Data and definitions provided by the Division of Statistical Analysis and Reporting within the NIH Office of Extramural Research's Office of Research Reporting and Analysis.

NIH Grant Awards by Sex, FY 2016–2020

Number of Awards

The analysis in this section compares two main categories of NIH grant awards: research project grants (RPGs)[14] and a subset of RPGs—the R01s and the R01-equivalent grants.[15] DSAR uses "RPGs" to include not only R01s but also many other types of mechanisms—larger grants such as the U's and smaller and shorter grants such as the R00, R03, R15, R21, and R56.

The R01 is the original and historically oldest grant mechanism used by NIH. Whether a grant is an R01-equivalent grant is determined by the specific activity code assigned by NIH to the grant from a particular Institute or Center (IC). R01 grants provide support for health-related research and development for a period of 3 to 5 years. R01s can be investigator-initiated or can be solicited via requests for applications.

Figures 18 and 19 illustrate the number of grant awardees by sex among all competing applications for R01-equivalent grants and all RPGs, respectively. In each year from FY 2016 to FY 2020, males received most of the R01-equivalent grants and RPGs. The proportion of female grantees over the past 5 years has increased only slightly.

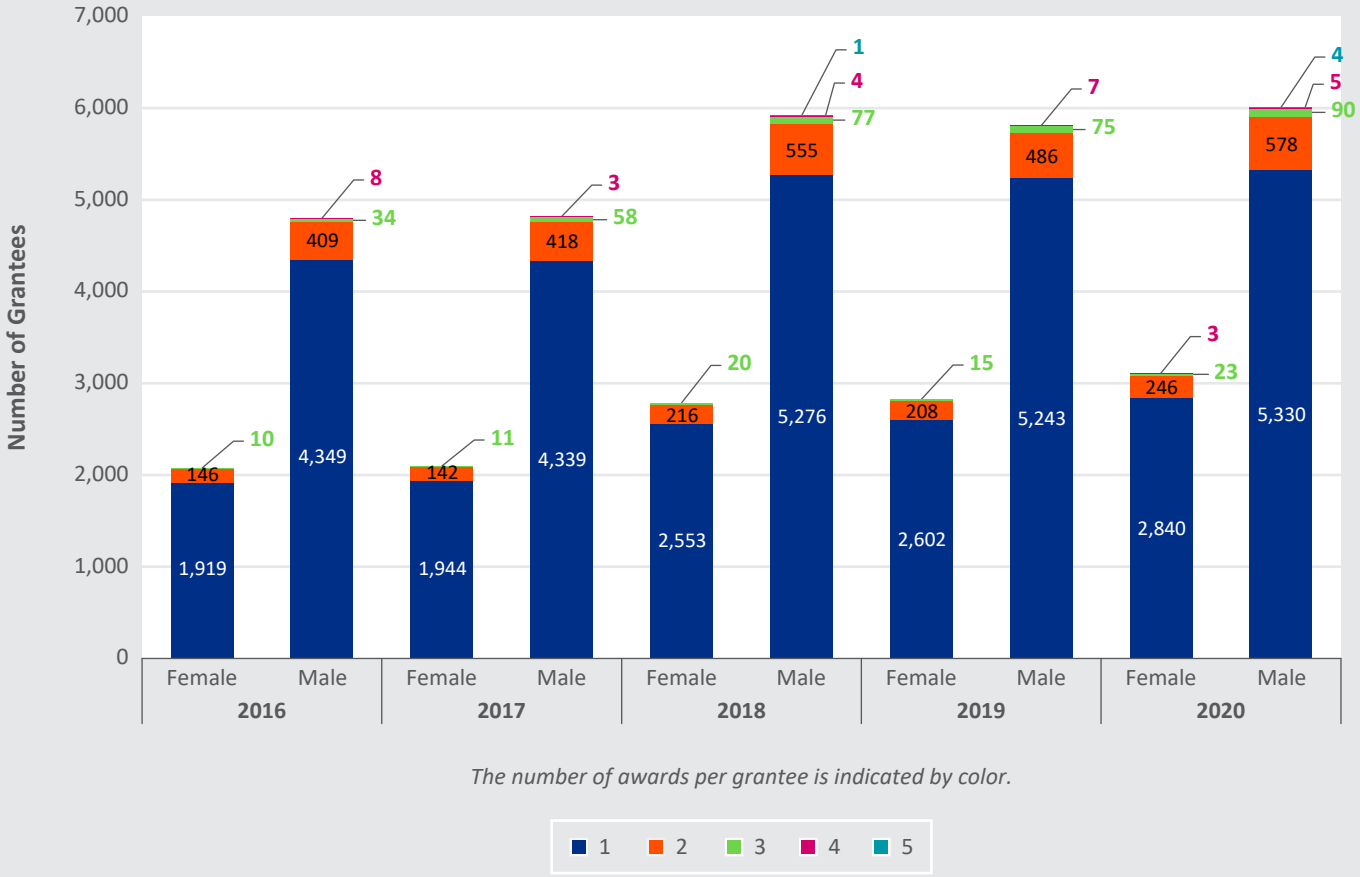
R01-Equivalent Grantees

Overall, more males than females received R01-equivalent awards among all competing applications in FY 2016-2020.

» For PIs who received only 1 award, the male-to-female ratios of grantees were 2.27, 2.23, 2.07, 2.01, and 1.88, respectively, for each fiscal year.

14. For FY 2020, RPGs are defined as activity codes DP1, DP2, DP3, DP4, DP5, P01, PN1, PM1, R00, R01, R03, R15, R21, R22, R23, R29, R33, R34, R35, R36, R37, R61, R50, R55, R56, RC1, RC2, RC3, RC4, RF1, RL1, RL2, RL9, RM1, UA5, UC1, UC2, UC3, UC4, UC7, UF1, UG3, UH2, UH3, UH5, UM1, UM2, U01, U19, and U34. Not all of these activities may be in use by NIH every year.
15. R01-equivalent grants are defined as activity codes DP1, DP2, DP5, R01, R37, R56, RF1, RL1, U01, and R35 from select National Institute of General Medical Sciences (NIGMS) and National Human Genome Research Institute (NHGRI) program announcements (PAs). Not all of these activities may be in use by NIH every year.

Figure 18. NIH Grantees by Sex: R01-Equivalent Grants (FY 2016–2020)



Notes:

1. *Includes direct budget authority only.*
2. *Includes fiscal years 2016–2020.*
3. *Includes all competing applications.*
4. *Includes both contact PI and multiple-PI (MPI) applications.*
5. *"RPG" is defined in 2020 as activity codes DP1, DP2, DP3, DP4, DP5, P01, PN1, PM1, R00, R01, R03, R15, R21, R22, R23, R29, R33, R34, R35, R36, R37, R61, R50, R55, R56, RC1, RC2, RC3, RC4, RF1, RL1, RL2, RL9, RM1, UA5, UC1, UC2, UC3, UC4, UC7, UF1, UG3, UH2, UH3, UH5, UM1, UM2, U01, U19, and U34. Research projects were first coded to the National Library of Medicine (NLM) in fiscal year 2007. Not all of these activities may be in use by NIH every year.*
6. *"R01-equivalent" is defined in 2020 as activity codes DP1, DP2, DP5, R01, R37, R56, RF1, RL1, U01, and R35 from select NIGMS and NHGRI program announcements (PAs). Not all of these activities may be in use by NIH every year.*

Source: *Data drawn from the frozen success rate demographic dataset as of 2/8/2021. Data produced by the Division of Statistical Analysis and Reporting within the NIH Office of Extramural Research's Office of Research Reporting and Analysis.*

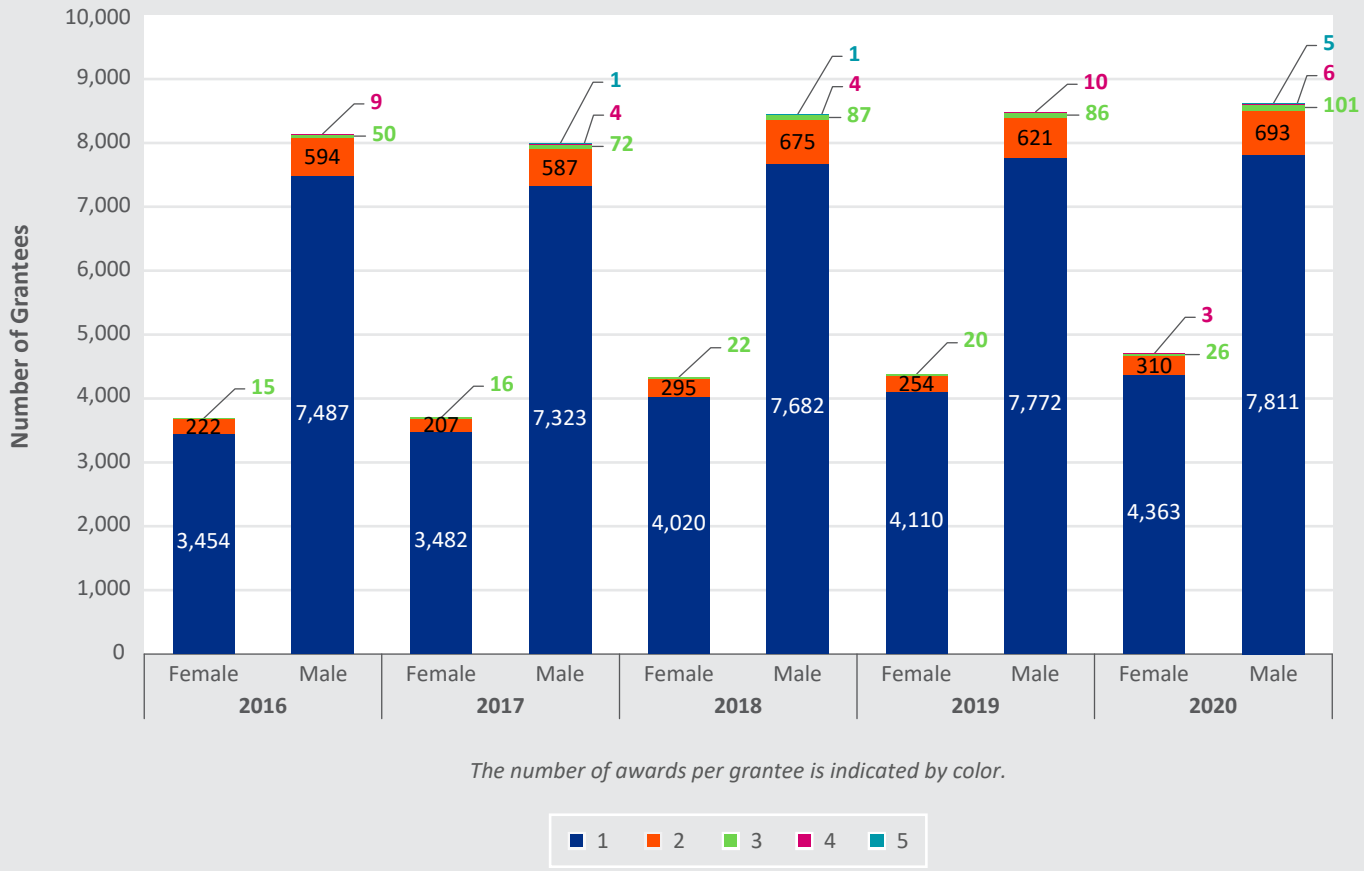
- For PIs who received 2 awards, the male-to-female ratios of awardees were 2.80, 2.94, 2.57, 2.34, and 2.35, respectively, for each fiscal year.
- For PIs who received 3 awards, the male-to-female ratios of awardees were 3.4, 5.27,3.85, 5.00, and 3.91, respectively, for each fiscal year.
- Only male PIs received 4 or 5 awards.

RPG Grantees

Overall, more males than females received RPG awards among all competing applications in FY 2016–2020.

- For PIs who received only 1 award, the male-to-female ratios of awardees were 2.17, 2.10, 1.91, 1.89, and 1.79, respectively, for each fiscal year.
- For PIs who received 2 awards, the male-to-female ratios of awardees were 2.68, 2.83, 2.29, 2.44, and 2.23, respectively, for each fiscal year.
- For PIs who received 3 awards, the male-to-female ratios of awardees were 3.33, 4.5, 3.95, 4.3, and 3.88, respectively, for each fiscal year.
- Only male PIs received 4 or 5 awards.

Figure 19. NIH Grantees by Sex: RPG (FY 2016–2020)



Notes:

1. *Includes direct budget authority only.*
2. *Includes all competing applications.*
3. *Includes both contact PI and multiple-PI (MPI) applications.*
4. *"RPG" is defined in FY 2020 as activity codes DP1, DP2, DP3, DP4, DP5, P01, PN1, PM1, R00, R01, R03, R15, R21, R22, R23, R29, R33, R34, R35, R36, R37, R61, R50, R55, R56, RC1, RC2, RC3, RC4, RF1, RL1, RL2, RL9, RM1, UA5, UC1, UC2, UC3, UC4, UC7, UF1, UG3, UH2, UH3, UH5, UM1, UM2, U01, U19, and U34. Not all of these activities may be in use by NIH every year.*
5. *The "Mixed RPG" category includes those mixed-gender MPI teams with unknown/withheld gender.*

Source: *Data drawn from the frozen success rate demographic dataset as of 2/8/2021. Data produced by the Division of Statistical Analysis and Reporting within the NIH Office of Extramural Research's Office of Research Reporting and Analysis.*

NIH Grant Application Success Rates by Sex or Gender and FY

"Success rate" is defined as the percentage of reviewed grant applications that received funding. This is the number of funded competing applications divided by the sum of the total number of competing applications reviewed plus the number of funded carryovers. Success rates were computed on a fiscal-year basis and included applications that had been peer-reviewed and either scored or unscored by an Initial Review Group (IRG). Applications with more than one submission for the same project in the same fiscal year were counted only once.

The success rate for RPGs and R01-equivalent grants, taken together, fluctuated between 17.1% and 22.4% from FY 2016 to FY 2020 across male-only PIs (either solo or as an MPI), female-only PIs (either solo or as an MPI), and mixed-sex[16] PI teams. During this 5-year time frame, the relative positions of the different PI groups changed for both RPGs and R01-equivalent grants, as discussed in the following sections. This is seen in Table 1.

16. For multiple-PI (MPI) grant applications.

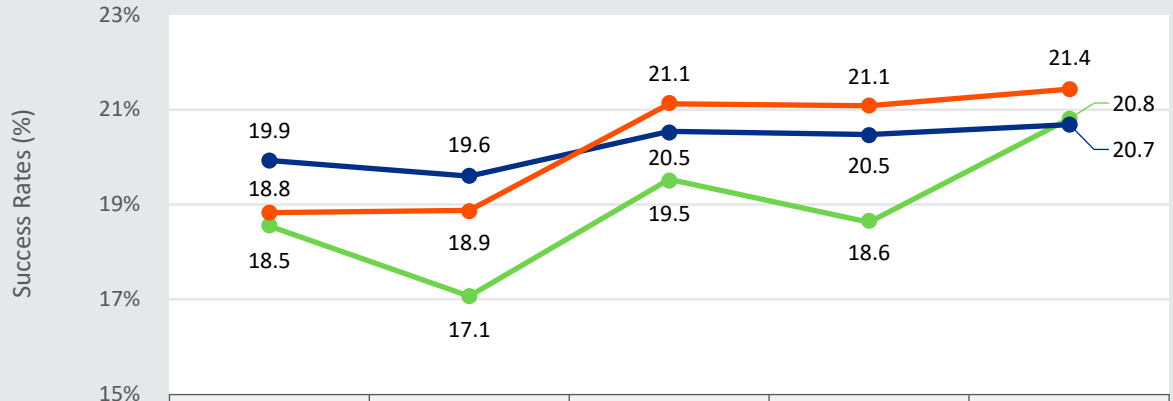
Table 1. NIH RPG and R01-Equivalent Success Rates by Investigators' Sex and FY

Activity Group	Fiscal Year	Female Only			Male Only			Mixed		
		Applications	Awards	Success Rate	Applications	Awards	Success Rate	Applications	Awards	Success Rate
RPG	2016	14,389	2,709	18.8%	33,046	6,586	19.9%	5,371	996	18.5%
	2017	14,307	2,700	18.9%	32,193	6,308	19.6%	5,953	1,016	17.1%
	2018	14,845	3,136	21.1%	31,992	6,573	20.5%	6,355	1,241	19.5%
	2019	14,766	3,113	21.1%	31,610	6,473	20.5%	6,690	1,246	18.6%
	2020	14,939	3,202	21.4%	31,168	6,448	20.7%	7,044	1,466	20.8%
R01-Equivalent	2016	7,760	1,515	19.5%	19,351	3,943	20.4%	3,183	577	18.1%
	2017	7,930	1,523	19.2%	19,271	3,870	20.1%	3,553	612	17.2%
	2018	8,740	1,954	22.4%	20,892	4,614	22.1%	4,344	877	20.2%
	2019	8,903	1,993	22.4%	20,895	4,431	21.2%	4,573	856	18.7%
	2020	9,428	2,088	22.1%	21,116	4,537	21.5%	4,915	1,027	20.9%

Notes:
1. *Includes direct budget authority only.*
2. *Includes all competing applications.*
3. *Includes both contact PI and multiple-PI (MPI) applications.*
4. *"RPG" is defined in FY 2020 as activity codes DP1, DP2, DP3, DP4, DP5, P01, PN1, PM1, R00, R01, R03, R15, R21, R22, R23, R29, R33, R34, R35, R36, R37, R61, R50, R55, R56, RC1, RC2, RC3, RC4, RF1, RL1, RL2, RL9, RM1, UA5, UC1, UC2, UC3, UC4, UC7, UF1, UG3, UH2, UH3, UH5, UM1, UM2, U01, U19, and U34. Not all of these activities may be in use by NIH every year.*
5. *The "Mixed RPG" category includes those mixed-gender MPI teams with unknown/withheld gender.*
6. *The table does not include the "Unknown/Withheld Sex Only" category.*

Source: *Data drawn from the frozen success rate demographic dataset as of 2/8/2021 and the NIH Success Rates by Demographics Dashboard: https://qlikview.nih.gov/QvAJAXZfc/opendoc.htm?document=ap_05_od%5Csuccess%20rate%20appl%20based%20pii%20dashboard.qvw&lang=en-US&host=QVS%40ProdQluster. (Only those with NIH credentials can access this.)*

Figure 20. NIH RPG Success Rates by Investigators' Gender and FY



	2016	2017	2018	2019	2020
Women-Only RPG	18.8%	18.9%	21.1%	21.1%	21.4%
Men-Only RPG	19.9%	19.6%	20.5%	20.5%	20.7%
Mixed-Gender RPG	18.5%	17.1%	19.5%	18.6%	20.8%

Notes:
1. *Includes direct budget authority only.*
2. *Includes all competing applications.*
3. *Includes both contact PI and multiple-PI (MPI) applications.*
4. *"RPG" is defined in FY 2020 as activity codes DP1, DP2, DP3, DP4, DP5, P01, PN1, PM1, R00, R01, R03, R15, R21, R22, R23, R29, R33, R34, R35, R36, R37, R61, R50, R55, R56, RC1, RC2, RC3, RC4, RF1, RL1, RL2, RL9, RM1, UA5, UC1, UC2, UC3, UC4, UC7, UF1, UG3, UH2, UH3, UH5, UM1, UM2, U01, U19, and U34. Not all of these activities may be in use by NIH every year.*
5. *The "Mixed RPG" category includes those mixed-gender MPI teams with unknown/withheld gender.*

Source: *Data drawn from the frozen success rate demographic dataset as of 2/8/2021. Data produced by the Division of Statistical Analysis and Reporting within the NIH Office of Extramural Research's Office of Research Reporting and Analysis.*

RPG Success Rates

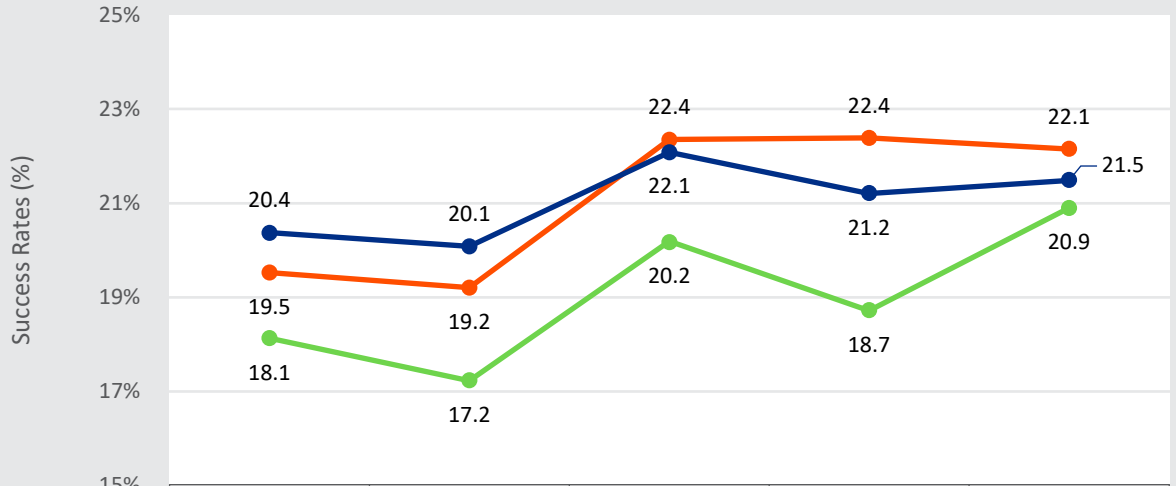
Between FY 2016 and FY 2020, the overall success rate for obtaining an RPG award fluctuated from 18.5% in 2016 to 21.4% in 2020, with a low of 17.1% in 2017 (Figure 20).

For men-only-PI RPGs, success rates remained relatively stable over the 5 years. The rate in FY 2020 was only slightly higher (0.8 percentage point) than the FY 2016 rate. (See Table 1.) For women-only PIs, there was a small increase in funding rates for RPG awards between FY 2016 and FY 2020 (from 18.8% in 2016 to 21.4% in 2020). Beginning in FY 2018, there were slight differences in success rates between women-only PIs and men-only PIs. From FY 2018 to FY 2020, women-only PIs' rates were marginally higher than men-only PIs', by about 0.7 percentage point (21.1%, 21.1%, and 21.4% for women, compared with 20.5%, 20.5%, and 20.7% for men). For most years, RPGs with mixed-gender PIs had lower success rates than both RPGs with men-only PIs and RPGs with women-only PIs—except in 2020, when they exceeded RPGs with men-only PIs by 0.1 percentage point. These are depicted in Figure 20.

R01-Equivalent Success Rates

The R01-equivalent grants' success rates ranged from a low of 17.2% in FY 2017 for mixed-gender MPI grant awards to a high of 22.4% in FY 2018 for women-only PIs (Figure 21). Over the 5 years (FY 2016–2020), the success rates of mixed-gender MPIs were consistently below the success rates of single-gender PIs, though the gap was smaller in FY 2020. Similar to the success rates for RPGs, R01-equivalent grants' success rates of men-only and women-only PIs switched over time, with men-only success rates being higher from FY 2016 to FY 2017 and women-only success rates being higher from FY 2018 to FY 2020. The differences were small (hovering around 1 percentage point) between the men and women PIs.

Figure 21. NIH R01-Equivalent Success Rates by Investigators' Gender and FY



	2016	2017	2018	2019	2020
Women-Only R01-Equivalent	19.5%	19.2%	22.4%	22.4%	22.1%
Men-Only R01-Equivalent	20.4%	20.1%	22.1%	21.2%	21.5%
Mixed-Gender R01-Equivalent	18.1%	17.2%	20.2%	18.7%	20.9%

Notes:
1. *Includes direct budget authority only.*
2. *Includes all competing applications.*
3. *Includes both contact PI and MPI applications.*
4. *"R01-equivalent" is defined in FY 2020 as activity codes DP1, DP2, DP5, R01, R37, R56, RF1, RL1, U01, and R35 from select NIGMS and NHGRI PAs. Not all of these activities may be in use by NIH every year.*
5. *The "Mixed R01-Equivalent" category includes those mixed-gender MPI teams with unknown/withheld gender. This category only applies to MPI applications.*

Source: *Data drawn from the frozen success rate demographic dataset as of 2/8/2021. Data produced by the Division of Statistical Analysis and Reporting within the NIH Office of Extramural Research's Office of Research Reporting and Analysis.*

NIH Grant Application Success Rates for Females from Underrepresented Racial and Ethnic Groups by FY

Comparison of success rates of applications submitted by female PIs (individuals and female-only teams) reveals differences across race and ethnicity.[17] The success rates for applications for both RPGs and R01-equivalent grants coming from females from underrepresented racial and ethnic groups were found to be considerably lower than the success rates for applications submitted by White female investigators (Table 2; Figures 22 and 23).

As shown in Figures 22 and 23, White female investigators had the highest rates of success among all females. Success rates among White females were consistently higher than the success rates among all females combined over the 5 years. (From Table 1: RPG success rates of all females combined from FY 2016 to FY 2020: 18.8%, 18.9%, 21.1%, 21.1%, and 21.4%, respectively.) RPG applications submitted by Black female investigators consistently had the lowest success rates among all females, hovering around 11.3% from FY 2016 to FY 2019 and improving to 16.9% in FY 2020 (green bar). Applications submitted by those in the "Other Non-White" category had higher success rates than those submitted by Black females over the 5 years, with RPG success rates switching from 14.6% in FY 2017

17. For this report, the combination of race and ethnicity is applied where Hispanic ethnicity takes priority over race, and the demographics are determined at the application level, where all PIs and MPIs on the same grant need to have the same demographics to be classified in a specific gender/racial/ethnic category. For example, all PIs and MPIs have to be Asian women to be classified as "Female Asian." This includes both teams of PIs and individual PI applicants. "Other Non-White" includes American Indians/Alaska Natives, those who are more than one race, and Native Hawaiians/Pacific Islanders who are not Hispanic.

Table 2. NIH RPG and R01-Equivalent Success of Females by Race and Ethnicity and FY

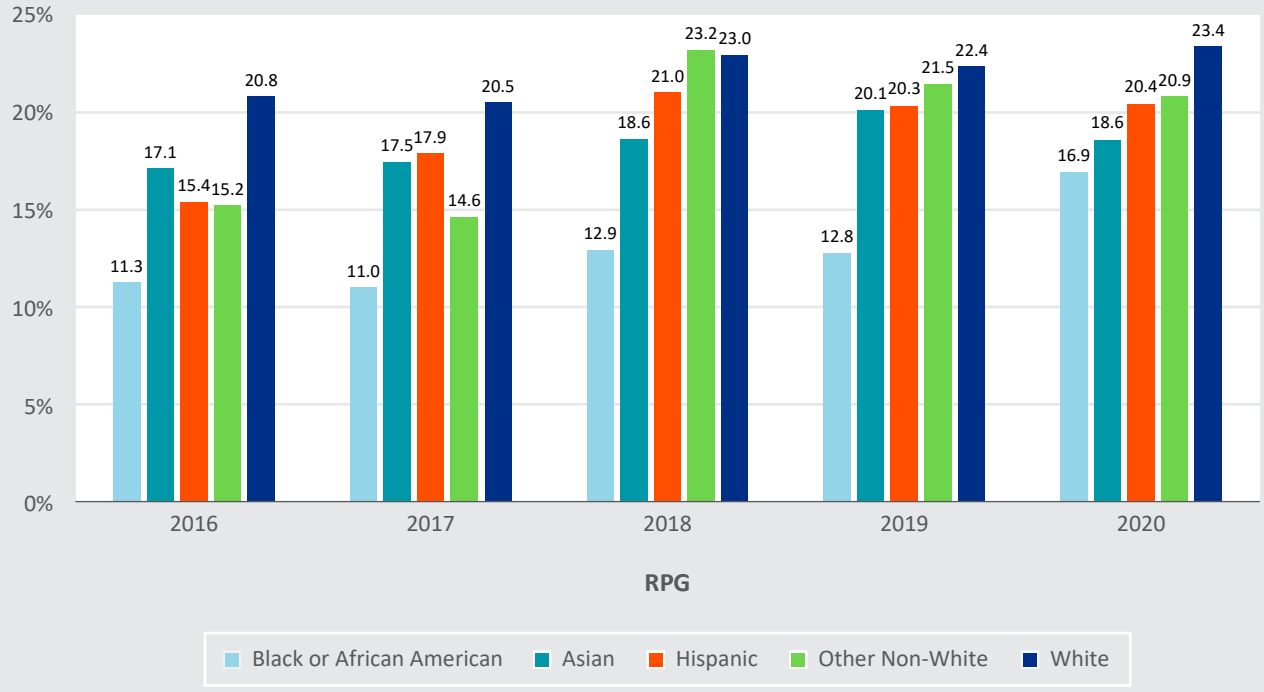
Activity Group	Fiscal Year	Black			Asian			Hispanic			Other Non-White			White		
		Applications	Awards	Success Rate	Applications	Awards	Success Rate	Applications	Awards	Success Rate	Applications	Awards	Success Rate	Applications	Awards	Success Rate
RPG	2016	408	46	11.3%	3,002	514	17.1%	720	111	15.4%	197	30	15.2%	8,982	1,871	20.8%
	2017	400	44	11.0%	3,131	547	17.5%	715	128	17.9%	212	31	14.6%	8,771	1,799	20.5%
	2018	433	56	12.9%	3,344	623	18.6%	751	158	21.0%	220	51	23.2%	8,928	2,051	23.0%
	2019	407	52	12.8%	3,340	672	20.1%	747	152	20.3%	219	47	21.5%	8,854	1,980	22.4%
	2020	425	72	16.9%	3,404	633	18.6%	769	157	20.4%	230	48	20.9%	8,908	2,084	23.4%
R01-Equivalent	2016	151	21	13.9%	1,629	309	19.0%	346	53	15.3%	101	15	14.9%	5,016	1,048	20.9%
	2017	165	22	13.3%	1,750	316	18.1%	366	74	20.2%	106	16	15.1%	4,971	1,008	20.3%
	2018	192	30	15.6%	2,007	400	19.9%	407	89	21.9%	110	26	23.6%	5,334	1,278	24.0%
	2019	191	23	12.0%	2,100	447	21.3%	418	97	23.2%	114	27	23.7%	5,351	1,261	23.6%
	2020	232	42	18.1%	2,156	415	19.2%	478	101	21.1%	121	26	21.5%	5,687	1,369	24.1%

Notes:

1. *Includes direct budget authority only.*
2. *Includes all competing applications.*
3. *Includes both contact PI and MPI applications.*
4. *"RPG" is defined in 2020 as activity codes DP1, DP2, DP3, DP4, DP5, P01, PN1, PM1, R00, R01, R03, R15, R21, R22, R23, R29, R33, R34, R35, R36, R37, R61, R50, R55, R56, RC1, RC2, RC3, RC4, RF1, RL1, RL2, RL9, RM1, UA5, UC1, UC2, UC3, UC4, UC7, UF1, UG3, UH2, UH3, UH5, UM1, UM2, U01, U19, and U34. Research projects were first coded to NLM in fiscal year 2007. Not all of these activities may be in use by NIH every year.*
5. *"R01-equivalent" is defined in FY 2020 as activity codes DP1, DP2, DP5, R01, R37, R56, RF1, RL1, U01, and R35 from select NIGMS and NHGRI PAs. Not all of these activities may be in use by NIH every year.*
6. *NIH has adopted the 1997 Office of Management and Budget (OMB) revised minimum standards for maintaining, collecting, and presenting data on race and ethnicity for all grant applications, contract and intramural proposals, and active research grants, cooperative agreements, and contract and intramural projects. The minimum standards are described in the 1997 OMB Statistical Policy Directive No. 15, https://www.govinfo.gov/content/pkg/FR-1997-10-30/pdf/97-28653.pdf. This directive revised minimum standards to include two ethnic categories ("Hispanic or Latino" and "Not Hispanic or Latino") and five racial categories ("American Indian or Alaska Native," "Asian," "Black or African American," "Native Hawaiian or Other Pacific Islander," and "White"). "Person reporting more than one race" under "race" indicates that an investigator indicated more than one race. "Withheld" under "race" indicates that the investigator chose not to disclose that information. "Unknown" indicates that the item was not completed and was missing in the IMPAC II database. Race and ethnicity are self-reported and subject to change.*
7. *For this report, the combination of race and ethnicity is applied where Hispanic ethnicity takes priority over race, and the demographics are determined at the application level, where all PIs and MPIs on the same grant need to have the same demographics to be classified in a specific gender/race/ethnicity category. For example, all PIs and MPIs have to be Asian women to be classified as "Female Asian." "Other Non-White" includes American Indians/Alaska Natives, those who are more than one race, and Native Hawaiians/Pacific Islanders who are not Hispanic.*

Source: *Data drawn from the frozen success rate demographic dataset as of 2/8/2021. Data produced by the Division of Statistical Analysis and Research within the NIH Office of Extramural Research's Office of Research Reporting and Analysis.*

Figure 22. NIH RPG Success Rates for Females by Race and Ethnicity



Notes:

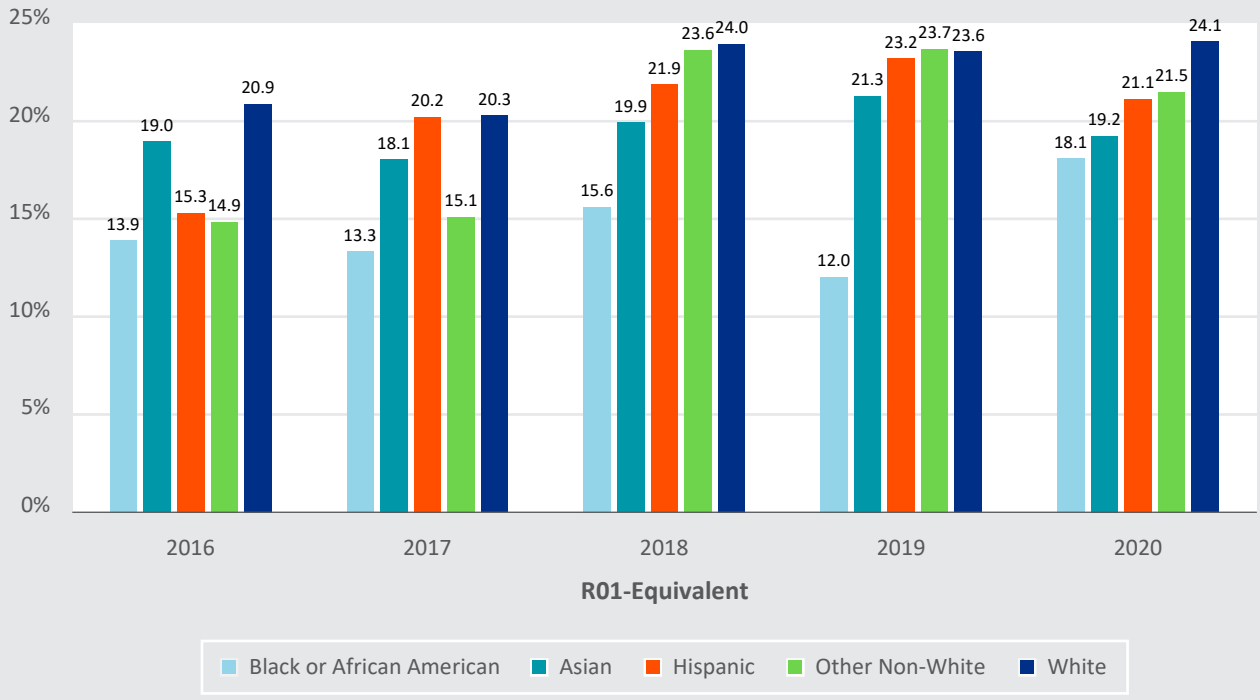
1. *Includes direct budget authority only.*
2. *Includes all competing applications.*
3. *Includes both contact PI and MPI applications.*
4. *"RPG" is defined in FY 2020 as activity codes DP1, DP2, DP3, DP4, DP5, P01, PN1, PM1, R00, R01, R03, R15, R21, R22, R23, R29, R33, R34, R35, R36, R37, R61, R50, R55, R56, RC1, RC2, RC3, RC4, RF1, RL1, RL2, RL9, RM1, UA5, UC1, UC2, UC3, UC4, UC7, UF1, UG3, UH2, UH3, UH5, UM1, UM2, U01, U19, and U34.*
5. *Not all of these activities may be in use by NIH every year.*
6. *NIH has adopted the 1997 Office of Management and Budget (OMB) revised minimum standards for maintaining, collecting, and presenting data on race and ethnicity for all grant applications, contract and intramural proposals, and active research grants, cooperative agreements, and contract and intramural projects. The minimum standards are described in the 1997 OMB Statistical Policy Directive No. 15, https://www.govinfo.gov/content/pkg/FR-1997-10-30/pdf/97-28653.pdf. This directive revised minimum standards to include two ethnic categories ("Hispanic or Latino" and "Not Hispanic or Latino") and five racial categories ("American Indian or Alaska Native," "Asian," "Black or African American," "Native Hawaiian or Other Pacific Islander," and "White"). "Person reporting more than one race" under "race" indicates that an investigator indicated more than one race. "Withheld" under "race" indicates that the investigator chose not to disclose that information. "Unknown" indicates that the item was not completed and was missing in the IMPAC II database. Race and ethnicity are self-reported and subject to change.*
7. *For this report, the combination of race and ethnicity is applied where Hispanic ethnicity takes priority over race, and the demographics are determined at the application level, where all PIs and MPIs on the same grant need to have the same demographics to be classified in a specific gender/racial/ethnic category. For example, all PIs and MPIs have to be Asian women to be classified as "Female Asian." "Other Non-White" includes American Indians/Alaska Natives, those who are more than one race, and Native Hawaiians/Pacific Islanders who are not Hispanic.*

Source: *Data drawn from the frozen success rate demographic dataset as of 2/8/2021. Data produced by the Division of Statistical Analysis and Reporting within the NIH Office of Extramural Research's Office of Research Reporting and Analysis.*

to 23.2% (0.2% higher than the rate among all females combined) in FY 2018 to 20.9% in FY 2020.

For R01-equivalent grants, success rates among females from underrepresented racial and ethnic groups were generally lower than those of all female investigators combined. (From Table 1: R01-equivalent success rates of all females combined from FY 2016 to FY 2020: 19.5%, 19.2%, 22.4%, 22.4%, and 22.1%, respectively.) Among all females from underrepresented racial and ethnic groups, this was most noticeable among Black female investigators, for whom success rates ranged from 12.0% to 18.1%—in FY 2019 and FY 2020, respectively. These unstable differences could be attributed to the smaller application and award counts. Differences also existed in the success rates of Asian female investigators, going from 19.0% in FY 2016 to a peak of 21.3% in 2019 and back to 19.2% in FY 2020. The differences in R01-equivalent grant success rates for Hispanic and "other non-White" female investigators narrowed from FY 2016 to FY 2020. Hispanic female investigators' success rate was 4.2 percentage points below that of all female investigators in FY 2016, at 15.3%, and 1 percentage point below that of all female investigators in FY 2020, at 21.1%, whereas the other non-White female investigators' success rate was 4.6

Figure 23. NIH R01-Equivalent Grant Success Rates for Females by Race and Ethnicity



Notes:

1. *Includes direct budget authority only.*
2. *Includes all competing applications.*
3. *Includes both contact PI and MPI applications.*
4. *"R01-equivalent" is defined in FY 2020 as activity codes DP1, DP2, DP5, R01, R37, R56, RF1, RL1, U01, and R35 from select NIGMS and NHGRI PAs. Not all of these activities may be in use by NIH every year.*
5. *NIH has adopted the 1997 OMB revised minimum standards for maintaining, collecting, and presenting data on race and ethnicity for all grant applications, contract, and intramural proposals, and active research grants, cooperative agreements, and contract and intramural projects. The minimum standards are described in the 1997 OMB Statistical Policy Directive No. 15, https://www.govinfo.gov/content/pkg/FR-1997-10-30/pdf/97-28653.pdf. This directive revised minimum standards to include two ethnic categories ("Hispanic or Latino" and "Not Hispanic or Latino") and five racial categories ("American Indian or Alaska Native," "Asian," "Black or African American," "Native Hawaiian or Other Pacific Islander," and "White"). "Person reporting more than one race" under race indicates that an investigator indicated more than one race. "Withheld" under "race" indicates that the investigator chose not to disclose that information. "Unknown" indicates that the item was not completed and was missing in the IMPAC II database. Race and ethnicity are self-reported and subject to change.*
6. *For this report, the combination of race and ethnicity is applied where Hispanic ethnicity takes priority over race, and the demographics are determined at the application level, where all PIs and MPIs on the same grant need to have the same demographics to be classified in a specific gender/racial/ethnic category. For example, all PIs and MPIs have to be Asian women to be classified as "Female Asian." "Other Non-White" includes American Indians/Alaska Natives, those who are more than one race, and Native Hawaiians/Pacific Islanders who are not Hispanic.*

Source: *Data drawn from the frozen success rate demographic dataset as of 2/8/2021. Data produced by the Division of Statistical Analysis and Reporting within the NIH Office of Extramural Research's Office of Research Reporting and Analysis.*

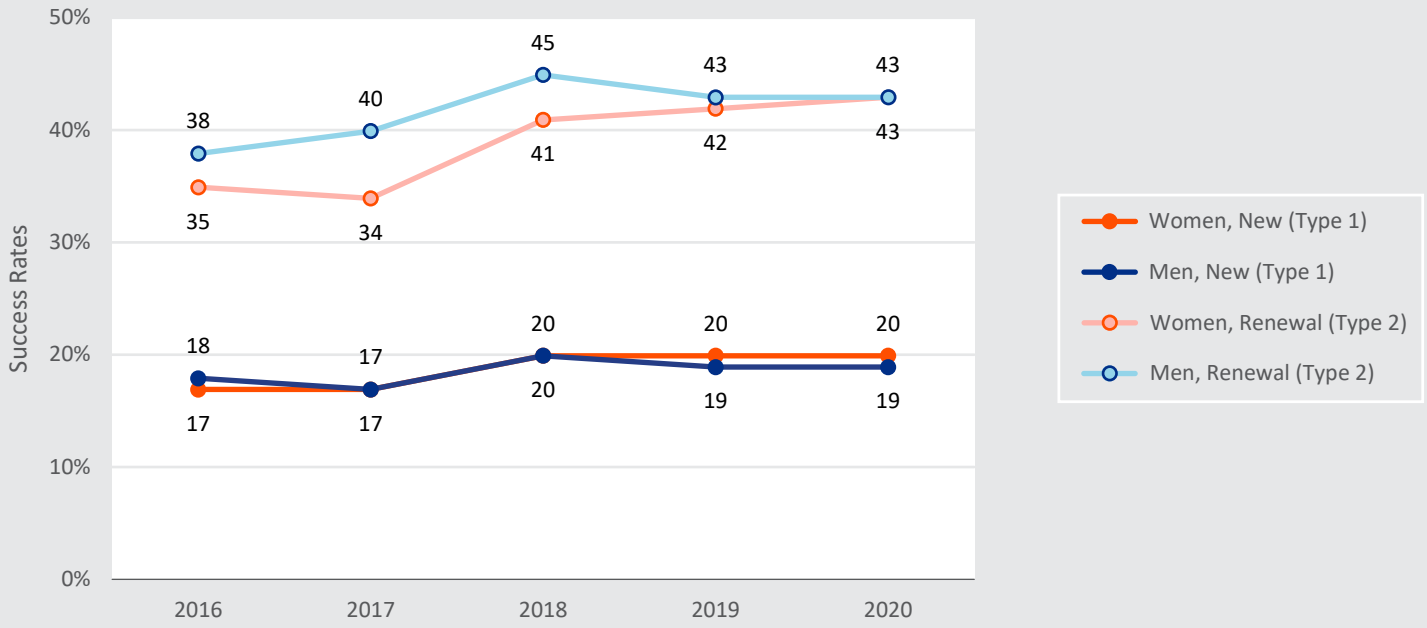
percentage points below that of all female investigators in FY 2016, at 14.9%, and 1.2 and 1.3 percentage points above all female investigators' rates in FY 2018 and FY 2019, respectively.

R01-Equivalent Grant Success Rates by Gender and Type of Application

Figure 24 illustrates the FY 2016 to FY 2020 success rate trends for R01-equivalent applications by gender and type of application. Specifically, Type 1 trends reflect new grant applications, whereas Type 2 trends correspond to renewals of the awarded grants. For new applications, success rates by gender increased slightly over the 5 years, ranging from 17% to 20% for women investigators in FY 2016 and FY 2020, respectively, and from 18% to 19% for men investigators in FY 2016 and FY 2020, respectively. Type 1 success rates changed for men and women over the 5 years. Men had higher Type 1 success rates than women in FY 2016. Men and women had equal success rates in FY 2017 and FY 2018. Women had higher success rates than men in FY 2019 and FY 2020; however, the differences were small.

For renewal grants (Type 2), the gap between women's and men's success rates fluctuated from year to year,

Figure 24. R01-Equivalent Success Rates by Gender and Type of Application



Notes:
1. *Excludes awards issued through supplemental COVID-19 appropriations. Special supplemental COVID-19 appropriations may include: (1) H.R. 6074 (Public Law 116–123) - Coronavirus Preparedness and Response Supplemental Appropriations Act, 2020. (2) H.R. 748 (Public Law 116–136) - Coronavirus Aid, Relief, and Economic Security (CARES) Act.*
2. *Beginning with FY 2009, awards made under reimbursable agreements, appropriations to NIH for superfund-related activities, gift funds, breast cancer research stamp funds, and NIH Office of the Director non–Common Fund appropriations have been excluded. Data include only awards made with direct budget authority funds.*
3. *For the last FY displayed, R01-equivalent grants are defined as activity codes DP1, DP2, DP5, R01, R37, R56, RF1, RL1, U01, and R35 from select NIGMS and NHGRI PAs. Not all of these activities may be in use by NIH every year. https://grants.nih.gov/grants/funding/ac_search_results.htm*
4. *The analysis is restricted to contact PIs who have reported their gender. Data on gender profiles are maintained by the investigator in the NIH eRA system and are subject to change.*

Source: *NIH IMPAC, Success Rate File - Data produced by the Division of Statistical Analysis and Reporting within the NIH Office of Extramural Research's Office of Research Reporting and Analysis (https://report.nih.gov/nihdatabook/report/131) and accessed on March 24, 2021.*

showing the biggest gap in FY 2017. In FY 2020, the gap diminished and there was no difference between women's and men's success rates. In FY 2016, men investigators had a success rate of 38%, and women investigators had a success rate of 35%. By FY 2020, the success rates for men and women for R01-equivalent renewal applications were the same—both at a higher rate of 43%.

Research Grant Investigators: Percentage of Women Awarded by Award Mechanism, Average Funding, and Fiscal Year

In addition to the RPGs and R01-equivalents, NIH research grant awards encompass a broad array of funding mechanisms. Research grants include extramural awards made to fund research centers and research projects, Small Business Innovation Research/ Small Business Technology Transfer (SBIR/STTR) program grants, and other grant mechanisms, such as training and career development awards. The grants covered within the research grant category include Institutional Training and Director Program Projects (DP1–DP5), research career development programs (K), the General Clinical Research Center program (M), research program projects and centers (P), research projects (R), research-related programs (S), cooperative agreements (U), construction cooperative agreements (UC6), and Research Centers in Minority Institutions awards (G12).[18] This analysis by gender was restricted to contact PIs who reported their gender. The following sections explore the proportions of women awarded different

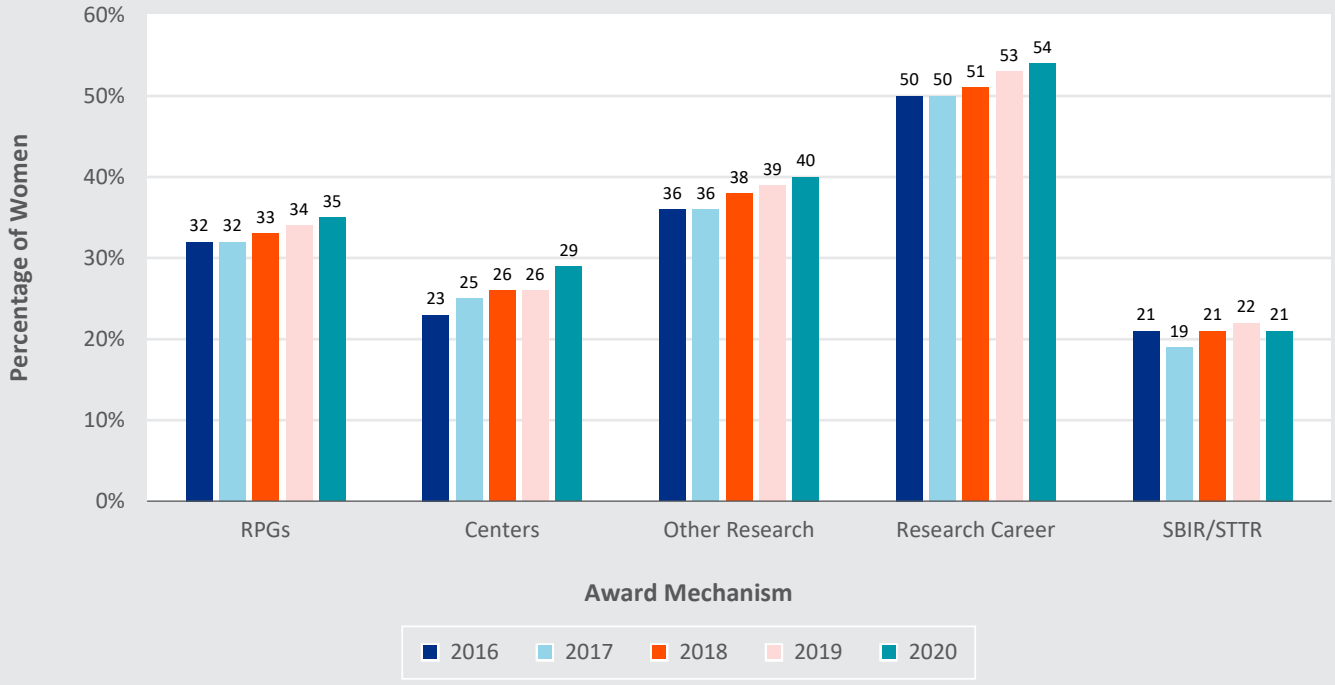
18. The activity codes associated with the grant programs are presented in parentheses. Please consult https://grants.nih.gov/grants/funding/ac_search_results.htm for a complete list of activity codes and associated grant.

types of research grants and the relative average funding they received compared with male awardees.

Percentage of Women Who Received Research Grants by Award Mechanism

Figure 25 presents the percentages of women NIH awardees by award mechanism and fiscal year. For most award mechanisms, the percentages of women awardees were consistently below those of men. However, the proportion of women to men awardees increased modestly from FY 2016 to FY 2020. Research center grants had the largest increase in the proportion of women awardees, from 23% in FY 2016 to 29% in FY 2020. RPGs, SBIR program grants, and STTR program grants had the smallest increase, only 3 percentage points, from 32% in FY 2016 to 35% in FY 2020 for RPGs and between 19% and 22% for SBIR and STTR awards over the 5 years. Although the proportion of women to men receiving research career awards was equal in FY 2016 and FY 2017 (50%), women overtook men in FY 2018 (51%), and in FY 2020, a larger majority (54%) of awardees receiving career development awards were women.

Figure 25. Research Grant Investigators: Percentage of Women by Award Mechanism and FY



Notes: *1. Excludes awards issued through supplemental COVID-19 appropriations. Special supplemental COVID-19 appropriations may include:*
(1) H.R. 6074 (Public Law 116–123) - Coronavirus Preparedness and Response Supplemental Appropriations Act, 2020.
(2) H.R. 748 (Public Law 116–136) - Coronavirus Aid, Relief, and Economic Security (CARES) Act.

2. The analysis is restricted to contact PIs who have reported their gender. Data on gender profiles are maintained by the investigator in the NIH eRA system and are subject to change.

3. For details about grant activities under each funding mechanism, please visit https://grants.nih.gov/grants/funding/ac_search_results.htm.

Source: *NIH IMPAC, Pub File - Data produced by the Division of Statistical Analysis and Reporting within the NIH Office of Extramural Research's Office of Research Reporting and Analysis (https://report.nih.gov/nihdatabook/report/169) and accessed on March 8, 2021.*

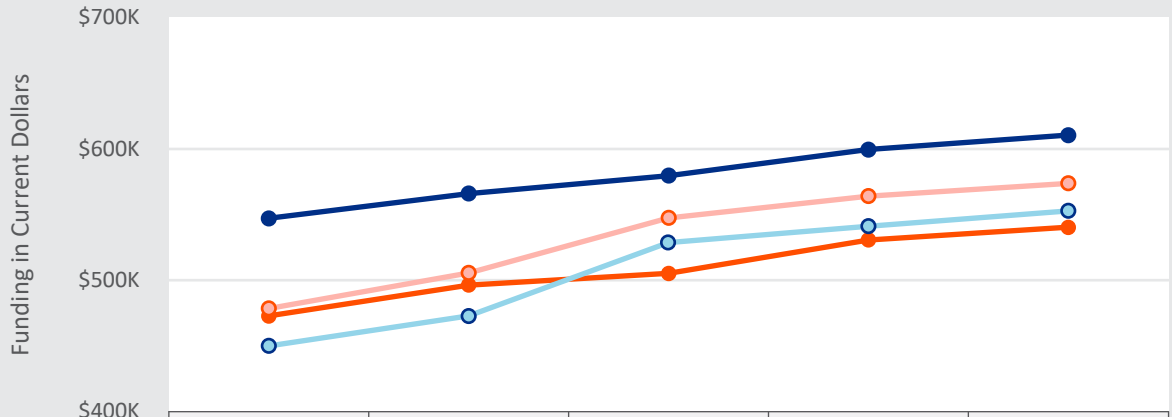
Average Funding for NIH Research Grants by Gender

Figure 26 presents the average amounts (in current dollars) awarded for all NIH research grants and the subset of R01-equivalent grants from FY 2016 to FY 2020 for men and women. Across all years, men PIs received higher average funding amounts than women PIs for research grants overall, with men receiving between $68,000 and $75,000 more than women on average. However, these differences decreased by 5.4% over the 5-year period, indicating a very slight narrowing of the gap.

Conversely, the average amounts awarded to women contact PIs for R01-equivalent grants were $18,000 to $29,000 higher than those awarded to men contact PIs throughout the 5-year period. However, during this period, the average amount awarded to men for R01-equivalent grants increased by 22.8% (from $450,130 to $552,810), while the average amount awarded to women for R01-equivalent grants increased at a lower rate of 19.9% (from $478,624 to $573,752).

The persistent gap in funding could be attributed to the imbalance in academia wherein men are more likely to be in higher ranks (full professors) and thus overseeing

Figure 26. NIH Research Grants and R01-Equivalent Grants: Average Funding in Current Dollars by Gender and FY



	2016	2017	2018	2019	2020
Research Project Grants Women	$472,889	$496,360	$505,271	$530,694	$540,256
Research Project Grants Men	$547,136	$566,037	$579,673	$599,511	$610,479
R01-Equivalent Grants Women	$478,624	$505,649	$547,492	$564,094	$573,752
R01-Equivalent Grants Men	$450,130	$472,930	$528,776	$541,184	$552,810

Notes:
1. *Excludes awards issued through supplemental COVID-19 appropriations. Special supplemental COVID-19 appropriations may include:*
   (1) H.R. 6074 (Public Law 116–123) - Coronavirus Preparedness and Response Supplemental Appropriations Act, 2020.
   (2) H.R. 748 (Public Law 116–136) - Coronavirus Aid, Relief, and Economic Security (CARES) Act.
2. *Each data point reflects only current dollars and is not adjusted for inflation.*
3. *For the last FY displayed, R01-equivalent grants are defined as activity codes DP1, DP2, DP5, R01, R37, R56, RF1, RL1, U01, and R35 from select NIGMS and NHGRI PAs. Not all of these activities may be in use by NIH every year.*
4. *Research grants are defined as extramural awards made for research centers, research projects, Small Business Innovation Research/Small Business Technology Transfer (SBIR/STTR) program grants, and other research grants. Research grants are defined by the following activity codes: R, P, M, S, K, U (excluding UC6), DP1, DP2, DP3, DP4, DP5, D42, and G12.*
5. *Analysis is restricted to contact PIs who reported their gender. Data on gender profiles are maintained by the investigator in the NIH eRA system and are subject to change.*

Source: *NIH IMPAC, Pub File - Data produced by the Division of Statistical Analysis and Reporting within the NIH Office of Extramural Research's Office of Research Reporting and Analysis (https://report.nih.gov/nihdatabook/report/173) and accessed on March 8, 2021.*

larger grants, such as the U01s and P01s, alongside smaller grants, such as the R21s (Figure 27).

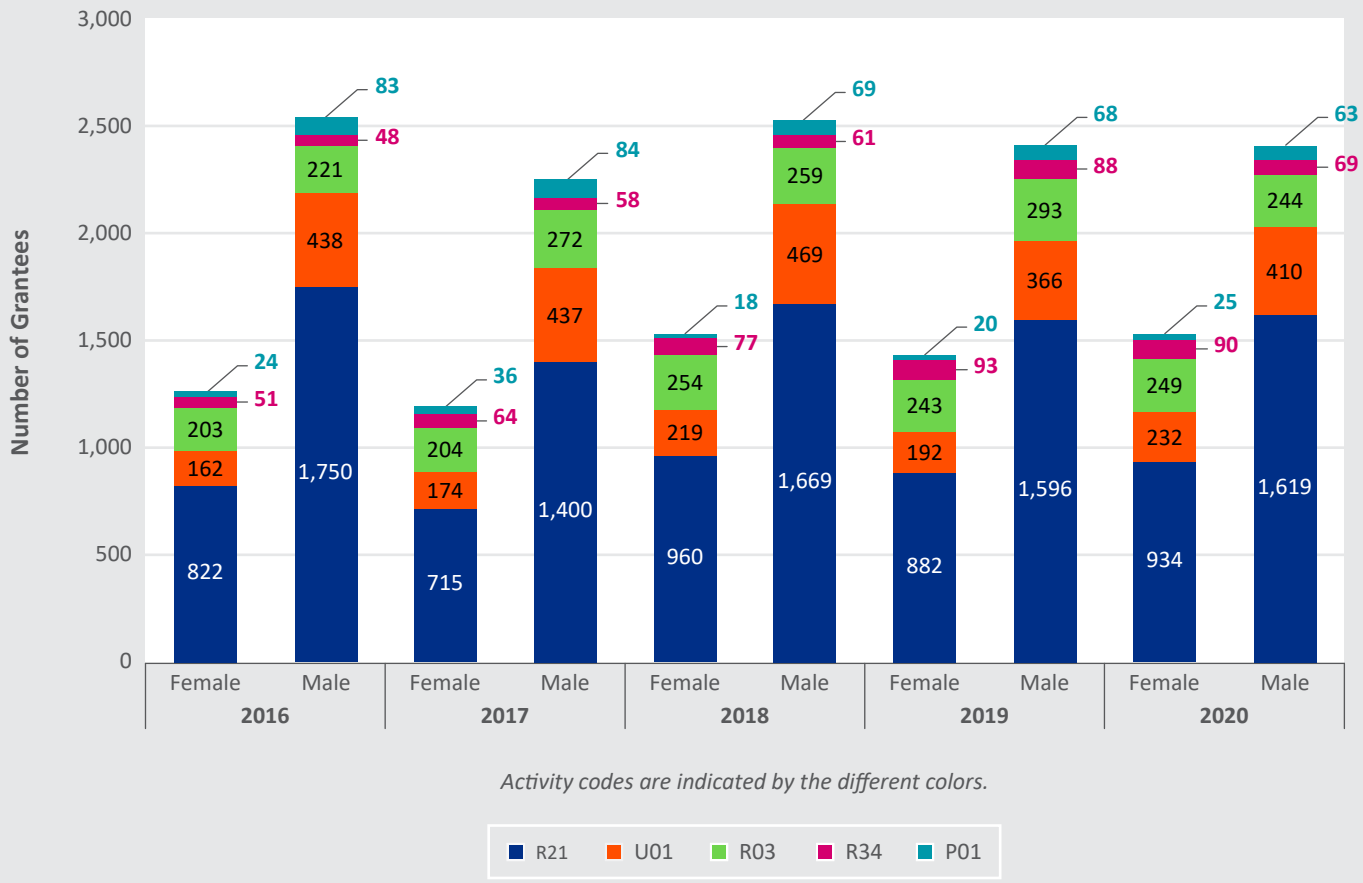
Career Stages and Development of PIs by Gender and Fiscal Year

R01-Equivalent Applications of Early-Stage Investigators

An early-stage investigator (ESI) is a PI or program director (PD) who has received a terminal research degree or reached the end of postgraduate clinical training, whichever date is later, within the past 10 years and who has not yet been awarded a substantial NIH independent research award (such as an R01). Figure 28 shows the number of applications from ESIs, broken down by gender and award status, from FY 2016 to FY 2020.

The number of ESI applications and the number of subsequent awards grew from FY 2016 to FY 2020. The increase in the number of applicants overall during the 5-year period was mostly driven by an increase in the number of women applicants. The number of R01-equivalent applications submitted by men ESIs increased slightly, by 227 applications (9.3%), from FY 2016 to FY

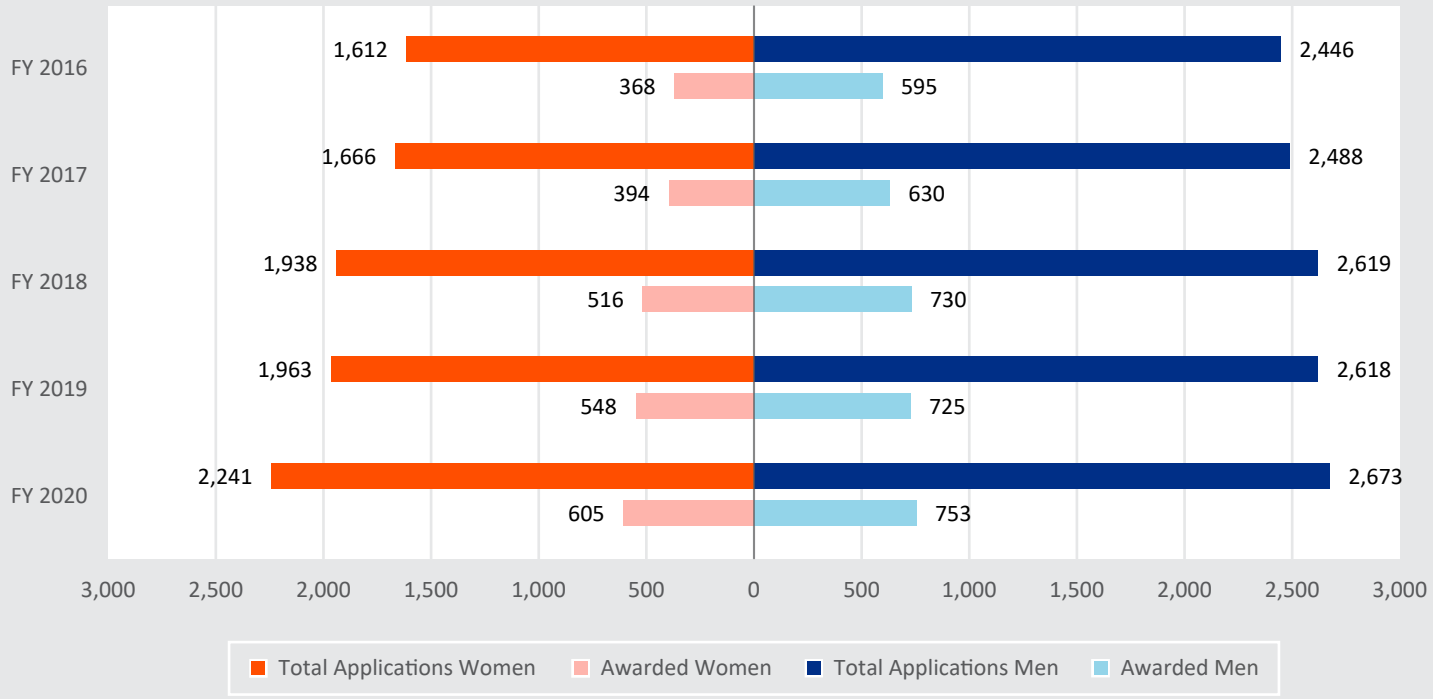
Figure 27. Number of Grantees by Activity Codes R21, U01, R03, R34, P01, and U01



Notes:
1. *Includes direct budget authority only.*
2. *Includes all competing applications.*
3. *Includes both contact PI and MPI applications.*

Source: *Data drawn from the frozen success rate demographic dataset as of 2/8/2021. Data produced by the Division of Statistical Analysis and Reporting within the NIH Office of Extramural Research's Office of Research Reporting and Analysis.*

Figure 28. NIH Type 1 R01-Equivalent: ESI Applicants and Awardees by FY and Gender



Notes:

1. *NIH definition of ESI: a PD or PI who has received a terminal research degree or reached the end of postgraduate clinical training, whichever date is later, within the past 10 years and who has not previously competed successfully as PD/PI for a substantial NIH independent research award. A list of NIH grants that a PD/PI can hold while still being considered an ESI can be found at https://grants.nih.gov/policy/early-investigators/list-smaller-grants.htm.*
2. *Includes Type 1 competing applications and Type 7 in year 2 in FY 2018–2020.*
3. *Includes contact PIs and MPIs.*
4. *"R01-equivalent" is defined in FY 2020 as activity codes DP1, DP2, DP5, R01, R37, R56, RF1, RL1, U01, and R35 from select NIGMS and NHGRI PAs. Not all of these activities may be in use by NIH every year.*

Source: *Data drawn from the frozen NGRI demographic dataset as of 2/8/2021. Data produced by the Division of Statistical Analysis and Reporting within the NIH Office of Extramural Research's Office of Research Reporting and Analysis.*

2020, while the number of R01-equivalent applications submitted by women ESIs increased by 629 (39%), from 1,612 applications in FY 2016 to 2,241 in FY 2020. The proportion of applications from women ESIs also increased, from 39.7% in FY 2016 to 45.6% in FY 2020.

The number of ESI awardees also increased overall during the 5-year period. The number of men ESIs awarded R01-equivalent grants increased by 26.6%, from 595 in FY 2016 to 753 in FY 2020. This corresponded to a small increase in the award rate, from 24.3% in FY 2016 (595 awardees out of 2,446 applicants) to 28.2% in FY 2020 (753 awardees out of 2,673 applicants). Over the same period, the number of women ESI awardees increased by 64.4%, from 368 in FY 2016 to 605 in FY 2020. Women ESIs also saw a small increase in the award rate, from 22.8% in FY 2016 (268 awardees out of 1,612 applicants) to 27% in FY 2020 (605 awardees out of 2,241 applicants). The proportion of women to men ESI awardees increased from 38.2% in FY 2016 to 44.6% in FY 2020, reflecting the increase in the number of women applicants over the period.

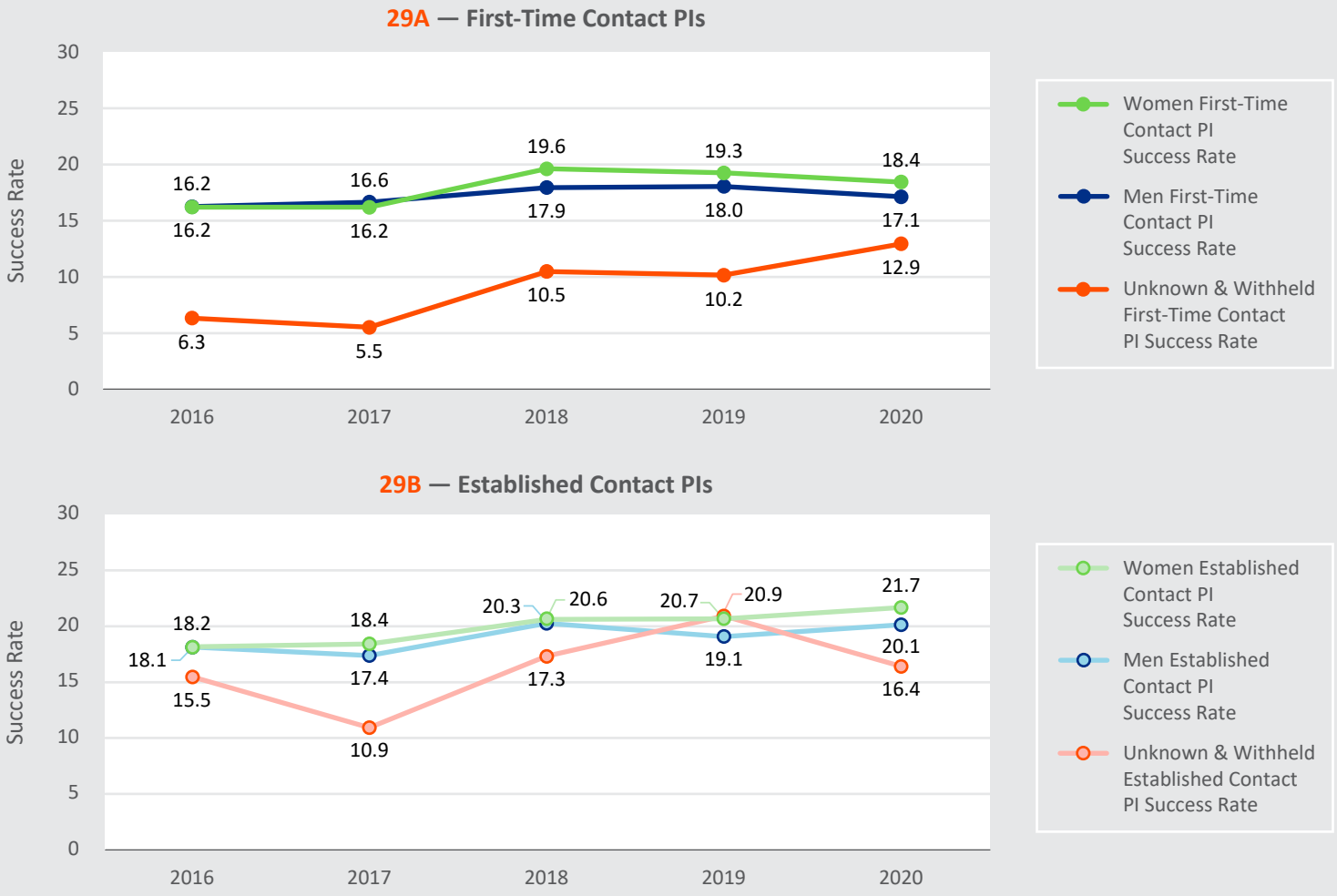
R01-Equivalent Success Rates for First-Time PIs and Established PIs

Figure 29 illustrates the NIH Type 1 R01-equivalent success rates by gender, fiscal year, and career stage (i.e., whether the PI was a first-time PI or an established PI). For both men and women, the success rates for first-time PIs were lower than those for established PIs. For first-time PIs, the success rates increased from 16.2% for both men and women in FY 2016 to 17.1% for men and 18.4% for women in FY 2020. For established PIs, the success rates were 18.2% for women and 18.1% for men in FY 2016 and 21.7% for women and 20.1% for men in FY 2020.

Women Receiving Career Development Awards

To support early- and mid-career scientists, NIH has instituted a variety of research training and career development awards, both to individuals (via awarding fellowships, or F's, and individual career development

Figure 29. NIH Type 1 R01-Equivalent Success Rates by Career Stage of Contact PI, FY, and Contact PI's Gender



Notes:

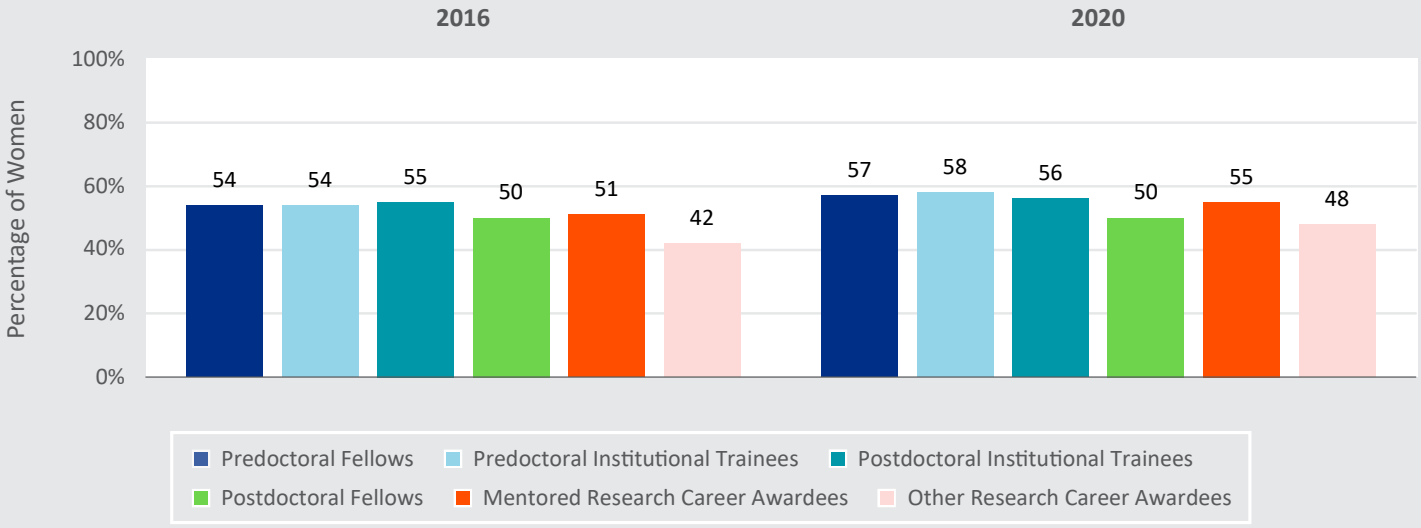
1. *Includes direct budget authority only.*
2. *Includes Type 1 competing applications only.*
3. *Includes only contact PI.*
4. *"R01-equivalent" is defined in FY 2020 as activity codes DP1, DP2, DP5, R01, R37, R56, RF1, RL1, U01, and R35 from select NIGMS and NHGRI PAs. Not all of these activities may be in use by NIH every year.*

Source: *Data drawn from the frozen success rate demographic dataset as of 2/8/2021. Data produced by the Division of Statistical Analysis and Reporting within the NIH Office of Extramural Research's Office of Research Reporting and Analysis.*

awards, or K's) and to institutions (via awarding institutional training awards to these institutions, such as K12s). The percentages of women recipients are shown in Figure 30 by type of award for both FY 2016 and FY 2020. Trends remained constant from FY 2017 to FY 2019, and data for those years are not illustrated in this figure. Aside from "other research career awardees," women received 50% or more of the training and career development awards in FY 2016 and FY 2020.

However, the growth in most grant categories remained small, between 1 and 4 percentage points. For example, there was slight growth in predoctoral awards—a 3-point increase in the percentage of predoctoral fellows who were women and a 4-point increase in the percentage of predoctoral institutional trainees who were women between FY 2016 (54% for both) and FY 2020 (57% and 58%, respectively).

Figure 30. NIH Research Career Development Award Recipients and Kirschstein-NRSA Trainees and Fellows: Percentage of Women by FY



Notes:
1. *Excludes awards issued through supplemental COVID-19 appropriations. Special supplemental COVID-19 appropriations may include: (1) H.R. 6074 (Public Law 116–123) - Coronavirus Preparedness and Response Supplemental Appropriations Act, 2020. (2) H.R. 748 (Public Law 116–136) - Coronavirus Aid, Relief, and Economic Security (CARES) Act.*
2. *Predoctoral fellowships include activity codes F30 and F31.*
3. *Postdoctoral fellowships include activity code F32.*
4. *Mentored research career awards include activity codes K01, K07, K08, K22, K23, K25, K99, KL1, and KL2.*
5. *"Other research career awards" are defined as any K activity code not included in mentored research career awards.*
6. *Kirschstein-NRSA training grants include activity codes T32, T34, T35, T36, T90, TL1, TL4, and TU2. Not all of these activities may be in use by NIH every year.*

Source: NIH IMPAC, Pub File - Data produced by the Division of Statistical Analysis and Reporting within the NIH Office of Extramural Research's Office of Research Reporting and Analysis (https://report.nih.gov/nihdatabook/report/170) and accessed on March 8, 2021.

Conclusions

This section of the women's health research biennial report examined the number and types of awards and award mechanisms, the dollar amounts of awards, career stage, and the success rates of applications by sex and/or gender, race, and ethnicity, and grant mechanism over 5 years, from FY 2016 to FY 2020. Men consistently received more R01-equivalent grants and research project grants (RPGs) than women, and they received more funding for RPGs. Women, on the other hand, received more funding, on average, for R01-equivalent grants. More men PIs than women PIs also hold multiple grants at any given time, as shown in Figures 29A and 29B.

For most types of awards examined as part of this report, men outnumbered women, except for career development and training awards (Figure 30), which women received as frequently or more frequently than men (i.e., the proportion of women awardees was 50% or higher across the 5-year period). Women also outnumbered men as predoctoral, postdoctoral, and K awardees.

In other types of awards—such as research center grants, RPGs, and SBIR/STTR program grants—women represented less than 50% of awardees over the 5 years. In some instances, women PI applicants had modestly higher success rates than men and mixed-gender PI applicants. As shown in Figures 20 and 21, in FY 2018, a crossover occurred between women and men with both the RPG and the R01-equivalent awards. Prior to FY 2018, men had higher success rates than both women and mixed-gender PI teams; however, in FY 2018 and beyond, women had higher success rates than the

other two groups, although the differences among the gender-based groups remained very small. Additionally, established women PIs had higher success rates in applying for and receiving R01-equivalent grants than their men counterparts. However, these differences were also small.

The success rates of applicants who are females from underrepresented racial and ethnic groups for RPGs and R01-equivalents, however, were below those of all female applicants in general. Black female investigators had the lowest success rates among all females from underrepresented racial and ethnic groups. The magnitude of differences between Black female investigators and the entire analytical universe of female investigators exceeded 4 percentage points across all fiscal years.

Overall, women's grant application outcomes and award opportunities have improved in recent years, though minimally. The sex and/or gender gap persists among NIH grants and awards, as the proportion of research

awards that are obtained by women overall is 30%. Although there is evidence that the representation of women among NIH grantees and awardees is increasing, this report reveals areas in which women are far from achieving parity in receiving NIH grants and awards.

Areas of Improvement

- Men consistently received more R01-equivalent grants and research project grants than women.
- Men outnumbered women in most types of awards. More men PIs than women PIs held multiple grants in any given year.
- Women represented less than 50% of awardees in research center grants, RPGs, and SBIR/STTR program grants over the 5-year period.
- Established women PIs had higher success rates in applying for and receiving R01-equivalent grants than their men counterparts—but the differences were small.
- The success rates for women of color were below those of all women applicants in general.

Areas of Parity

- Women are receiving more average funding for R01-equivalent grants.
- Women are receiving career development awards as frequently or more frequently than men.
- Women outnumbered men as predoctoral, postdoctoral, and K awardees.

IV. ORWH Biomedical Career Development

The National Institutes of Health (NIH) Office of Research on Women's Health (ORWH) recognizes the vital contributions that women who pursue careers in science, technology, the computational sciences, and biomedicine make to the health and welfare of the Nation. Therefore, a key component of ORWH's mission is to promote the recruitment, retention, re-entry, and advancement of women in biomedical careers. To advance these goals, ORWH took the critical step in 2020 of dedicating a section of the office to creating and promoting programs that nurture women's participation and advancement in biomedical careers and to addressing barriers that impede their professional growth.

This chapter summarizes major areas supported by ORWH in FYs 2019 and FY 2020. They include:

1. Support for interdisciplinary research, career development programs, and programs for re-entry into the workforce;
2. Creation of new initiatives that facilitate the transition and retention of women scientists during critical life events;
3. Recognition of institutions that have addressed faculty diversity and gender equity issues successfully, thus showcasing effective approaches that can be replicated by others; and
4. Dissemination of information relevant to advancing women's careers in science through the use of various platforms, including digital media, social networks, educational resources, and participation in the Women's Congressional Policy Institute's STEAM (science, technology, engineering, the arts, and mathematics) Fair.

Building Interdisciplinary Research Careers in Women's Health

ORWH's research and career development programs are based on the premise that interdisciplinary approaches are essential to advancing the science of women's health and increasing awareness of the ways sex and gender influence human health and disease. Career development programs that use NIH's K12 institutional grant mechanism are an effective means of achieving these goals and ultimately translating knowledge into evidence-based clinical practice.

ORWH designed, developed, and implemented the Building Interdisciplinary Research Careers in Women's Health (BIRCWH) K12 program to develop a cadre of women's health investigators who study the influences of sex and gender on health. BIRCWH (pronounced like "birch") provides a framework for mentored research training and career development opportunities that prepare investigators for independent scientific careers. The scientists are then equipped to design and conduct research that will benefit the health of women, advance research on sex and gender influences on health, and expand the use of interdisciplinary research methodologies. BIRCWH funding provides opportunities for training and development that would not otherwise be available, and it has been especially effective at facilitating the transition to research independence for junior faculty researchers (known as BIRCWH Scholars). The first K12 awards were given to BIRCWH Scholars in the fall of 2000, and this program will celebrate its 20th anniversary in the fall of 2020 with a new round of awardees.

ORWH and the other NIH Institutes, Centers, and Offices (ICOs) consider interdisciplinary mentoring teams an essential component of the BIRCWH program. Mentors have expertise in diverse disciplines, including medicine, dentistry, nursing, pharmacology, biotechnology, the social sciences, bioengineering, anthropology, and genetics. They—together with principal investigators and sponsoring/cooperating departments, centers, and institutes—form a collaborative unit that advises and supports a BIRCWH Scholar in the transition from trainee to independent researcher. This interdisciplinary team approach has been continually emphasized and enhanced since the BIRCWH program was initiated, because it has successfully bridged the basic and clinical sciences and generated new models of collaboration and institutional support. The BIRCWH program has also been instrumental in incorporating NIH's goals and objectives for women's health research, described in

Advancing Science for the Health of Women: The Trans-NIH Strategic Plan for Women's Health Research, at its various sites.

Since the BIRCWH program's inception, ORWH has sponsored more than 730 BIRCWH Scholars through institutional career development grant awards. The program has substantially expanded the number of scientists and clinicians who possess the interdisciplinary research skills necessary to stimulate innovative research on women's health and on sex and gender differences. At the end of FY 2020, there were 22 funded BIRCWH program sites across the U.S. (Table 3).

ORWH oversees the programmatic aspects of the BIRCWH program, while the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development manages the issuance of the grants. Additional ICO partners include:

- National Cancer Institute
- National Institute on Aging
- National Institute on Alcohol Abuse and Alcoholism
- National Institute of Allergy and Infectious Diseases
- National Institute of Arthritis and Musculoskeletal and Skin Diseases
- National Institute of Dental and Craniofacial Research
- National Institute on Drug Abuse
- National Institute of Environmental Health Sciences
- National Institute of Mental Health
- Office of AIDS Research

A recent evaluation assessed the BIRCWH program's impact from 2000 to 2018. The surveys were designed to acquire metrics that could indicate success toward achieving the BIRCWH program's overarching goals. The following questions were addressed:

- What are the career trajectories of the BIRCWH Scholars after their period of training?

Table 3. FY 2019–2020 BIRCWH Program Sites

Institution	Lead PI
Brigham and Women's Hospital	Jill Goldstein, Ph.D.
Duke University	Nancy Andrews, M.D., Ph.D.
Emory University	Ighovwerha Ofotokun, M.D., M.S.
Johns Hopkins University	Daniel Ford, M.D., M.P.H.
Magee-Womens Research Institute & Foundation	Yoel Sadovsky, M.D.
Mayo Clinic	Kejal Kantarci, M.D., M.S.
Medical University of South Carolina	Jacqueline McGinty, Ph.D.
Oregon Health & Science University	Jeanne-Marie Guise, M.D., M.P.H.
Tufts University	Karen Freund, M.D., M.P.H.
Tulane University	M.A. "Tonette" Krousel-Wood, M.D.
University of California, Davis	Nancy E. Lane, M.D.
University of California, San Francisco	Claire D. Brindis, Dr.P.H., M.P.H.
University of Colorado	Judith Regensteiner, Ph.D.
University of Kentucky	Thomas Curry, Ph.D.
University of Illinois Chicago*	Pauline Maki, Ph.D.
University of Minnesota	Jerica M. Berge, Ph.D., M.P.H.
University of North Carolina at Chapel Hill	Kim Boggess, M.D.
University of Pennsylvania	Maria A. Oquendo, M.D., Ph.D.
University of Texas Medical Branch	Abbey Berenson, M.D., M.M.S., Ph.D.
University of Utah	Michael Varner, M.D.
University of Wisconsin–Madison*	Elizabeth Burnside, M.D., M.P.H.
Vanderbilt University	Katherine Hartmann, M.D., Ph.D.

**Newly funded programs for 2020.*

- What are the career trajectories of the principal investigators (PIs) and the mentors involved in the program?
- To what extent have underrepresented minorities (URMs) been recruited as BIRCWH Scholars?
- What is the career advancement of URMs trained within the program?
- How have the institutions that employ BIRCWH Scholars leveraged the BIRCWH program?

The December 2019 *Changing the Culture to End Sexual Harassment* report, developed by the NIH Advisory Committee to the Director Working Group on Changing the Culture to End Sexual Harassment, provides recommendations for NIH, NIH-funded institutions, and scientific and professional societies to change the culture at every level of the research enterprise. This further supports the BIRCWH program's overarching goals by seeking to ensure safe, diverse, and inclusive research and training environments.

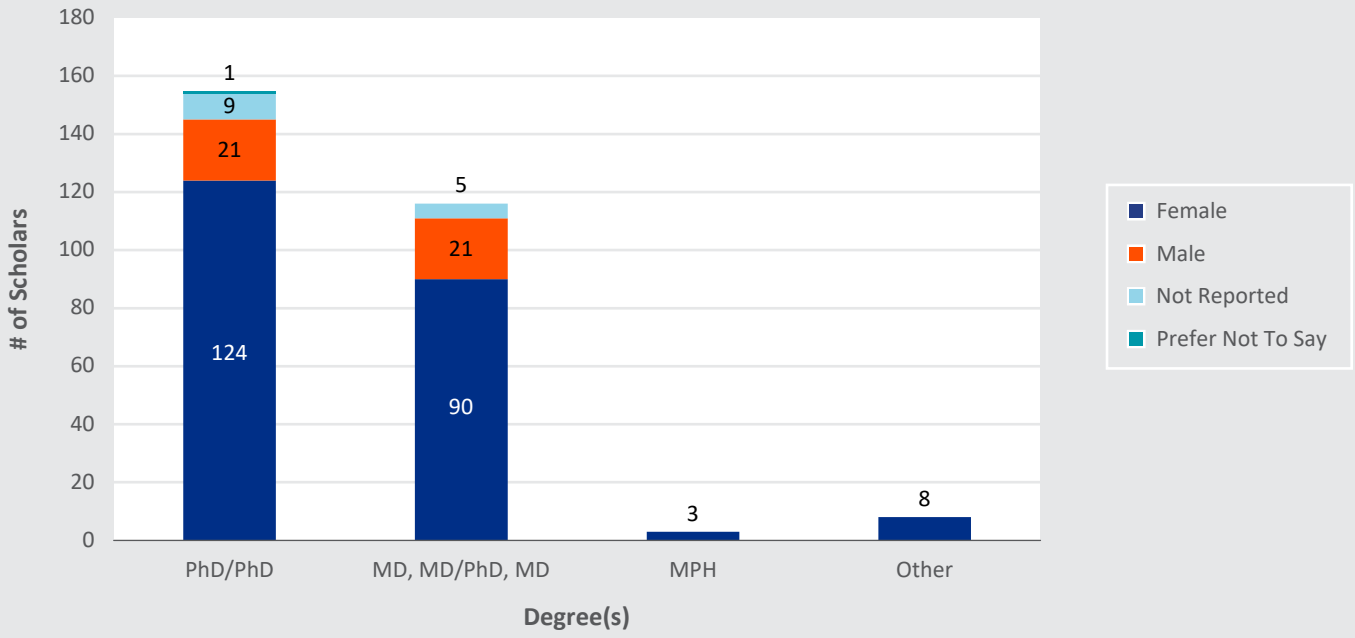
Over the 18-year period, the BIRCWH program had awarded 88 grants to 44 institutions and supported 687 junior faculty/Scholars. The response rates to survey questions for PIs, Scholars, and mentors were as follows:

- All living PIs (n=88): 64% response rate, representing 78% of BIRCWH program sites
- Sample of 391 Scholars from all BIRCWH institutions: 72% response rate
- Sample of 80 mentors recommended by PIs: 79% response rate

During the evaluation period, most Scholars held a Ph.D. or equivalent degree; more than 40% held a medical degree or medical degree combined with another advanced degree; and other Scholars held advanced degrees in nursing, pharmacy, dentistry, public health, and veterinary medicine. The evaluation confirmed that the BIRCWH program had successfully recruited physician-scientists (Figure 31). Eighty percent of the BIRCWH Scholars reported as female, and 20% reported as male.

Although the BIRCWH program was not specifically designed to function as a career development program for members of underserved racial and ethnic groups,

Figure 31. FY 2019–2020 Terminal Degree(s) Credentials for BIRCWH Scholars



*Notes: * In addition to the PhD, includes degrees such as MPH, DVM, PharmD, MSW, DDS, and DC.*
*** In addition to MD degree, includes MPH, MS, DPH, MSPH, ScM, and MSc.*
**** In addition to MPH degree, includes MS and MSci degrees.*
Other: Includes DPH, DO, DPT Sc, PharmD, PsyD degrees.

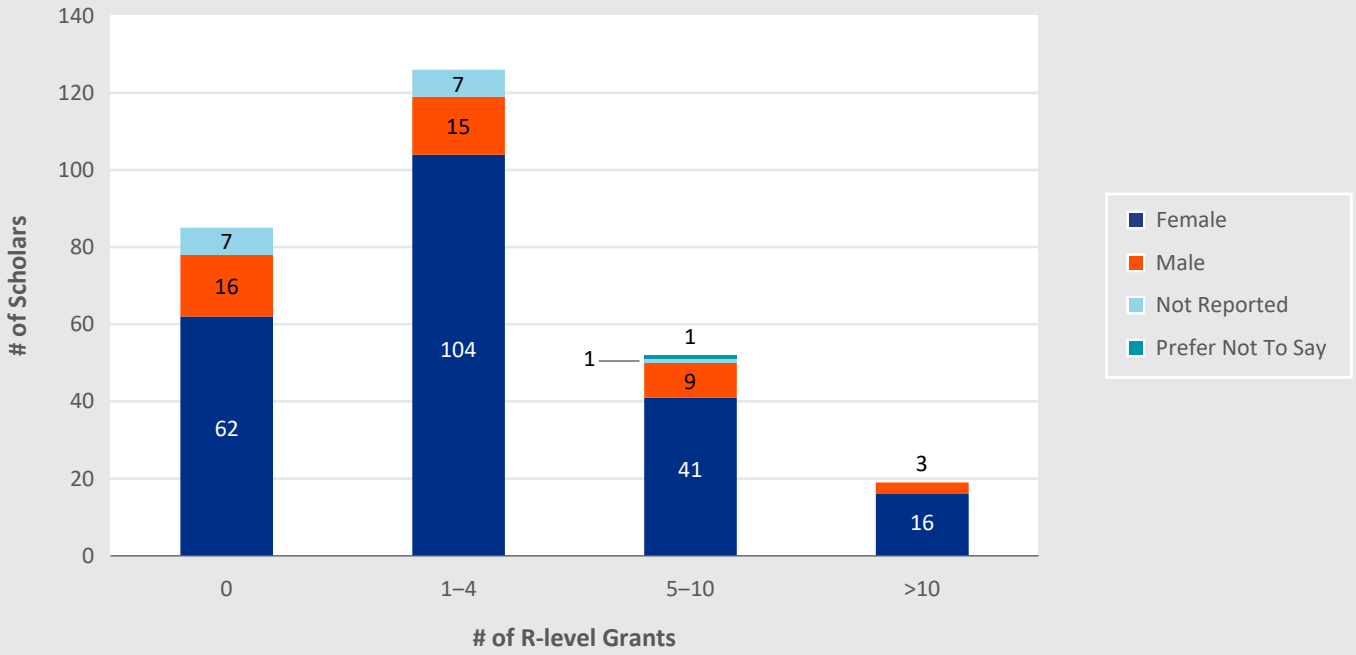
it has been successful in this regard. Over the 18-year reporting period, 13% of BIRCWH Scholars reported being in an underrepresented racial or ethnic group, which NIH defines as a person belonging to the Black or African American, American Indian or Alaska Native, or Native Hawaiian and other Pacific Islander racial group or to the Hispanic or Latino ethnic group. From 2015 to 2018, more than 21% of Scholars belonged to at least one of those groups. Moreover, the BIRCWH program collaborates with several historically Black colleges and universities (HBCUs) and is in the process of expanding its network to include more minority-serving institutions. ORWH will continue to analyze responses to this section of the evaluation and utilize trans-NIH resources so that additional measures can be identified that will permit further recruitment and retention of URM faculty.

BIRCWH Scholars have been successful at securing Federal funding for their research and publishing their results. In FY 2019 and FY 2020, 70% of the Scholars reported holding at least one NIH R-level grant; the largest group reported having one to four grants, with a median of two (Figure 32). Analysis of their publication records is ongoing, but preliminary results suggest the Scholars have a median of 33 publications per person, a mean of 45, and a range from 1 to 278.

ORWH will continue to analyze the BIRCWH evaluation data to refine and enhance the program. Overall, BIRCWH Scholars have shown high levels of success as research scientists by securing funding from various sources and publishing many articles in medical or health-related journals. Data suggest the BIRCWH program has been instrumental in fostering mutually beneficial mentor–mentee relationships. PIs report that the BIRCWH program has leveraged itself across their institutions to accrue several advantages. There have been greater levels of interdisciplinary research, more mentorship and networking opportunities, new courses in women's health research, more visibility within their home institutions, and a greater focus on women's health and sex differences research in general.

Additional analysis is planned to ascertain the impact of publications authored by the BIRCWH Scholars and ways that the interdisciplinary team science has evolved since the program was created in 2000. Most of the programs include multiple schools of health professions—such as medicine, nursing, public health, dentistry, and pharmacy—that encourage cross-disciplinary research.

Figure 32. FY 2019–2020 R-Level NIH Grants Received by BIRCWH Scholars



Notes: The mean number of R level grants was 3.18 (SD = 4.24). The median was 2 grants.

Further evaluation of academic advancement and career pathways will be performed as the Scholars provide updated employment information. Given the data on earned degrees, the type of research settings in which they work, and their publication and sponsored research records, comparisons can be made along the more successful career trajectories.

NIH hosts the BIRCWH Annual Meeting to bring together the Scholars, PIs and their research staff, NIH staff members, and others interested in the BIRCWH program. These meetings include the Ruth L. Kirschstein Memorial Lectureship, plenary panel discussions, and mentorship sessions led by experienced NIH research staff members. The 2020 Annual BIRCWH Meeting, which will celebrate the 20th anniversary of the BIRCWH program, will be delivered virtually because of the COVID-19 pandemic and will feature a special Legacy of Leadership lecture and a virtual poster session. Abstracts submitted by the BIRCWH Scholars for the FY 2019 and FY 2020 meetings will be published in the *Journal of Women's Health*. Videos of the presentations and additional information about the program will be posted on the ORWH website.

Women's Reproductive Health Research Career Development Program

The Women's Reproductive Health Research (WRHR) Career Development Program was initiated by the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development in 1998 and has been co-sponsored by ORWH since its inception. Its goal is to provide opportunities for junior obstetrician-gynecologists (OB-GYNs) to obtain intensive mentored research training in basic, translational, and/or clinical research in women's reproductive health.

There are 15 WRHR sites in OB-GYN departments throughout the U.S., and each site has the capacity to support two scholars. Senior investigators from established OB-GYN research programs and collaborating departments form an intellectual and technical research base for mentoring WRHR scholars. These sites enable OB-GYN junior faculty members to obtain state-of-the-art training in women's reproductive health research in an academic setting and to increase the research capacity of OB-GYN departments.

Program eligibility is limited to obstetrician-gynecologists with an M.D. or D.O. who have recently completed their clinical training and are strongly committed to an academic research career. Scientific topics of interest encompass all areas of women's reproductive health, including maternal–fetal medicine, gynecologic oncology, reproductive endocrinology and infertility, female pelvic medicine and reconstructive surgery, and family planning and menopause. More than 235 OB-GYN junior faculty members have been appointed to the WRHR program since its inception.

FY 2019 Program Sites: Sites 1–6 were active in FY 2019 and FY 2020 but were discontinued as of June 30, 2020. Grant numbers indicate funding received from July 1, 2018, to June 30, 2019, and from July 1, 2019, to June 30, 2020.

1. Augusta University Women's Reproductive Health Research Career Development Plan.

   Institution: Augusta University (formerly Georgia Regents University); Augusta, Georgia.

   Principal Investigator (PI): Sharad A. Ghamande, M.D.

   Grant: K12 HD085817-04 & K12 HD085817-05.

2. Brown University/Women & Infants Hospital (WIH) Women's WRHR Career Development Program: Improving Women's Health through Career Development in Clinical Research.

   Institution: WIH Rhode Island/Brown University; Providence, Rhode Island.

   PI: Maureen G. Phipps, M.D., M.P.H.

   Grant: K12 HD050108-14 & K12 HD050108-15.

3. Continuation of Wayne State University's Successful Development of Physician-Scientists as Independent Researchers in the Area of Women's Reproductive Health.

   Institution: Wayne State University; Detroit, Michigan.

   PI: Chaur-Dong Hsu, M.D., M.P.H.

   Grant: K12 HD001254-19 & K12 HD001254-20.

4. Fast Forwarding Women's Reproductive Health Research: University of Michigan WRHR Career Development Program.

   Institution: University of Michigan; Ann Arbor, Michigan.

   PI: Dee E. Fenner, M.D.

   Grant: K12 HD065257-9 & K12 HD065257-10.

5. Magee-Womens Basic and Translational Reproductive Health Training Program.

   Institution: Magee-Womens Research Institute & Foundation; Pittsburgh, Pennsylvania.

   PI: Robert P. Edwards, M.D.

   Grant: K12 HD063087-9 & K12 HD063087-10.

6. OB/GYN Faculty Research Career Development Program.

   Institution: University of Alabama at Birmingham; Birmingham, Alabama.

   PI: Todd R. Jenkins, M.D.

   Grant: K12 HD 001258-19 & K12 HD 001258-20.

7. Colorado Women's Reproductive Health Research Career Development Center.

   Institution: University of Colorado Denver; Denver, Colorado.

   PI: Nanette F. Santoro, M.D.

   Grant: K12 HD001271-19 & K12 HD001271-20.

8. The Penn Center for Career Development in Women's Health Research.

   Institution: University of Pennsylvania; Philadelphia, Pennsylvania.

   PIs: Deborah A. Driscoll, M.D., and Samuel I. Parry, M.D.

   Grant: K12 HD001265-19 & K12 HD001265-20.

9. Women's Reproductive Health Research.

   Institution: University of California, San Francisco; San Francisco, California.

   PI: Amy P. Murtha, M.D.

   Grant: K12 HD001262-19 & K12 HD001262-20.

10. Women's Reproductive Health Research at the University of Washington.

    Institution: University of Washington; Seattle, Washington.

    PI: Barbara A. Goff, M.D.

    Grant: K12 HD001264-19 & K12 HD001264-20.

11. University of California, San Diego (UCSD) Women's Reproductive Health Research Program.

    Institution: University of California, San Diego; San Diego, California.

    PI: Charles W. Nager, M.D.

    Grant: K12 HD001259-19 & K12 HD001259-20.

12. The Yale WRHR Career Development Center.

    Institution: Yale University; New Haven, Connecticut.

    PI: Hugh Smith Taylor, M.D.

    Grant: K12 HD047018-14 & K12 HD047018-15.

13. Research Career Development in Obstetrics and Gynecology.

    Institution: Northwestern University; Chicago, Illinois.

    PI: Serdar E. Bulun, M.D.

    Grant: K12 HD050121-14 & K12 HD050121-15.

14. Utah Women's Reproductive Health Research Career Development Program.

    Institution: University of Utah; Salt Lake City, Utah.

    PI: Robert M. Silver, M.D.

    Grant: K12 HD085816-04 & K12 HD085816-05.

15. Women's Reproductive Health Research K12 Program.

    Institution: Oregon Health & Science University; Portland, Oregon.

    PI: Aaron B. Caughey, M.D., Ph.D.

    Grant: K12 HD085809-04 & K12 HD085809-05.

FY 2020 Program Sites: Sites 1–9 include those that were continued from July 1, 2018, to June 30, 2019, and from July 1, 2019, to June 30, 2020, and are ongoing; sites 10–15 include those that began on July 1, 2020. Only grant numbers starting on July 1, 2020, are indicated.

1. Colorado Women's Reproductive Health Research Career Development Center.

   Institution: University of Colorado Denver; Denver, Colorado.

   PI: Nanette F. Santoro, M.D.

   Grant: K12 HD001271-21.

2. The Penn Center for Career Development in Women's Health Research.

   Institution: University of Pennsylvania; Philadelphia, Pennsylvania.

   PI: Elizabeth A. Howell, M.D., M.P.P.

   Grant: K12 HD001265-21.

3. Women's Reproductive Health Research.

   Institution: University of California, San Francisco; San Francisco, California.

   PI: Amy P. Murtha, M.D.

   Grant: K12 HD001262-21.

4. Women's Reproductive Health Research at the University of Washington.

   Institution: University of Washington; Seattle, Washington.

   PI: Barbara A. Goff, M.D.

   Grants: K12 HD001264-21.

5. University of California, San Diego (UCSD) WRHR Program.

   Institution: University of California, San Diego; San Diego, California.

   PI: Linda Brubaker, M.D.

   Grant: K12HD001259-21.

6. The Yale WRHR Career Development Center.

   Institution: Yale University; New Haven, Connecticut.

   PI: Hugh Smith Taylor, M.D.

   Grant: K12 HD047018-16.

7. Research Career Development in Obstetrics and Gynecology.

   Institution: Northwestern University; Chicago, Illinois.

   PI: Serdar E. Bulun, M.D.

   Grant: K12 HD050121-16.

8. Utah Women's Reproductive Health Research Career Development Program.

   Institution: University of Utah; Salt Lake City, Utah.

   PI: Robert M. Silver, M.D.

   Grant: K12 HD085816-06.

9. Women's Reproductive Health Research K12 Program.

   Institution: Oregon Health & Science University; Portland, Oregon.

   PI: Aaron B. Caughey, M.D., Ph.D.

   Grant: K12 HD085809-06.

10. Transdisciplinary Harvard WRHR Career Development for Gynecologists and Obstetricians.

    Institution: Brigham and Women's Hospital; Boston, Massachusetts

    PI: Nawal M. Nour, M.D., M.P.H.

    Grant: 1K12HD103096-01 (Started on July 1, 2020).

11. Duke Women's Reproductive Health Research Scholars.

    Institution: Duke University; Durham, North Carolina.

    PI: Matthew Barber, M.D.

    Grant: 1K12HD103083-01 (Started on July 1, 2020).

12. Stanford WRHR Career Development Program.

    Institution: Stanford University; Palo Alto, California.

    PI: Leslee L. Subak, M.D.

    Grant: 1K12HD103087-01. (Started on July 1, 2020).

13. Baylor College of Medicine and Texas Children's WRHR Center of Excellence.

    Institution: Baylor College of Medicine; Houston, Texas.

    PI: Michael A. Belfort, M.D., Ph.D.

    Grant: 1K12HD103087-01. (Started on July 1, 2020).

14. Advancing Women's Health through Research: University of North Carolina (UNC) WRHR Career Development Program.

    Institution: University of North Carolina at Chapel Hill; Chapel Hill, North Carolina.

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

    Grant: 1K12HD103085-01. (Started on July 1, 2020).

15. Johns Hopkins WRHR Career Development Program.

    Institution: Johns Hopkins University; Baltimore, Maryland.

    PI: Andrew J. Satin, M.D.

    Grant: 1K12HD103036-01. (Started on July 1, 2020).

Research Supplements to Promote Re-Entry into Biomedical and Behavioral Research Careers

The NIH research supplements to promote re-entry into biomedical and behavioral research careers (PA-18-592) assist individuals with high potential to re-enter an active research career after an interruption for family responsibilities or another qualifying event. The program began as a pilot in 1992 using administrative supplements to support full- or part-time researchers working on existing NIH grants. It includes three components that help re-establish awardees as independent competitive research scientists:

1. Full participation in an ongoing NIH-funded research project;
2. An opportunity to update and enhance research capabilities; and
3. A carefully planned mentoring program developed by the mentor and awardee.

As of FY 2020, over 150 applications had been received and over 60 grants had been awarded to investigators, with support from 19 NIH Institutes, Centers, and Offices (ICOs).

The funding opportunity announcement is set to be renewed by September 2021 and will allow maximum flexibility for the ICOs to support an individual who has been out of the research environment for less than 6 months or support individuals, including graduate students, who are seeking to transition out of unsafe environments.

NIH Working Group on Women in Biomedical Careers

The NIH Working Group on Women in Biomedical Careers (WgWBC) was established in 2007 to lead NIH-wide efforts to address career barriers for women in science, including the development of innovative strategies to promote entry, recruitment, retention, and sustained advancement of women in biomedical and research careers. The WgWBC is co-chaired by the directors of NIH and ORWH, and its members include NIH deputy directors, senior staff members from the NIH Office of the Director, NIH Institute and Center (IC) directors, IC scientific directors, and other NIH intramural and extramural staff members. (FY 2019 and FY 2020 members are listed in Appendix C.) It hosts several committees related to its mission, including the Committee on Women of Color in Biomedical Careers and the Committee on the NIH Intramural Research Program. The working group and its committees have sponsored national workshops, seminars, and research symposia on career development trends and interventions; issued reports on best practices; created public outreach websites; developed a grant program to study barriers that impede women's career development; and published articles on topics relevant to the advancement of women in biomedical careers.

FY 2020 activities of the WgWBC include the publication of two continuity supplements aimed at supporting and enhancing retention of early-career biomedical investigators during critical life events. The notice of special interest (NOSI) titled *Administrative Supplements to Promote Research Continuity and Retention of NIH Mentored Career Development (K) Award Recipients and Scholars* (NOT-OD-20-054) announced support for the transition and retention of investigators from mentored career development to research independence, with a goal of minimizing departures from the biomedical research workforce at this critical juncture. The supplements are intended to ensure continuity of research among recipients of mentored career development (K) awards by providing supplemental research support to help sustain the investigators' research during critical life events.

The NOSI titled *Administrative Supplement for Continuity of Biomedical and Behavioral Research Among First-Time Recipients of NIH Research Project Grant Awards* (NOT-OD-20-055) aims to enhance retention of investigators who are facing critical life events and are transitioning to the first renewal of their first independent research project grant award or to a second, new NIH research project grant award. Retention at the first renewal is crucial for sustaining both the research investments NIH has made and retaining diversity in the biomedical research workforce. This program supports "at-risk" investigators as identified in the NIH Next Generation Researchers Initiative.

Another activity of the WgWBC in FY 2020 is the NIH Prize for Enhancing Faculty Gender Diversity in Biomedical and Behavioral Science, which seeks to recognize institutions whose biomedical and behavioral science departments, centers, or divisions have achieved sustained improvement in gender diversity. Critical goals of this competition are the identification of best practices, the sharing of lessons learned, and the delineation of evidence-based approaches that can be replicated by other institutions.

NIH Women in Biomedical Careers Website and Newsletter Articles

ORWH maintains the NIH Women in Biomedical Careers website (https://womeninscience.nih.gov) for the NIH Working Group on Women in Biomedical Careers (WgWBC). The website provides the history of the working group, accomplishments of NIH women in biomedical careers, names of committees in the working group, and a list of programs supported by the WgWBC. It also includes pages with information on grants, resources for career development, and profiles of prominent women in the sciences. In addition, the website links to the Women of Color Research Network (WOCRN) group on LinkedIn, which features NIH diversity efforts, prominent women-of-color researchers, and networking and research opportunities. The website, often referred to as the "Women in Science website," is also home to the ORWH "Pearls of Wisdom" video series, which highlights distinguished women in science and medicine who share words of wisdom about advancing in careers in the biomedical field. The wisdom shared by these leaders raises awareness of the crucial role that women in science play and also highlights the importance of their accomplishments. Finally, ORWH began work in FY 2020 on significant updates to the NIH Women in Biomedical Careers website, both with respect to content and by migrating the site to a more modern platform. It is expected to launch in FY 2021.

The ORWH quarterly publication, *Women's Health in Focus at NIH (In Focus)*, has prominently featured WgWBC-related content in its Women in Science section since the periodical's launch in FY 2018. This section features scientist spotlights, timely research updates and perspectives, and current news and reports. Articles address important steps for career development and best practices for retention at universities and institutions, and they provide an overview of NIH policies and programs relevant to women in the sciences. In the 12-month period from October 2019 through September 2020, ORWH website pageviews increased by 44% (from 20,976 to 30,289 views), and ORWH garnered a 5.4% increase in social media followers (54,326 to 57,263 followers). Spikes in visits and followers coincided with releases of new issues of *In Focus*.

Activities of the Committee on Women of Color in Biomedical Careers

The Committee on Women of Color in Biomedical Careers, part of the NIH Working Group on Women in Biomedical Careers, is charged with addressing the unique challenges facing women scientists of color. One challenge faced by women scientists of color is difficulty gaining visibility and recognition. Toward that end, the committee regularly identifies and nominates exceptional women researchers for the prestigious NIH Director's Wednesday Afternoon Lecture Series (WALS). For the WALS seasons in FY 2019 and FY 2020, the committee successfully nominated six lecturers, which accounted for 10% of the WALS lecturers each season. Two FY 2020 speakers were rescheduled for the FY 2021 WALS season because of disruptions from the COVID-19 pandemic. In FYs 2019 and 2020, the committee held three meetings that featured two NIH Earl Stadtman tenure-track investigators and the Deputy Director of the National Institute on Minority Health and Health Disparities to discuss their research and their career journeys as women scientists of color. The committee also maintains the Women of Color Research Network (WOCRN) on LinkedIn to promote networking among women scientists of color. WOCRN provides information, mentoring, and career development opportunities for women of color in biomedical careers and for those who support racial, ethnic, and gender diversity in the scientific workforce. The WOCRN LinkedIn group has over 1,300 members.

Activities of the Committee on the NIH Intramural Research Program

In FYs 2019 and 2020, the Committee on the NIH Intramural Research Program of the NIH Working Group on Women in Biomedical Careers (IRP WgWBC) has remained focused on improving and enhancing the NIH work environment to support the advancement of women. This committee has played an active role in synthesizing ideas and integrating goals from several mission-related groups and committees, including the NIH Office of Equity, Diversity, and Inclusion; the Women Scientists Advisors (WSA); the NIH Equity

Committee (NEC); the NIH Civil Program; the NIH Child Care Board; and committees within the NIH Office of Intramural Training and Education (OITE).

Meetings of the IRP WgWBC focus on specific actions that can support the advancement of women scientists. They provide committee members with an opportunity to discuss and evaluate metrics needed to identify trends, monitor progress, address challenges, and develop constructive solutions. The committee's efforts in the past 2 years have provided support for gathering information, evaluating policies, and developing strategies to make the culture in the NIH Intramural Research Program (IRP) more equitable.

Information Gathering

Postdoc Exit Survey: A postdoc exit survey was initiated by the WSA, is supported by the IRP WgWBC, and is being administered by the Foundation for Advanced Education in the Sciences. The survey aims to obtain information from departing postdocs about their career track, including why they chose a particular track and what type of mentoring they received. Responses to the survey are strictly confidential, and answers are only presented in aggregate form. Data from the postdoc exit survey will be posted to a dashboard platform and made available to scientific directors and training directors as the data accumulate. The feedback will be used to improve postdoctoral training at NIH.

COVID-19 Impact Survey: Members of the IRP WgWBC collaborated with several other groups to develop a COVID-19 impact survey that assessed levels of job satisfaction among IRP scientists during the pandemic, whether they believed they were effective when working remotely, and what types of work they were accomplishing. It queried a wide variety of topics related to the impact of the pandemic on their professional lives; the effectiveness of institutional communication regarding health, wellness, and work status; satisfaction with the level of support they were receiving to remain productive; experience with issues of harassment or discrimination; changes in caregiving responsibilities; reductions in use of public transportation; levels of comfort returning to the physical workplace; the impact of being physically separated from co-workers; and the overall impact on productivity. Employees' responses provided important feedback to NIH on how to meaningfully adapt its policies and communication practices to optimize remote working conditions through full and partial shutdowns.

Policy Development

Resources Task Force: The IRP WgWBC partnered with the NEC to develop a policy that would make it easier for principal investigators (PIs) to request accommodations and/or resources to cover for themselves or a staff member who requires leave for family responsibilities. The effort aimed to produce a policy statement and checklist that would facilitate discussions between the PI and lab/branch chief or scientific director. This strategy arose from the model used for the successful Keep the Thread program, developed previously by the IRP WgWBC. A further effort has been to ensure everyone in the IRP is aware of these policies and can access them through a website and sourcebook faculty page when necessary. The policies are intended to supplement existing family leave policies and are designed to support lab productivity.

Alleviating the Impact of COVID-19 on Women in Biomedical Careers: The IRP WgWBC engaged in monthly discussions to share information with and seek input from working group members who represented the various IRP committees relevant to women in biomedical careers. Through these exchanges, the committee provided valuable input to leadership that helped frame policies for teleworking and return-to-work arrangements. The task force tracked publications that assessed how women scientists' publication rate was affected in relation to men's during stay-at-home directives and called attention to data indicating a need for policies to extend time for boards of scientific counselors' reviews and tenure reviews.

Development of Rigorous Review Processes for Lab and Branch Chiefs: The IRP WgWBC, in conjunction with the NEC and other committees on gender equity, made significant contributions to the framing and development of a process to rigorously review performance of laboratory and branch chiefs in the IRP. The goal was to ensure outstanding performance of NIH's laboratory and branch chiefs in the domains of science management, ethical oversight, and administrative practice. Failure to meet these high standards might result in a decision to replace chiefs with highly qualified scientists either at NIH or recruited from extramural organizations.

Scientific Director and Clinical Director Review Processes: The IRP WgWBC's collaborations with the NEC led to the development of an external review process for NIH scientific directors and clinical directors. One component of this review is to evaluate the scientific and clinical directors' performance in building a diverse, equitable, and inclusive community of scientists. The NEC and IRP WgWBC also endorsed a plan to provide NIH Institute and Center (IC) directors with their respective ICs' NEC reports so that the clinical directors and scientific directors can develop plans to respond to recommendations effectively.

Culture Change

Ongoing Contributions to Mentoring Tenure-Track Investigators: The IRP WgWBC has continued to review processes to evaluate and improve the quality of mentorship provided by tenure-track investigators (TTIs) and senior investigators, including laboratory and branch chiefs. Training for TTIs has included a 1-day course that is delivered by IRP staff members and OITE, and recently the course has been supplemented by a series of professional development workshops throughout the year. In addition, the IRP WgWBC and the WSA have supported development of regular discussion groups for early-career scientists that are organized around shared research interests and mentoring goals.

NIH Anti-Harassment Training: Discussions within the IRP WgWBC and WSA and feedback from NIH staff members helped prompt NIH leadership to explore ways to create systemwide changes in culture and climate that will prevent harassment and discrimination. Initiatives designed to promote a safe and inclusive culture at NIH that resulted from this effort included the development of a sexual harassment survey by the Scientific Workforce Diversity Office, support for a hotline to receive anonymous complaints, and establishment of the NIH Civil Program.

Recommendation to Establish Diversity Oversight Positions Within Institutes: Based on the NEC reviews of scientific directors, the group explored additional strategies to promote diversity. It was proposed that a senior person at each NIH Institute, Center, and Office have the responsibility to build a diverse community of inclusive excellence. The IRP WgWBC is currently debating the nature of this position and its responsibilities, and plans are underway to supplement this effort through the NIH UNITE initiative, with the goals of producing more diverse recruitment portfolios and conducting searches to enhance inclusivity.

Recruitment and Retention of Women and People in Underrepresented Racial and Ethnic Groups: The IRP WgWBC is currently developing programs to increase recruitment of scientists who are women and members of underrepresented racial and ethnic groups. The effort involves developing support for re-entry programs for people seeking to switch to a full-time research position from another scientific career or a teaching position with limited research opportunities. It also includes programs to recruit senior investigators by expanding the IRP Distinguished Scholars Program and developing sabbatical programs at NIH for a diverse group of senior scientists. Finally, the IRP WgWBC promotes programs that improve retention of women in research careers by increasing support during the transition from postdoc to faculty, with particular attention to child care, office spaces on campus, and flexible tenure processes.

Retention and Continuity Administrative Supplement Programs of the Working Group on Women in Biomedical Careers

In January 2020, ORWH and the Division of Biomedical Research Workforce in the NIH Office of Extramural Research published two linked pilot continuity supplement programs on behalf of the NIH Working Group on Women in Biomedical Careers that aim to support and enhance retention of early-career biomedical investigators at crucial branching or transition points in their careers. The notice of special interest (NOSI) titled *Administrative Supplements to Promote Research Continuity and Retention of NIH Mentored Career Development (K) Award Recipients and Scholars* (NOT-OD-20-054) supports investigators who are experiencing critical life events and transitioning from mentored career development to research independence in order to minimize departures from the biomedical research workforce at this critical juncture. The NOSI titled *Administrative Supplement for Continuity of Biomedical and Behavioral Research Among First-Time Recipients of NIH Research Project*

Grant Awards (NOT-OD-20-055) aims to enhance the retention of investigators who are facing critical life events and are transitioning from their first independent research award to sustained research funding. The awards target these two career transition points because they are stages when women investigators are disproportionately affected compared with men, according to NIH Data Book and National Science Foundation data. Retaining investigators at these critical junctures will protect the research investment made via the parent NIH awards and enhance the diversity of the investigator pool.

In FY 2020, NIH received over 140 applications for the supplements promoting research continuity and retaining K award recipients (NOT-OD-20-054), and over 105 were funded. In the same period, NIH received approximately 30 applications for the research project grant (RPG) continuity supplement program (NOT-OD-20-055), and approximately 20 were funded. In FY 2020, ORWH provided over $1 million to the participating NIH Institutes, Centers, and Offices in support of launching these new programs, which accounted for 10% of the funded mentored career development continuity supplements and approximately 30% of the funded RPG continuity supplements.

NIH Prize for Enhancing Faculty Gender Diversity in Biomedical and Behavioral Science

The NIH Prize for Enhancing Faculty Gender Diversity in Biomedical and Behavioral Science will recognize institutions that have successfully addressed faculty gender diversity and equity issues in biomedical and behavioral science departments, centers, and divisions. The goal is to acknowledge transformative structures, systems, projects, programs, and processes that were implemented to successfully enhance and sustain gender diversity within institutions. Critical to this prize competition will be the identification of best practices, the sharing of lessons learned, and the delineation of evidence-based approaches through crowdsourcing, which will then be broadly translated to and replicated by other institutions via an NIH-supported national toolkit. Conceptually originating from the NIH Working Group on Women in Biomedical Careers, this prize competition is a critical step in addressing a recommendation of a National Academies of Sciences, Engineering, and Medicine consensus study report to deepen the evidence base for programs, policies, and practices to improve gender diversity in academia. It was launched on September 2020, and prizes are expected to be awarded by the end of FY 2021.

Activities of the NIH Advisory Committee to the Director Working Group on Changing the Culture to End Sexual Harassment

The NIH Advisory Committee to the Director (ACD), established in 1965, provides advice on matters relevant to NIH mission responsibilities in the conduct and support of biomedical research, medical science, and biomedical communications. ACD includes several active working groups with specific objectives and charges. The ORWH Director serves as a member of the ACD Working Group on Changing the Culture to End Sexual Harassment, which comprises experts in addressing sexual harassment from several different perspectives. This working group is charged with performing the following actions:

- Assessing the current state of sexual harassment allegation investigation, reporting, remediation, and disciplinary procedures at NIH-funded organizations;
- Advising on oversight, accountability, and reporting measures for awardee institutions, which will encourage a reduction in and prevention of sexual harassment in biomedical research laboratories;
- Proposing actions and policies that would promote a safe and inclusive culture at NIH-supported research conferences;
- Suggesting systemwide changes to culture and climate to prevent harassment and gender discrimination through diffusion of hierarchical environments by mentoring networks and committee-based advisement and through strong and diverse leadership; and

» Developing strategies for encouraging research on anti-harassment policies, procedures, and training, as well as measures and evaluations of their effectiveness.

The ACD Working Group on Changing Culture to End Sexual Harassment recently developed resources that comprehensively outline NIH policies, practices, and initiatives to address sexual harassment at NIH, at NIH-supported institutions, and anywhere NIH research activities take place. In December 2019, this working group published a report to the ACD, titled *Changing the Culture to End Sexual Harassment*, which provides recommendations for ending sexual harassment at every level of the research enterprise. The NIH Director accepted the report.

Office of Intramural Training and Education

The NIH Office of Intramural Training and Education's (OITE) mission is to enhance the training experience of students and fellows on all NIH campuses. It works closely with the NIH Institutes and Centers (ICs). OITE programs provide NIH Intramural Research Program trainees at all career stages and on all campuses with opportunities to develop the scientific and professional skills to become leaders in the biomedical research community.

High School Scientific Training and Enrichment Programs: HiSTEP and HiSTEP 2.0

In FY 2019, ORWH provided funds to support students in the High School Scientific Training and Enrichment Programs (HiSTEP and HiSTEP 2.0). These programs expand the pipeline of students interested in biomedical and health care careers by providing internship opportunities for students from high schools with large populations of financially disadvantaged students. The programs target students from Washington, DC, Maryland, and Virginia, where more than 30% of students receive free or low-cost lunches from the National School Lunch Program. Students from these lower-resourced schools traditionally struggle to obtain internships in research groups, even when they show great potential.

Rising high school juniors are selected for HiSTEP through a two-part application process and participation in career exploration, leadership, and professional development training opportunities; they are guided by HiSTEP staff members. HiSTEP 2.0 supports competitively selected rising high school seniors and HiSTEP alumni who have little or no research experience and provides them with the opportunity to conduct biomedical research at NIH for 8 weeks. Students are paired with and work side by side with scientists on the main campus of NIH in Bethesda, Maryland. Through these experiences, HiSTEP and HiSTEP 2.0 students develop their research and scientific skills; explore biomedical, translational, and/or basic science in depth; and sharpen their critical thinking skills. In addition to research experience, all students participate in a curriculum designed to enhance leadership and communication skills, experience mentorship during and beyond the summer, and gain access to resources that help them in the transition from high school to college. As a required part of the program, students present research results at a "Summer Poster Day" alongside other NIH summer interns.

In 2019, 25 students from 15 schools were selected for HiSTEP, 16 (64%) of whom were girls and 9 (36%) of whom were boys. The entire 2019 HiSTEP cohort completed the program. Students ranked the hands-on laboratory experience and the college application preparation sessions as their favorite aspects of the program. The participants began their senior years with plans to attend college. When surveyed, 100% of the 2019 participants said they would recommend HiSTEP to a friend. Overall, 98% of HiSTEP alumni from the 2015–2018 programs said they would recommend HiSTEP to a friend.

The 2019 HiSTEP 2.0 cohort consisted of 24 students, 8 (33%) of whom were HiSTEP alumni. The gender distribution in this cohort included 16 (67%) girls/women and 8 (33%) boys/men. Twenty-three students completed the program, and one individual withdrew. In a survey, all HiSTEP 2.0 students (100%) said they would recommend the program to a friend who is interested in conducting biomedical research, and 83% said they felt more prepared for college after program completion. In fact, the students ranked the "Transition to College Series" as one of the most helpful components. By the end of the program, students indicated improvement

in their abilities to (1) communicate with peers and mentors, (2) lead presentations at laboratory meetings and poster sessions, (3) use networking skills to expand their professional networks, (4) develop their research and scientific skills, and (5) manage time and stress effectively.

Representative feedback from 2019 HiSTEP and HiSTEP 2.0 students is listed below:

- "This program prepared me for applying to college and broadened my knowledge in the STEM-M field."
- "There is so much I learned from this program. I think it really helps to prepare students for life after high school."
- "It is truly amazing having a program which teaches, mentors, tutors, and supports students who lack that in their lives."
- "This program gave me a taste of almost everything possible with science/ It definitely broadened my knowledge and proved that STEM is not restrictive."
- "I think this is the best program for kids our age about to enter 12th grade that are interested in STEM, especially medicine and research."
- "I'm so glad I had an opportunity to be a part of this."
- "It was so beneficial, and I gained so much and in various ways such as personally and professionally."
- "Once in a lifetime experience and an open door to many more opportunities."
- "It is a valuable experience that can change one's future."
- "This program has taught me a lot about STEM-M careers and has also given/improved my life skills that can virtually be applied anywhere."
- "It is an amazing experience. We feel like we are part of something bigger than us and it is such an amazing environment."
- "It is a great experience for STEM careers and people interested in research. They will be able to get the full experience."
- "It really gets you ahead preparing you for the STEMM field."

Because of the COVID-19 pandemic, the NIH 2020 Summer Internship Program in Biomedical Research (SIP) was canceled, and OITE withdrew its application for ORWH co-funding for the HiSTEP and HiSTEP 2.0 programs. To provide students with a summer-long series of activities that would help them sharpen their science skills and develop both professionally and personally, OITE created the 2020 NIH Virtual Summer Enrichment Program (VSEP). The online offerings focused on the science at NIH and on important career and professional development topics for students at all educational levels. The NIH Career Development Series for High School Students and Recent Graduates was a 6-week lecture series that covered topics such as applying to college, career exploration, and success in college. Students who attended at least five workshops were eligible to receive a certificate of completion. VSEP is discussed in more detail in the next section.

Training in Mentorship, Leadership, Management, and Related Topics

For many years, ORWH has partnered with OITE to support the development and dissemination of materials to enhance mentoring and interpersonal skills in the intramural and extramural communities. In response to the COVID-19 pandemic in 2020, OITE converted all services and activities from in-person to virtual formats. An immediate benefit was the opportunity for trainees from all NIH campuses to participate equally in OITE programming and interact with their peers across NIH. In addition, OITE opened many events to trainees around the world and thus increased participation and broadened the reach of its programming in the areas of resilience and wellness, mentoring, and leadership. More recently, training focused on enhancing emotional intelligence, resilience, self-care, and wellness was added because the COVID-19 pandemic dramatically increased the need for such efforts.

OITE was able to continue its programs to improve leadership and management skills of its trainees without disruption during the pandemic. All major events and offerings were held online and were accessible to NIH trainees at all locations. Additionally, many events have been opened to trainees outside of NIH.

2020 NIH Virtual Summer Enrichment Program (VSEP): After the cancellation of SIP, OITE created VSEP, with a curriculum that included series on (1) career development for high school students, (2) preparation for graduate and/or professional school, (3) becoming a resilient scientist, and (4) career and professional development for scientists. On Fridays, 13 ICs joined the NIH Science at Home presentations. There were a total of 35 talks, panels, and workshops. It was a highly successful virtual program; the NIH Career Development Series for High School Students and Recent Graduates had over 3,700 session views (Table 4), and VSEP had over 10,000 (Table 5).

Table 4. NIH Career Development Series for High School Students and Recent Graduates "Attendance"

Date	Event Name	TOTAL Views
6/15/2020	I. Applying to College	836
6/22/2020	II. Leadership: Self-Awareness and Relationships with Others	723
6/29/2020	III. Effective Communication	664
7/6/2020	IV. Career Exploration	596
7/13/2020	V. Presenting Yourself: Resumes and Social Media	508
7/27/2020	VI. Success in College	401
	TOTAL	3,728

Workplace Dynamics Series: NIH trainees are encouraged to participate in this four-part series, which aims to improve and build interpersonal and communication skills using experiential learning and examples relevant to research groups. It begins by enhancing self-awareness and understanding of others. Then it examines different communication and learning styles, builds understanding of workplace conflicts, provides strategies to communicate feedback, and encourages skills in team dynamics and team behaviors. And it closes with a session on how to utilize diversity. Postdocs, clinical fellows, and advanced graduate students who complete the Workplace Dynamics Series are eligible for a 2-day management course that provides an overview of common management concepts. Topics include emotional intelligence, personal and organizational resilience, hiring, managing conflict as a supervisor, establishing expectations and motivating others, and building an inclusive and diverse work group. This capstone course has provided valuable knowledge and skills that help advanced trainees transition to their first positions as direct supervisors. In 2020, this series was moved to an online format.

Table 5. 2020 Virtual Summer Enrichment Program "Attendance"

Date	Event Name	TOTAL Views
6/11/2020	Essential Leadership Skills for Future Scientists and Health Care Professionals	1,074
6/12/2020	Virtual Interviews	363
6/16/2020	What Can You Do in College to Enhance Your Chances of Getting into Medical or Graduate School	994
6/18/2020	Career Planning for Scientists	851
6/23/2020	Choosing and Applying to Medical School	761
6/23/2020	Research Careers in the Intramural Research Program	544
6/25/2020	General Information about Secondary Applications to Medical School	302
6/25/2020	Ethics in Research Environment for Summer Students	302
6/30/2020	Choosing and Applying to Graduate School	898
7/2/2020	Networking, Informational Interviews and Using LinkedIn for Career Success	600
7/7/2020	Writing Personal and Research Statements for Graduate Programs	773
7/9/2020	Creating and Presenting Virtual Posters	486
7/14/2020	Interviewing for Medical School	464
7/16/2020	Resumes/CVs/Cover Letters: Essential Job Search Documents	786
7/28/2020	New Beginnings: Making Successful Transitions	178
7/30/2020	Job Search Strategies	318
8/13/2020	Talking Science: Designing and Delivering Successful Oral Presentations	403
	TOTAL VIEWS	10,097

Wellness Activities: OITE has developed resources for all trainees on topics such as stress management, mindfulness, holistic self-care, resilience, self-compassion, and wellness. In response to the COVID-19 pandemic, the number of OITE Wellness Advisors was increased, new wellness and resilience offerings were created, and the frequency of offerings was increased to meet trainee needs.

For many years, OITE has offered wellness and mental health seminars, with the latest series titled "The Mental Health and Well-Being of Biomedical Researchers." It addresses the impact of stress on physical and mental health and presents strategies to

enhance well-being. These quarterly workshops are intended to explore how to build resilience as a scientist and how to nurture one's mental health and well-being.

OITE-guided mindfulness meditation groups provide an informal atmosphere to explore topics such as body–mind relaxation, breath awareness, and stillness practice. To meet trainee needs during the pandemic, the meditation sessions were increased to three sessions per week. A weekly wellness group explores topics such as sleep hygiene, cognitive distortions, spiritual health, and social support.

Resilience discussion groups met with a trained counselor to discuss conflict in workplace environments, strategies to manage stress of job/school applications, and other work-related topics. The office also offers discussion groups for trainees of color, international trainees, and LGBTQ+ trainees. During the pandemic, session frequency was increased from 5 to 10 sessions per week, and topics were added to address loneliness, isolation, stress, sleep, addictive behaviors, and processing loss. Journaling for Career Development and Personal Growth sessions are offered twice per month and help trainees to tune in to their thoughts and emotions, work through challenges, and support their goals.

Because individuals embrace wellness initiatives through different media, recordings of all wellness seminars and lecture series are available on the OITE YouTube channel. During the pandemic, more than 22,000 individuals, at NIH and in the broader biomedical training community, participated in virtual wellness/resilience workshops between mid-March and the end of August. OITE has also utilized social media, such as Twitter and Instagram, to hold interactive wellness challenges. The OITE Career Blog has included posts on taking time to recharge, managing the winter blues, managing stress during the pandemic, and caring for your mental health. When needed, OITE Wellness Advisors meet individually with trainees to help them navigate life stressors and workplace environments.

In 2020, OITE hosted "How to Teach and Advise Biomedical Graduate Students and Postdocs Around Career and Professional Development: A Train-the-Trainers Event" for a third time. Its goal is to share best practices on how to engage students individually and in groups. The 2020 event was attended by academic deans, graduate and postdoctoral program directors, and career counseling staff members from STEMM fields. It was held virtually over 4 days. One track focused on standard career development needs, such as career advising skills, helping trainees navigate career decisions, and executive functioning and attention. The second track helped participants develop skills in helping trainees through stressful situations, self-care, and the impact of current events on trainee health and wellness. Small group discussions and role-playing events on mental health/wellness topics and career advising were held on the two remaining days. Participants practiced difficult conversations related to stress, anxiety, and depression. The small group sessions were facilitated by a cohort of therapists from the community, who provided guidance and feedback to participants on their verbal and nonverbal communication. Participants could register for one or both tracks and group discussions.

The 2020 virtual Train-the-Trainers event participation was nearly four times as high as the participation in the 2018 event. Additional session data are provided below (Table 6). Participants represented over 200 institutions and 4 countries. OITE is planning similar workshops every 2 to 3 years, as funding allows.

Table 6. Train-the-Trainer 2020 Attendance Data

Day	Total Attendance	NIH Attendance
Monday, July 20	727	98
Tuesday, July 21	607	89
Thursday, July 23	490	79
Mental Health Discussions	398	Unable to report
Career Discussions	386	Unable to report

Overall attendee number: 823, including 117 from NIH; data for daily attendance are from Zoom webinar; discussion group numbers are from Zoom meetings.

NIH attendee breakdown:

PI: 31

OITE: 29

Training Office Staff: 25

Admin/Support Staff: 20

Fellows: 6

Staff Scientists: 6

Finally, prior to the COVID-19 pandemic, the OITE Director traveled to many universities and national

scientific meetings to discuss wellness and resilience with institutional leaders, faculty, and trainees. These visits have supported many institutions in their efforts to improve the health and well-being of the biomedical workforce. When the pandemic began, these outreach activities continued through online events and meetings.

Wellness Skill-building Groups: OITE recently launched a series of wellness skill-building groups that offer NIH trainees a space to reflect on areas of growth, explore tools to support their wellness, and practice skill development. Each group session provides NIH trainees with tangible strategies related to the overall theme. Topics include stress management, mindfulness, emotional regulation, and assertiveness. Each series lasts 4–6 weeks. The sessions are facilitated by OITE Wellness Advisors.

NIH Fogarty International Center Global Health Training Program

In FYs 2019 and 2020, ORWH continued its support for the Fogarty International Center Global Health Training Program (RFA-TW-16-002), which provides mentorship, research opportunities, and a collaborative research environment for early-stage investigators from the U.S. and low- and middle-income countries. The program aims to enhance scientists' global health research expertise, with a focus on the careers of women in biomedical science. Many projects address women's health and maternal and child health. In FYs 2019 and 2020, ORWH co-funded eight awards focused on training and career development, a research project on the role of human papillomavirus genome diversity in cervical cancer, a project on precancerous lesions in women with HIV, and a project on the efficacy of an antifibrinolytic (tranexamic acid) in preventing postpartum hemorrhage after elective cesarean section. In FY 2019, 63 of 116 scholars (54%) were women; in FY 2020, 61 of the 93 scholars (66%) were women.

NIH/National Medical Association Travel Award

Several NIH Institutes, Centers, and Offices (ICOs) contributed to the National Medical Association (NMA) Travel Award, which allows senior residents, fellows, and junior faculty members interested in careers in biomedical research and/or academic medicine to attend the NIH/NMA Academic Career Development Workshop. The National Institute of Diabetes and Digestive and Kidney Diseases leads the program. Other participating ICOs include ORWH, the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, and the National Heart, Lung, and Blood Institute. ORWH continued its support for these travel awards in FYs 2019 and 2020 through participation of the ORWH Director in the annual workshops. Held in conjunction with the NMA Annual Convention and Scientific Assembly, the event covers topics ranging from grantsmanship to time management skills. Awardees must attend the entire workshop. NIH anticipates that this opportunity will allow more physicians from medically underserved communities to receive research training.

Women's Congressional Policy Institute's Annual STEAM Fair and Reception

The Women's Congressional Policy Institute's annual STEAM Fair and Reception showcases innovative efforts to encourage girls to pursue—and young women to remain in—careers in science, technology, engineering, the arts, and mathematics (STEAM). This interactive Capitol Hill event features remarks from the leadership of the Congressional Caucus for Women's Issues and exhibits by Federal, corporate, labor, and nonprofit advocacy partners that promote STEAM programs to women and girls. ORWH is a regular Federal partner for this annual event and has been joined in the past by the National Aeronautics and Space Administration, the U.S. Department of Veterans Affairs, the National Science Foundation, and the U.S. Department of Energy. As partners, ORWH representatives hosted a presentation booth at the 7th and 8th annual fairs on July 16, 2019, and July 23, 2020, respectively, where content on the office's mission and activities was shared with participants. Because of the COVID-19 pandemic, the 2020 STEAM Fair was hosted virtually, but it still reached girls across the Nation.

V. Monitoring Adherence to the NIH Policy on the Inclusion of Women and Minorities as Subjects in Clinical Research

Historical Perspective

The establishment of policies for the inclusion of women and minorities in National Institutes of Health (NIH)–funded clinical research originates from the women's health movement. After the U.S. Public Health Service Task Force on Women's Health Issues issued its report in 1985, NIH established a policy urging the inclusion of women in clinical research. This policy was first published in the *NIH Guide for Grants and Contracts* in 1987. Later that year, NIH published a policy encouraging the inclusion of minorities in clinical studies.

To ensure that NIH implements the inclusion policies, Congress made previous policy into public law through a section in the NIH Revitalization Act of 1993 (Public Law 103) titled "Women and Minorities as Subjects in Clinical Research." In 1994, NIH revised its inclusion policy[19] to comply with the statutory language. The NIH Revitalization Act essentially reinforced certain existing NIH policies, stating that NIH should ensure:

- That women and minorities and their subpopulations are included in all clinical research;
- That women and minorities and their subpopulations are included in Phase III clinical trials in a way that allows for valid analysis;
- That cost is not allowed as an acceptable reason for excluding these groups; and
- That it initiates programs and support for outreach efforts to recruit and retain women and minorities and their subpopulations as participants in clinical studies.

In October 2015, the Government Accountability Office (GAO) released a report examining women's participation in NIH research, titled *Better Oversight Needed to Help Ensure Continued Progress Including Women in Health Research* (GAO 16–13).[20] GAO examined (1) women's enrollment and NIH efforts to monitor this enrollment in NIH-funded clinical research and (2) NIH efforts to ensure that NIH-funded clinical trials are designed and conducted to analyze potential sex differences when applicable. GAO recommended that NIH examine and report more detailed data on women's enrollment in NIH-funded studies and collect, examine, and report data on the extent to which these studies include analyses of potential differences between men and women. NIH agreed with the report and has implemented four of the five GAO recommendations. NIH addresses the final GAO recommendation, to report summary data and the results of analyses of awardees' plans to conduct analyses of potential sex differences, in this report.

Since the NIH Revitalization Act was enacted, the overall number of women, minorities, and children included in NIH-funded studies has increased. However, as the GAO report pointed out, attention is still needed to ensure scientifically appropriate inclusion, as well as analyses and reporting of population-specific information. Moreover, the inclusion of groups in disease and condition areas should be monitored and reported.

NIH has taken the following several steps to address these issues: (1) Institute and Center–level enrollment data are now accessible online through NIH's RePORT website.[21] (2) As recommended in the GAO report and required by section 2038 of the 21st Century Cures Act, inclusion data by research, condition, or disease category are now available on the NIH RePORT website.[22] (3) NIH added questions regarding required valid analysis for NIH-defined Phase III clinical trials to the NIH-wide checklist used by program officers beginning in FY 2016. And (4) NIH has analyzed the

19. https://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm
20. https://www.gao.gov/products/GAO-16-13
21. https://report.nih.gov/recovery/inclusion_research.aspx
22. https://report.nih.gov/RISR

percentages of NIH-defined Phase III clinical trials that need valid analysis, and data are included in this report, in Appendix E.

The 21st Century Cures Act and the Inclusion Across the Lifespan Policy

The 21st Century Cures Act (Public Law 114–255), enacted December 13, 2016, included several new reporting requirements for inclusion of sex/gender in clinical research. As a result, NIH updated its policy on the inclusion of women and minorities as subjects in clinical research on November 28, 2017, to require studies that are both NIH-defined Phase III clinical trials and applicable clinical trials to report the results of analyses by sex/gender and race and ethnicity in ClinicalTrials.gov. This requirement is effective for competing grant awards on or after December 13, 2017, as well as contract solicitations and intramural studies initiated after this date. Additionally, NIH held a workshop on age groupings and exclusions in clinical research on June 1–2, 2017, and revised its Inclusion of Children in Clinical Research policy on December 19, 2017. The revision, now called NIH Policy and Guidelines on the Inclusion of Individuals Across the Lifespan as Participants in Research Involving Human Subjects, requires individuals of all ages (including children and older adults) to be included in clinical research unless there are scientific or ethical reasons not to do so. The policy also requires investigators conducting clinical research to submit individual-level data on sex/gender, race, ethnicity, and age of participants at enrollment in annual progress reports. The policy applies to all applications submitted on or after January 25, 2019. On September 2, 2020, NIH held a follow-up Inclusion Across the Lifespan-II Workshop[23] to gather stakeholders in the scientific community in order to examine the state of the science, discuss lessons learned, and share evidence-based practical advice to consider in the implementation of the Inclusion Across the Lifespan policy.

In response to 21st Century Cures Act requirements and as recommended by the GAO report, NIH has made available inclusion data by disease or condition category on the NIH RePORT website. The NIH RCDC Inclusion Statistics Report allows users to view the number and proportion of participants in NIH clinical research by sex/gender, race, or ethnicity for each category in the Research, Condition, and Disease Categorization (RCDC) system. Users can view these data for each IC and use filters to exclude single-sex/gender, single-race, or single-ethnicity studies.

Inclusion Monitoring Activities

Communication and Outreach Efforts to the Scientific Community

NIH regularly updates application, contract proposal, and intramural project instructions and guidance to ensure that investigators address inclusion as required and report inclusion enrollment data at least annually. Numerous policy documents, podcasts, answers to frequently asked questions, and other resources are available for investigators and NIH staff on the Office of Research on Women's Health (ORWH) and Office of Extramural Research (OER) websites. Tools to help investigators understand the new policies and their implementation, including a decision tree and infographic, are available on the OER website. These resources are intended to help the extramural research community understand and implement NIH requirements for monitoring inclusion in clinical research.

NIH staff members have authored several publications to communicate inclusion requirements to the scientific community and the general public. The blog of the NIH Deputy Director for Extramural Research, "Open Mike," has published an entry announcing the availability of the *Inclusion Across the Lifespan-II Workshop Report*,[24] available on the NIH Extramural Nexus website.[25] In addition, the NIH Extramural Nexus has published numerous articles highlighting inclusion requirements on topics such as submission of inclusion plans and enrollment data and the availability of NIH inclusion data.[26]

NIH also conducts outreach to the extramural community through educational sessions at scientific meetings and conferences. For example, OER discusses inclusion policies at its NIH Regional Seminars.[27]

The Center for Scientific Review (CSR) and OER provide training for reviewers and applicants. OER has

23. Workshop report available at https://grants.nih.gov/sites/default/files/IAL-II-Workshop-Report.pdf.

24. https://grants.nih.gov/sites/default/files/IAL-II-Workshop-Report.pdf

25. https://nexus.od.nih.gov/all/?s=inclusion&submit=Search

26. https://nexus.od.nih.gov/all/tag/inclusion

27. https://grants.nih.gov/news/contact-in-person/seminars.htm

online training tools designed for applicants.[28] These training and outreach efforts improve understanding of the inclusion policies and help extramural and NIH intramural investigators appropriately address these issues throughout the research funding process. Specifically, these tools help applicants understand how NIH monitors inclusion, reviews the importance of reporting the race and ethnicity of clinical research participants, and describes how grantees and applicants should report race and ethnicity.

NIH Inclusion Outreach Toolkit

ORWH launched a revised NIH Inclusion Outreach Toolkit[29] to help researchers recruit and retain women participants in their clinical studies. The new version of the NIH Inclusion Outreach Toolkit includes information on the history of inclusion at NIH, current policies, case studies and testimonials, regulations, checklists, seminars, and other resources. These resources will help investigators and their research teams to fulfill their responsibilities for including women in clinical research and ensure that the distribution of study participants by sex, gender, race, ethnicity, and age reflects the population needed to accomplish the scientific goals of the clinical study. The toolkit features case studies with researchers' experiences with including women in their studies. Topics include recruiting young urban women into an HIV prevention clinical trial, cervical cancer prevention, treatments for menopause symptoms, caries prevention in young children, and diabetes prevention.

Peer Review Expectations

Scientific review groups (SRGs) are instructed to focus on scientific considerations when assessing the enrollment for a proposed study described in an NIH grant application. The SRGs evaluate the inclusion plans and find them unacceptable if the applicant (1) fails to provide enough information about the planned sample, (2) does not adequately justify limited inclusion or lack

28. https://grants.nih.gov/grants/funding/women_min/inclusion_training.htm

29. https://orwh.od.nih.gov/toolkit

of inclusion of women or minorities, or (3) does not realistically address recruitment. Reviewers on NIH peer review panels are given specific guidance on reviewing inclusion based on sex/gender, race, ethnicity, and age when considering clinical research applications. For NIH-defined Phase III clinical trials, the SRGs also evaluate the description of plans for valid analyses and whether investigators need to examine differences in the intervention effect by sex/gender, racial, and/or ethnic groups. Valid analyses refer to stratified analyses that explore how well the intervention works among sex/gender and racial and ethnic groups. Although they may or may not have high statistical power, these trials provide essential information to inform future studies. Previous data suggesting that differences may exist could indicate a need to consider specific analyses.

Unacceptable inclusion plans must be reflected in the priority score of the application and documented in the minutes of the review session. Initial review groups make recommendations on the acceptability of the proposed study population with respect to inclusion policies. If issues are raised during the review, program staff notify the principal investigators (PIs), who are required to address these issues prior to funding. Applications with unacceptable inclusion plans cannot receive funding; an award is not issued until an acceptable resolution is received. NIH staff members must be assured that the revised plans meet inclusion policy requirements.

Communication and Outreach Efforts Within NIH

The Extramural Activities Working Group (EAWG), established by the NIH Director as a working group of the NIH Steering Committee, facilitates the governance for the policies, procedures, and utilization of resources for extramural research and research training. The Inclusion Governance Committee (IGC) was formed in 2011 as a subcommittee of the EAWG to discuss policy issues related to inclusion. The IGC is currently co-chaired by the ORWH Director and the National Institute on Aging Deputy Director. Members of the IGC are primarily senior-level staff members from the NIH Office of the Director and various ICs; other participants represent business areas involved in the implementation of inclusion policy.

CSR, which handles approximately 70% of the grant applications that NIH receives, offers a robust resource page that includes training, resources, and updates for scientific review officers (SROs) and program officers. In addition, OER regularly provides trainings for institute program officials/program directors, grants management staff, and SROs on implementation of the NIH policies for the inclusion of women, minorities, and individuals across the lifespan. In coordination with other NIH Institutes, Centers, and Offices (ICOs), OER provided two online trainings on NIH staff procedures for implementing inclusion policies in 2020. These trainings continue to be available to staff on the NIH extramural intranet website.

Monitoring Compliance and Inclusion Enrollment Outcomes

NIH staff members continue to monitor and document compliance with the inclusion policies and work with grantees to ensure compliance. Program officers and staff members provide technical assistance to investigators as they develop their applications and proposals. Program staff members monitor actual enrollment progress in annual progress reports and provide consultation when necessary. In preparation for peer review meetings, SROs remind reviewers of the guidelines for evaluating investigators' plans for the inclusion of women and minorities in clinical research. Also discussed during these preparatory meetings are the instructions and requirements for reviewing NIH-defined Phase III clinical trials, particularly how the proposed work considers plans for valid analyses of sex differences. Program staff members note whether valid analyses of sex differences are required prior to awarding grants. When new and competing continuation applications that were selected for payment are deficient in meeting inclusion policy requirements, NIH staff members are required to withhold funding until the PI has satisfactorily addressed the policy requirements. Grants management staff members ensure that appropriate terms and conditions of award are included in the Notice of Award and ensure that this information is appropriately documented in the official grant file. At the time of award and at the time of submission of progress reports, program officials monitor and verify that progress with inclusion is appropriate for the scientific goals under study.

Inclusion enrollment data aggregated across the ICs are presented in this report in summary figures and aggregate data tables (Appendix E), providing

documentation of inclusion monitoring with some analysis. Caution should be used in interpreting these figures. Conclusions that can be reasonably drawn from the data are provided.

When assessing inclusion data, NIH avoids directly comparing enrollment figures with national census figures. The goal of the NIH policy is to ensure that the scientific knowledge acquired through NIH-defined clinical research ultimately will be generalizable to the appropriate population(s), not to satisfy any proportional target based on census data. The numbers of women, men, and representatives of racial and ethnic groups included in a study depend on the scientific question(s) being addressed and may consider several factors, such as the prevalence among women, men, or racial and ethnic groups of the disease, disorder, or condition under investigation; gaps in scientific knowledge; and disparities in health risks or outcomes. A key principle of the inclusion policies is that inclusion is integral to conducting good science. Inclusion should not be considered based on absolute numbers of individuals in the population groups; rather, the focus should be on whether a given study has the right people for its scientific goals and how sex/gender, race, and ethnicity may affect outcomes in those groups.

NIH Human Subjects System (HSS)

NIH has monitored aggregate inclusion data for study populations since fiscal year (FY) 1994. All ICs have well-established practices for monitoring compliance with NIH's inclusion policies. NIH has used the Electronic Research Administration (eRA) Human Subjects System (HSS) to monitor inclusion data since June 9, 2018. This system consolidates study-level human subjects and clinical trial information in one place. HSS facilitates data collection, allows submission of participant-level enrollment data in comma-separated values (CSV) format, and reduces the need for duplicate data entry in other systems, such as ClinicalTrials.gov. NIH staff members use HSS to manage all human subjects' information associated with a grant, cooperative agreement, or contract, including plans for inclusion and inclusion enrollment data. HSS provides an electronic means of entering, storing, approving, monitoring, and reporting the planned and actual enrollment of research participants based on sex/gender, race, and ethnicity. HSS promotes increased transparency by displaying the same information to grant recipients and NIH staff. In 2019, NIH introduced an indicator to monitor requirements for valid analysis by sex/gender and race and ethnicity for NIH-defined Phase III clinical trials. The use of this indicator allows NIH to more easily monitor

and report requirements for analysis by sex/gender, race, and ethnicity in NIH-defined Phase III clinical trials.

Summary Report of NIH Inclusion Data for FYs 2019 and 2020

Reporting of sex/gender, racial, and ethnic categories is based on self-identification of the participants, who always have the option not to identify. Although inclusion is mandated for all clinical research projects conducted or supported by NIH, for the summary report, the primary focus of the racial and ethnic analyses is on studies involving populations in the U.S. Appendix E contains data tables describing inclusion data for all clinical research and NIH-defined Phase III clinical trials from FY 2010 to FY 2020.

Important Considerations When Interpreting NIH Inclusion Data

Analysis of aggregate NIH inclusion data demonstrates that substantial numbers of women and men and individuals of different races and ethnicities have been included as research subjects in NIH clinical research studies and NIH-defined Phase III clinical trials. In addition, multi-year data are provided to show inclusion trends over time. As explained in the section titled "Monitoring Compliance and Inclusion Enrollment Outcomes," ORWH recommends using caution to avoid overinterpreting the figures and data tables provided in this chapter.

- **Portfolio Composition:** The NIH portfolio is diverse in terms of the types of clinical research studies it supports, the size of the studies, and the expectations for inclusion within them. The size of clinical research and clinical trial portfolios and the studies within those portfolios vary substantially across the ICOs, depending on such factors as an ICO's budget and mission and the scientific goals of a given study. Some ICOs do not conduct NIH-defined Phase III clinical trials or support very few of them.
- **Funding Life Cycle:** It is crucial to consider the nature of the funding life cycle at NIH and how that can affect inclusion enrollment information. The average length of an NIH grant award is 4 years. This means that every year, approximately 25% of the NIH funding portfolio turns over to newly funded awards or competing continuation awards. However, funding can be as short as 1 year or can last up to 10 years. The total amount of funding can vary from year to year, and at times, spikes or dips in appropriations may affect inclusion enrollment. Changes caused by the funding life cycle may create noticeable shifts in inclusion enrollment data, particularly for ICOs with small clinical research or clinical trial portfolios. This life cycle also affects the reported enrollment numbers. In any given year, some projects have just begun, so enrollment is low. Other projects have higher enrollment rates in later years. Furthermore, some other projects have ended, so their data are no longer reported. These fluctuations across studies also can lead to notable shifts in enrollment numbers from year to year.
- **Coding Categories:** The NIH-defined clinical research category includes not only NIH-defined Phase III clinical trials but also many other types of clinical studies, such as observational and epidemiological studies, exploratory studies, and other phases of clinical trials, all of which are monitored for compliance with the inclusion policies. The NIH-defined Phase III clinical trial category is a subset of all NIH-defined clinical research.

Summary of Key Trends

The following sections summarize data on the inclusion of women and minorities in NIH-funded clinical research and NIH-defined Phase III clinical trials. Appendix D summarizes all available inclusion data from FY 2010 to FY 2020. The key trends from the inclusion data summary are as follows:

- Investigators reported that in FYs 2019 and 2020, a total of 13,241,413 and 13,705,659 participants, respectively, enrolled in NIH-funded clinical research **(Appendix E, Table 1A)**. If we exclude studies conducted outside the U.S., the enrollment count was 10,356,075 and 11,080,871 in the corresponding years **(Table 1B)**.
- Enrollment of women in all NIH-funded clinical research in FY 2019 was 52.1%. This figure increased to 55.1% in FY 2020 **(Appendix E, Table 1A)**.
- Enrollment of clinical research participants from racial minority groups across all NIH research was 40.1% in FY 2019 and remained at a similar level (39.6%) in FY 2020 **(Appendix E, Table 2E)**. Participation of the Hispanic/Latino population was

also stable—approximately 11% in FYs 2019 and 2020 **(Appendix E, Table 2F)**.

» NIH-defined Phase III clinical trials are a subset of NIH clinical research studies. In FY 2019, 61.4% of participants in NIH-defined Phase III clinical trials were female, and 61.8% were female in FY 2020 **(Appendix E, Table 1E)**.

» Racial minority inclusion in NIH-defined Phase III clinical trials increased substantially, from 46.6% in FY 2019 to 67.1% in FY 2020 **(Appendix E, Table 3A)**. Likewise, increased enrollment of ethnic minorities was observed. In FY 2019, approximately 9.9% of participants recruited to NIH-defined Phase III clinical trials were Hispanic/Latino. This figure increased to 14.5% in FY 2020 **(Appendix E, Table 3F)**.

Source of Inclusion Data

The following summary is based on inclusion data tabulated from human subjects involved in NIH-funded clinical research and NIH-defined Phase III clinical trials. NIH defines human clinical research as patient-oriented, epidemiological, behavioral, outcomes, or health services research that includes human subjects. Patient-oriented research is research conducted with human subjects (or on material of human origin, such as tissues, specimens, and cognitive phenomena) in which an investigator directly interacts with human subjects. Excluded from this definition are *in vitro* studies that use human tissues that cannot be linked to a living individual. Patient-oriented research includes (a) mechanisms of human disease, (b) therapeutic interventions, (c) clinical studies, and (d) development of new technologies. Studies falling under 45 CFR 46, Exemption 4 for human subject research are not considered clinical research by this definition. Exemption 4 applies to secondary research uses of identifiable private information or identifiable biospecimens that meet specific criteria outlined in 45 CFR 46.104(d)(4) of the revised Common Rule.[30]

Clinical trials are a subset of clinical research studies. They are research studies in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebos or other controls) to evaluate their effects on health-related biomedical or behavioral outcomes. Clinical trials test treatment, prevention, and diagnostic strategies and include studies of drugs, devices, surgical techniques, health care delivery systems, and strategies to change health-related behavior, such as diet and therapy.

NIH-defined Phase III clinical trials are a subset of clinical trials. NIH-defined Phase III clinical trials usually compare interventions with other standard or experimental interventions (biomedical or behavioral) in large groups of people, from several hundred to several thousand. Typically, these trials monitor adverse effects and collect information that will allow the interventions to be used safely.

NIH-defined Phase III clinical trials require valid analyses by sex/gender, race, and ethnicity. NIH program staff members monitor requirements for these analyses, and ICOs report the number of NIH-defined Phase III trials requiring valid analyses in their triennial inclusion reports. The 21st Century Cures Act requires reporting of valid analyses for studies that are both NIH-defined Phase III clinical trials and applicable clinical trials. "Applicable clinical trial" is the term used in Title VIII of the Food and Drug Administration Amendments Act (FDAAA) of 2007 (Public Law 110–85) to designate the scope of clinical trials that may be subject to the registration and results reporting requirements of the FDAAA. Clinical trials that are subject to the regulation are, in general, clinical trials of drug, biological, and device products regulated by the Food and Drug Administration (FDA). A pediatric post-market surveillance study of a device product required by FDA is also subject to the regulation.[31] Applicable NIH-defined Phase III clinical trials require reporting of results of valid analyses in ClinicalTrials.gov.

In FY 2015, NIH expanded inclusion monitoring to require submission of planned and actual enrollment data for additional funding mechanisms, such as career development (K) awards and individual fellowship (F) awards. In addition, NIH eliminated most previously allowable exceptions to include monitoring for clinical research studies, such as secondary analyses, tissue repositories, early feasibility studies, studies with small sample sizes, and those determined by the ICOs not to be clinical research.

The following summary of inclusion of women and minorities in NIH research was derived from HSS data

30. https://www.ecfr.gov/cgi-bin/text-idx?SID=851e9dd3244b65d1d25893d2c-c226feb&mc=true&node=se45.1.46_1104&rgn=div8

31. https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-014.html

to facilitate the congressional report required biennially by statute (Public Health Service Act section 492B, 42 U.S.C. section 289a-2). The data are aggregated across all ICs. Each IC has reviewed and approved its inclusion data used in this report. Individual IC reports are made available triennially on the NIH RePORT website. In FY 2019, investigators submitted 20,976 inclusion enrollment reports (IERs), with 14,225 IERs reporting enrollment of 13,241,413 participants. The remaining 6,751 IERs indicated that participants had not yet been enrolled. In FY 2020, investigators submitted 23,856 IERs, with 14,260 IERs reporting enrollment of 13,705,659 participants. The remaining 9,596 IERs for FY 2020 indicated that participants had not yet been enrolled.

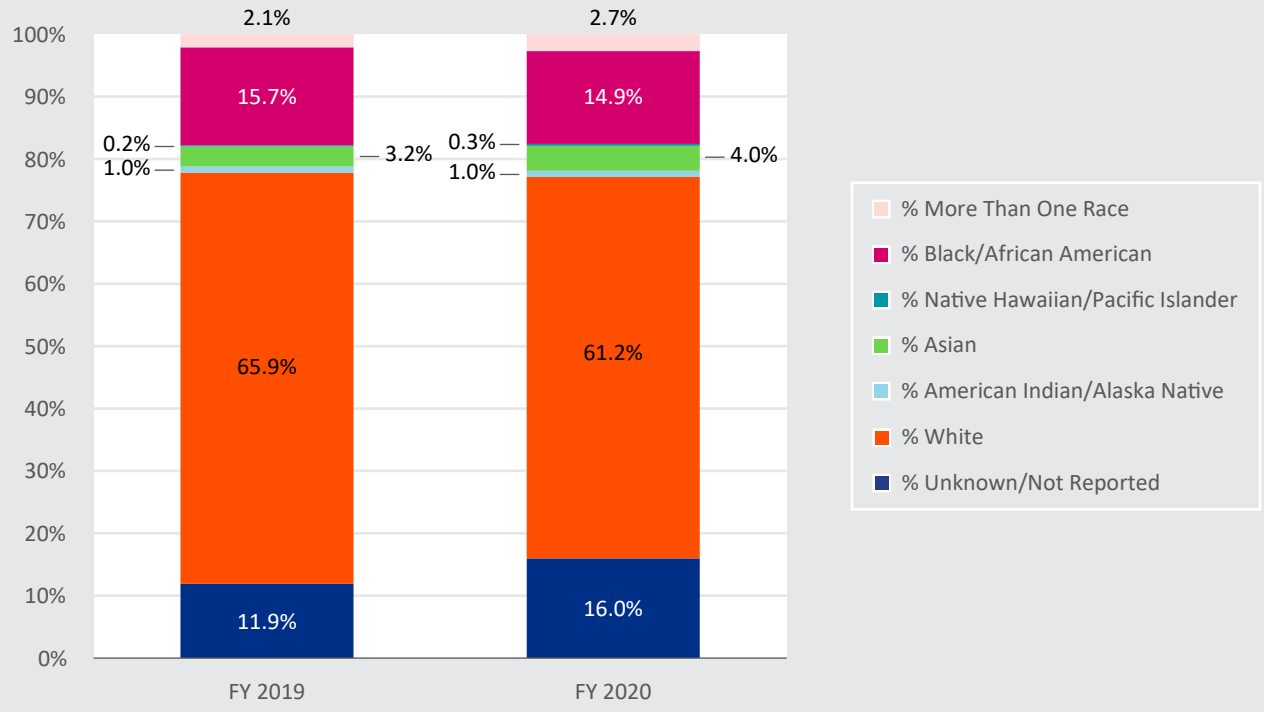
Inclusion Summaries

This report defines population subgroups by research participants' sex, race, and ethnicity. The percentage of female participants in NIH-funded clinical research is the proportion of enrolled participants who selected "female" as their sex. In FY 2019, 52.1% of the participants were women. During FY 2020, 7,552,684 enrollees were women, which accounted for 55.1% of NIH-defined clinical research participants. The FY 2020 enrollment count for men was 5,532,650, constituting 40.4% of the study population. Sex was unknown or not reported for 3.1% and 4.5% of participants in FY 2019 and FY 2020, respectively **(Appendix E, Table 1A)**.

Across all NIH-funded clinical research studies, the race of participants was unknown or not reported for 10.6% in FY 2019 and 14.2% in FY 2020 **(Appendix E, Table 2E)**. As for ethnic minorities, 10.5% of individuals did not report their Hispanic/Latino identity in FY 2019, and the rate slightly increased to 11.9% in FY 2020 **(Appendix E, Table 2F)**. Subsetting clinical research conducted at U.S. sites demonstrated a higher percentage of unknown racial and ethnic identity. A total of 11.9% and 16% of study participants did not report their races in FY 2019 and FY 2020, respectively **(Appendix E, Table 2G)**. The proportion of unknown Hispanic/Latino origin was 11.5% in FY 2019 and increased to 13.4% in the subsequent year **(Appendix E, Table 2H)**.

Figure 33 displays the racial composition of participants enrolled in NIH-funded clinical research at U.S. sites for FY 2019 and FY 2020. The rate of enrollment of White participants was 65.9% in FY 2019 but declined to 61.2% the following year. In FY 2020, enrollment of Black/African American participants was 14.9%, a minor

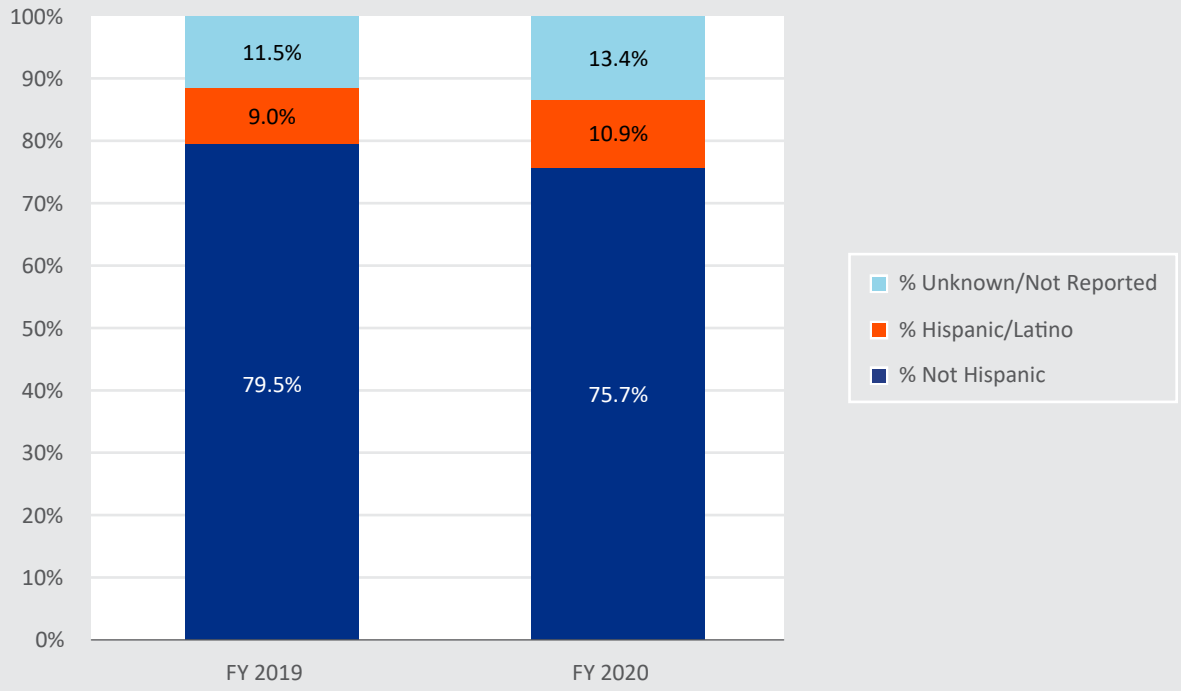
Figure 33. Enrollment for All NIH Clinical Research at U.S. Sites Racial Categories for FY 2019 and FY 2020



decrease compared with the previous year's 15.7%. Although Asian, Native Hawaiian/Pacific Islander, and individuals who identified as more than one race had an increase in clinical research participation, the magnitude was marginal and never exceeded 1%.

The ethnic breakdown of participants in **Figure 34** indicates that the rate of enrollment of non-Hispanic participants decreased from 79.5% in FY 2019 to 75.7% in FY 2020. While the rate of enrollment of Hispanic/Latino participants increased from 9% to 10.9% during this interval, the percentages of participants of unknown/not reported ethnicity were substantial; these participants accounted for 11.9% and 16% of enrollment in FY 2019 and FY 2020, respectively.

Figure 34. Enrollment for All NIH Clinical Research at U.S. Sites Ethnic Categories for FY 2019 and FY 2020



Inclusion Trends in NIH-Funded Clinical Research

Data regarding enrollment of women and minorities for NIH-funded clinical research in FY 2019 and FY 2020 are presented in **Figures 35–38** in the following pages. In each figure, the data are summarized for (a) all NIH clinical research, (b) all NIH clinical research at U.S. sites, (c) clinical research supported by the NIH Extramural Research Program conducted at U.S. sites, and (d) clinical research conducted through the NIH Intramural Research Program at U.S. sites. All clinical research at U.S. sites includes studies conducted through the Extramural Research Program and the Intramural Research Program.

The information in this report represents new data collected prospectively. Studies that analyzed retrospective data using extant datasets were excluded from the report. The exclusion of retrospective data prevents possible inflation of enrollment counts, which may have been analyzed and reported previously.

Figure 35 summarizes the percentages of enrollees who were women in NIH-funded clinical research for FY 2019 and FY 2020. All categories except for NIH-funded intramural clinical research at U.S. sites had an increase in women's participation. For all NIH-funded clinical research categories, women accounted for 52.1% of research participants in FY 2019 and 55.1% in FY 2020. When we exclude female-only studies from the enrollment counts, women accounted for 40.4% of participants in FY 2019 and 41.7% in FY 2020 **(Appendix E, Table 1A)**.

Appendix D, Table 1B presents enrollment information for NIH-funded clinical research at U.S. sites from FY 2015 to FY 2020. It shows that enrollment of women has been 49.1% or higher, whereas for men, the recruitment rate since FY 2015 has been 37.2% or higher. Across all years, women had a higher percentage of enrollment than men.

Figure 36 demonstrates the percentages of participants in NIH-funded clinical research who are members of racial and ethnic minority groups. For all clinical studies conducted at U.S. sites, minority participants accounted for 29.9% of enrollees in FY 2019, compared with 32.1% in FY 2020. The rates of enrollment of minority participants in U.S. site studies supported through the Extramural Research Program were larger than those in U.S. site studies supported through the Intramural Research Program in both FY 2019 (18.2% for intramural, versus 32.3% for extramural) and FY 2020 (17.7% for intramural, versus 34.8% for extramural).

Figure 35. Percentage of Participants in NIH-Funded Clinical Research that are Female FY 2019 and FY 2020

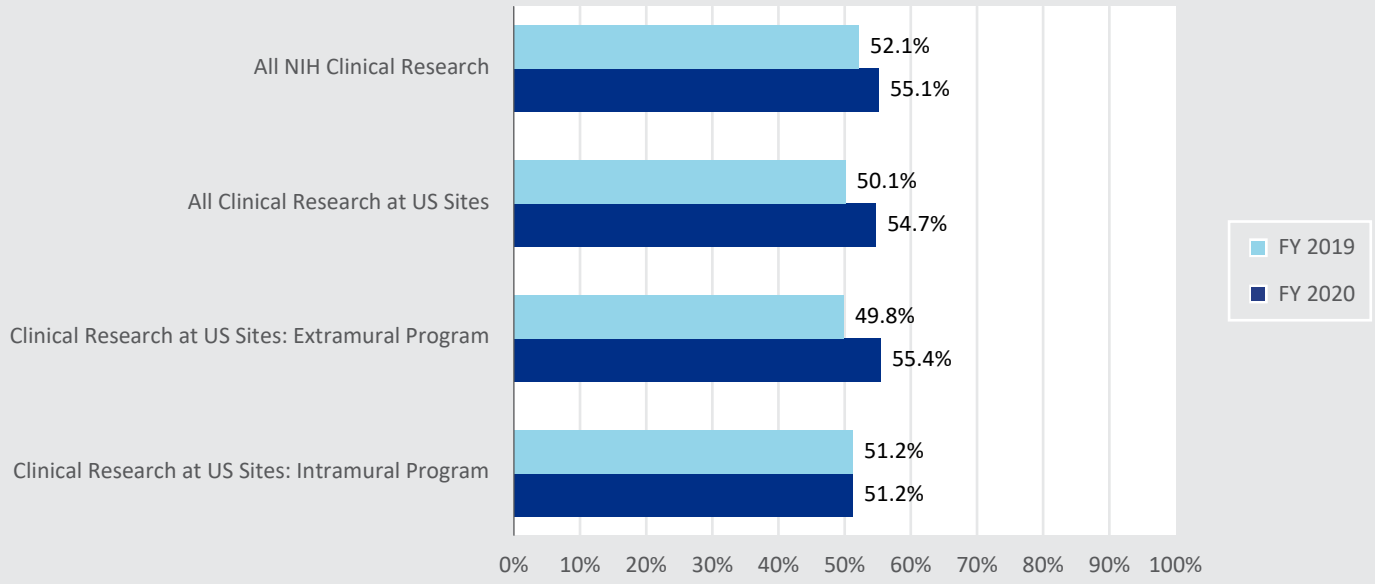
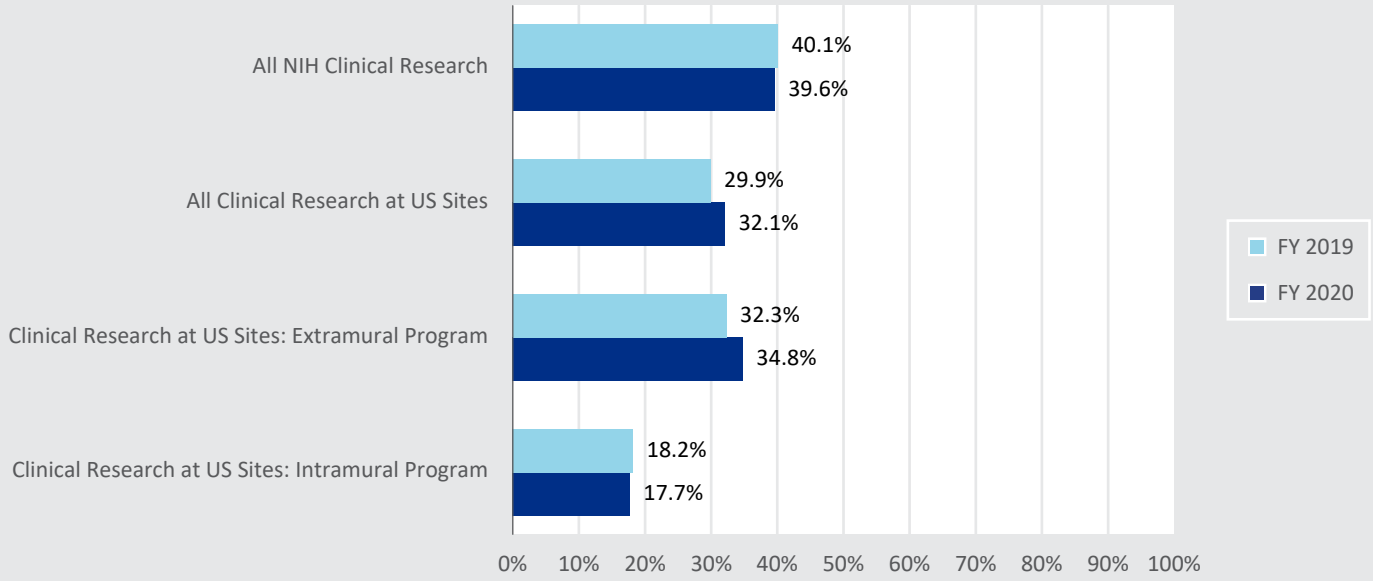


Figure 36. Percentage of Participants in NIH-Funded Clinical Research that are Members of Minority Groups FY 2019 and FY 2020



To illustrate a complete picture of minority enrollment in clinical research, **Figures 37 and 38** provide an enrollment summary for female and male minority participants. In terms of all NIH-funded clinical research, the rate of enrollment of minority female participants was 43.9% in FY 2019 and 41.5% in FY 2020. Conversely, there was an increase in the rate of enrollment of female minority participants in clinical research conducted at U.S. sites, from 32.4% in FY 2019 to 34.2% in FY 2020. The percentage in the U.S. site Extramural Research Program category also increased, by 1.8 points **(Figure 37)**.

Figure 37. Percentage of Female Participants in NIH-Funded Clinical Research that are Members of Minority Groups FY 2019 and FY 2020

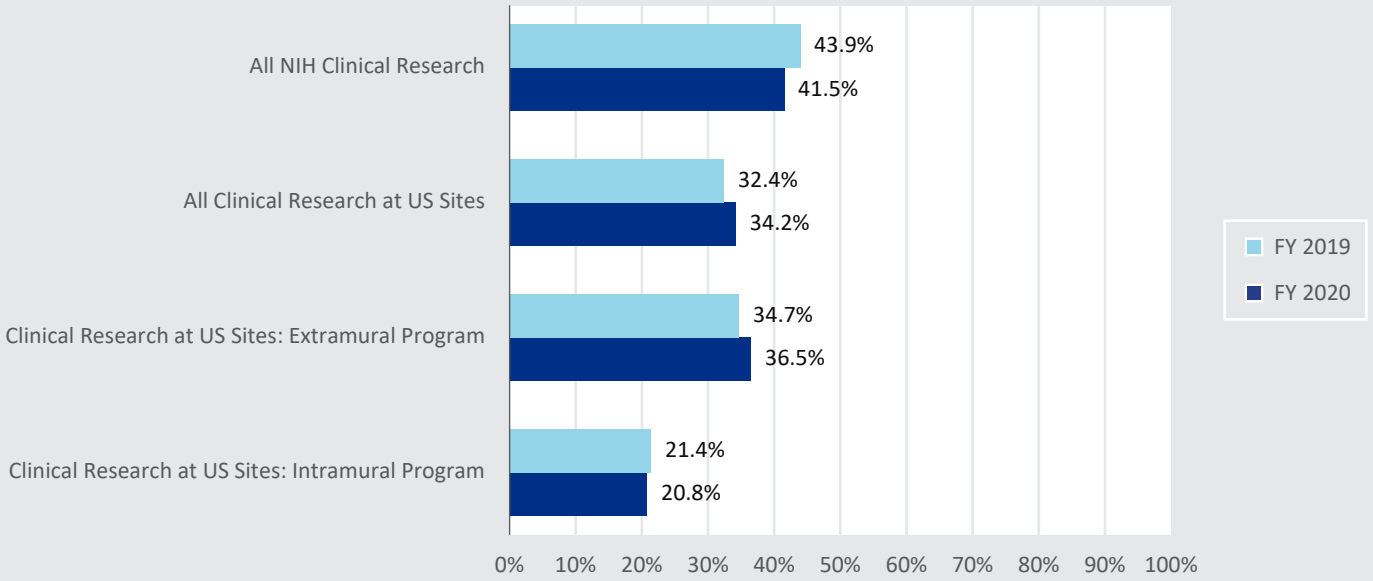


Figure 38. Percentage of Male Participants in NIH-Funded Clinical Research that are Members of Minority Groups FY 2019 and FY 2020

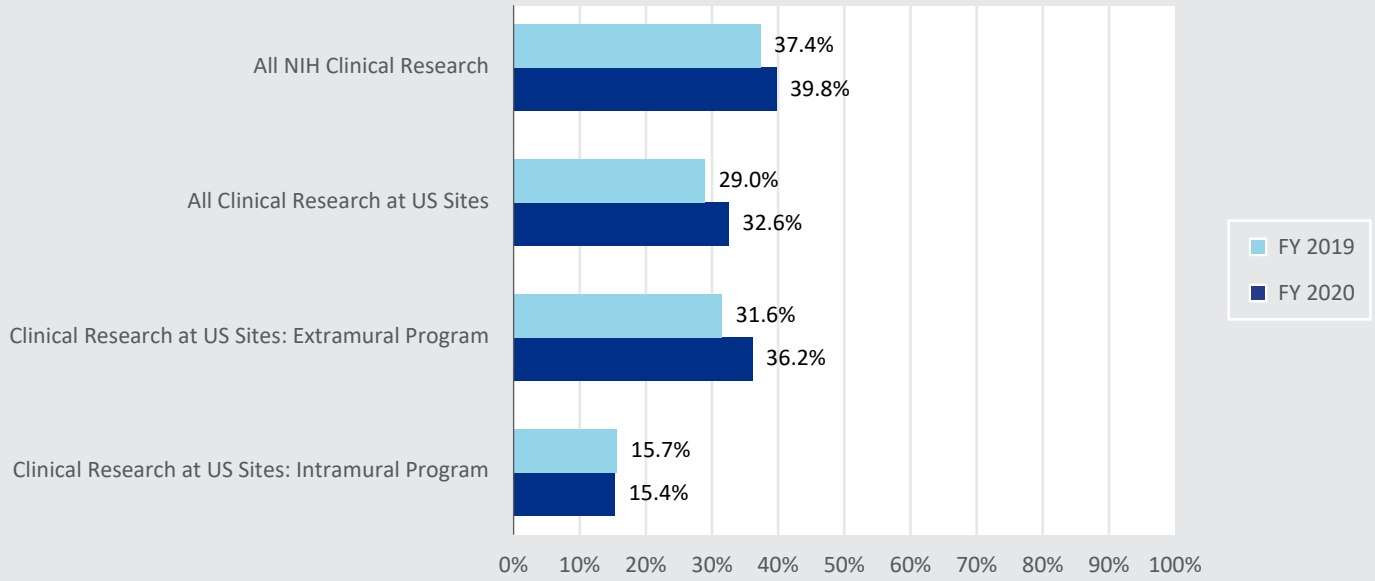
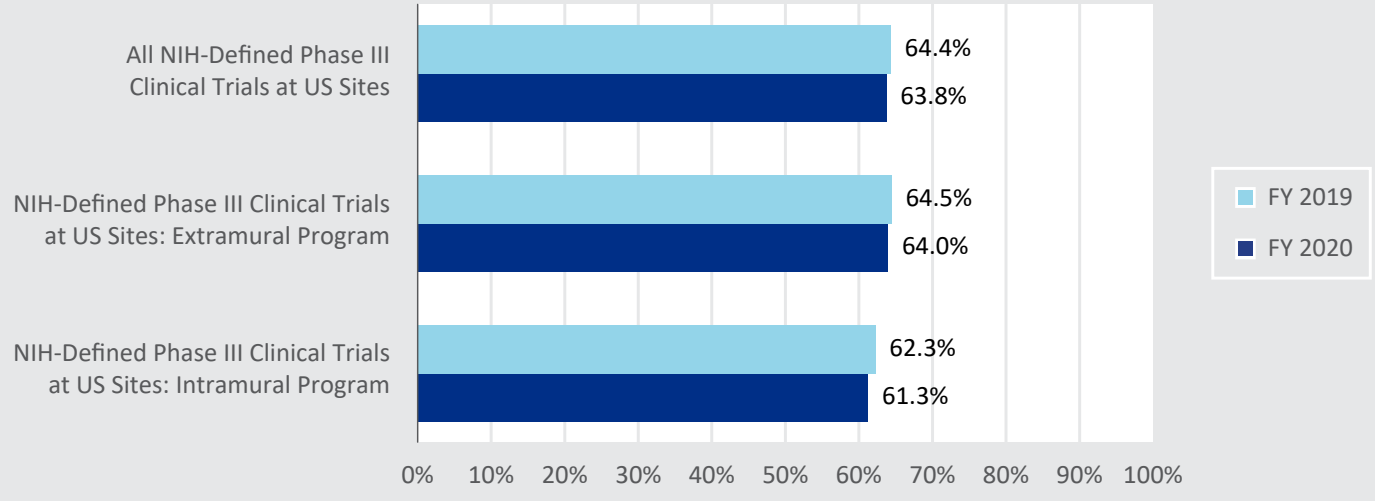


Figure 38 demonstrates minority men's clinical research participation. Of clinical research conducted at U.S. sites, the rate of enrollment of minority male participants was 29% in FY 2019 and subsequently increased to 32.6% in FY 2020. The percentage of male minority participants in the U.S. site extramural studies also increased, by 4.6 points. Note that for both minority men and minority women, the percentages of intramural research participants were unchanged between FY 2019 and FY 2020 **(Figures 37 and 38)**.

Tables 4A–4D in **Appendix E** provide details on inclusion from FY 2015 to FY 2020 for male and female participants in clinical research who are members of minority groups. **Tables 4I–4L** provide a detailed breakdown of enrolled participants by race and ethnicity of male and female enrollees for FY 2019 and FY 2020.

Figure 39. Percentage of Participants in NIH-Defined Phase III Clinical Trials at US Site that are Female FY 2019 and 2020



Inclusion Trends in NIH-Defined Phase III Clinical Trials

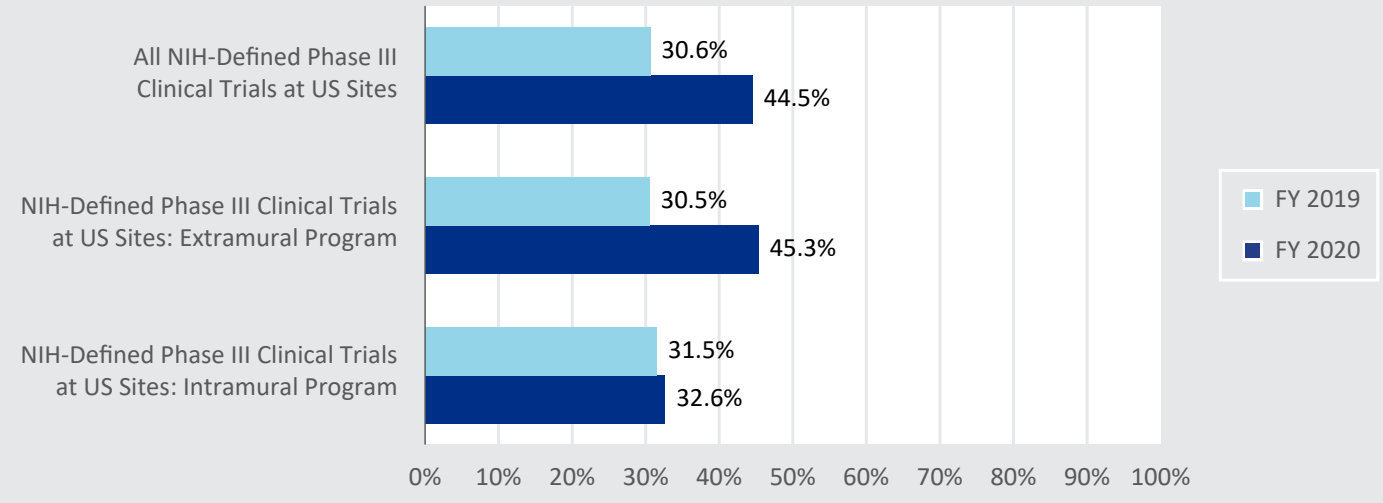
NIH-defined Phase III clinical trials are a subset of NIH clinical research studies. Enrollments for Phase III clinical trials conducted at U.S. sites are shown in **Figures 39–42**.

Figure 39 illustrates the percentages of women enrolled in NIH-defined Phase III clinical trials at U.S. sites in FY 2019 and FY 2020, with a subset analysis for extramural and intramural research enrollments. The rate of enrollment of female participants in Phase III clinical trials at U.S. sites was 64.4% in FY 2019 and 63.8% in FY 2020. For extramural Phase III clinical trials, the rate of enrollment of female participants was 64.5% in FY 2019 and 64% in FY 2020. Women's enrollment in the intramural Phase III clinical trials also exceeded 61% in both years.

Figure 40 presents minority participants' enrollment data in NIH-defined Phase III clinical trials. Of the Phase III clinical trials performed at U.S. sites, the minority enrollment rate was 30.6% in FY 2019 and 44.5% in FY 2020. U.S. site studies supported by the NIH Extramural Research Program also had a noticeable upsurge—from 30.5% in FY 2019 to 45.3% in FY 2020.

Tables 3A–3D in **Appendix E** show minority enrollment in NIH-defined Phase III clinical trials from FY 2015 to FY 2020. **Tables 3E–3L** provide a detailed breakdown of NIH-defined Phase III clinical trials' enrollment by race and ethnicity from FY 2015 through FY 2020.

Figure 40. Percentage of Participants in NIH-Defined Phase III Clinical Trials at US Sites that are Members of Minority Groups FY 2019 and FY 2020



Figures 41 and 42 illustrate enrollment by sex/gender of minority participants at U.S. sites. The rate of enrollment in NIH-defined Phase III clinical trials for women who are members of minority groups increased remarkably, from 30% in FY 2019 to 45% in FY 2020. Minority women's participation in extramural Phase III clinical trials also demonstrated a significant increase, from 29.7% in FY 2019 to 45.4% in FY 2020. However, the magnitude of increase for NIH-defined Phase III clinical trials conducted by the Intramural Research Program was minimal **(Figure 41)**.

As with females, the participation of minority males in NIH-defined Phase III clinical trials had a substantial increase, from 31.9% in FY 2019 to 44.2% in FY 2020 **(Figure 40)**. For U.S. site trials supported by the

Figure 41. Percentage of Female Participants in NIH-Defined Phase III Clinical Trials at US Sites that are Members of Minority Groups FY 2019 and FY 2020

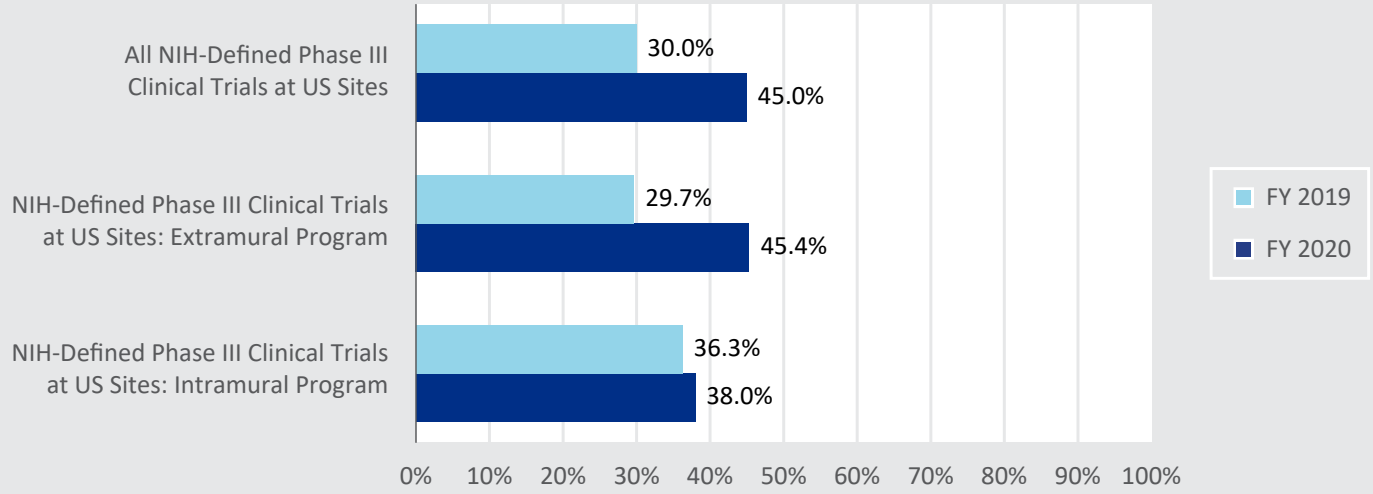
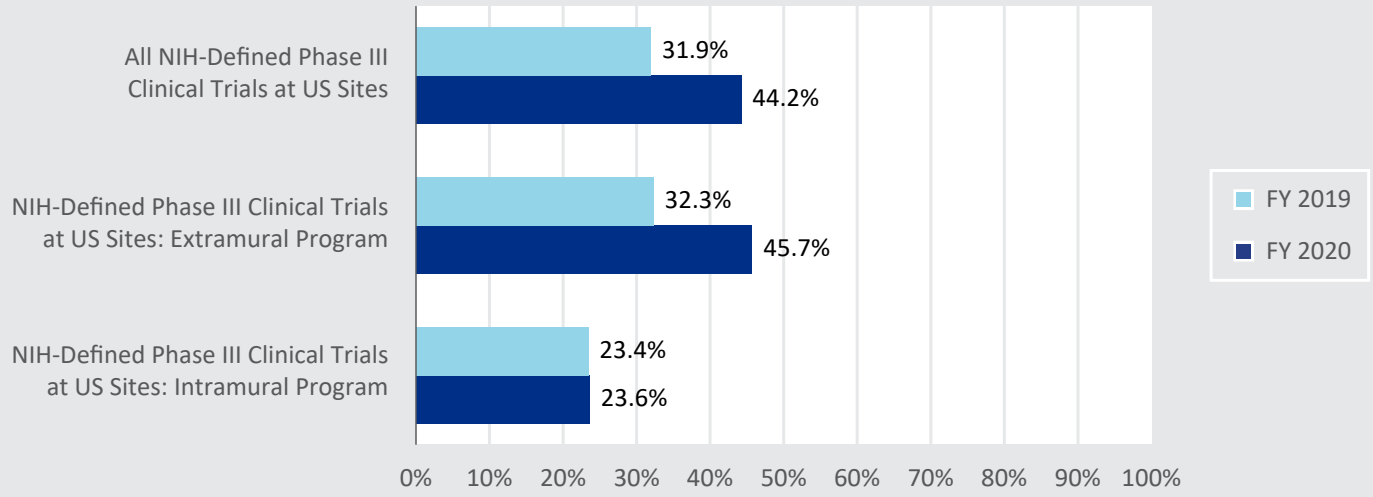


Figure 42. Percentage of Male Participants in NIH-Defined Phase III Clinical Trials at US Sites that are Members of Minority Groups FY 2019 and FY 2020



Intramural Research Program, enrollment rates for minority men were lower than those for minority women. In FY 2019, the difference was about 12.9 percentage points. The discrepancy was increased by 14.4 percentage points in FY 2020 **(Figures 41 and 42)**.

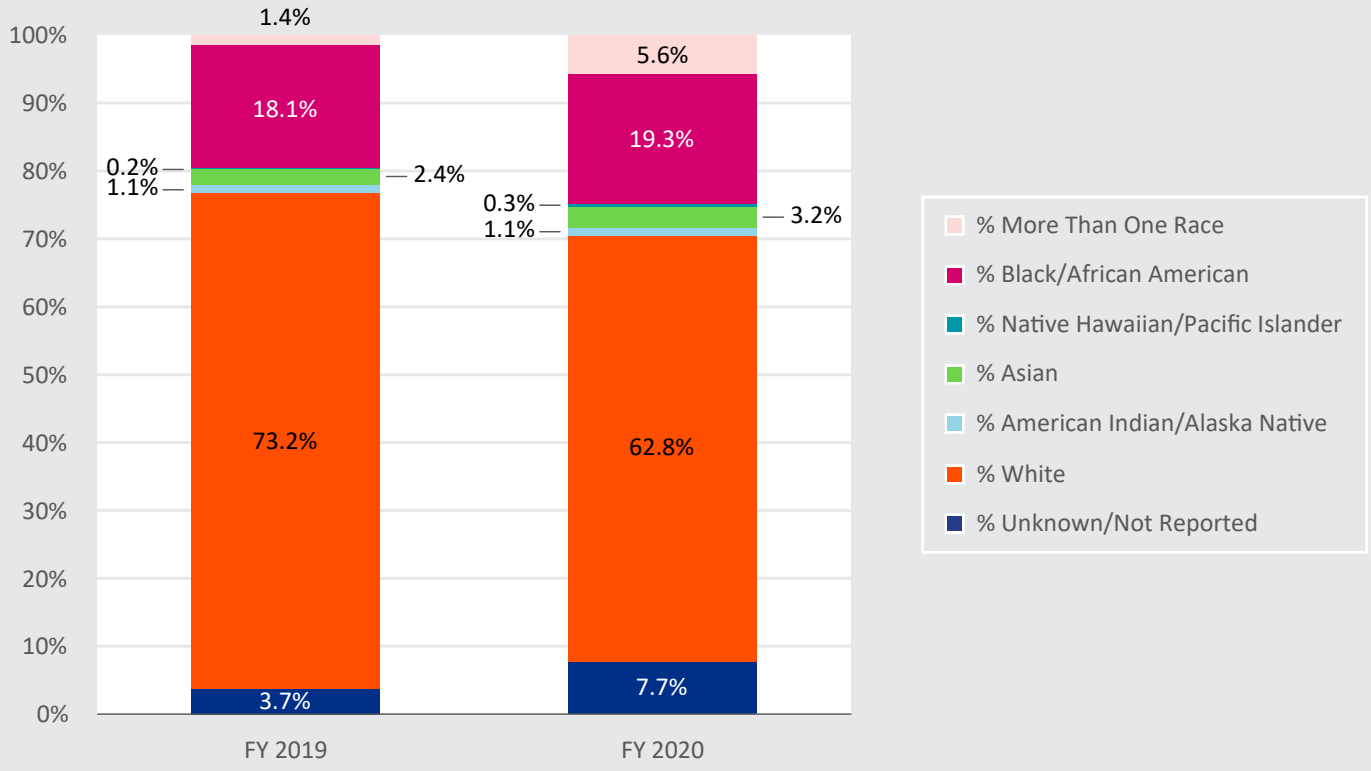
Tables 4F–4H in **Appendix E** provide details on inclusion from FY 2015 to FY 2020 for minority male and female participants in NIH-defined Phase III clinical trials at U.S. sites. **Tables 4N–4P** further break down enrolled participants by race and ethnicity of male and female enrollees for FY 2019 and FY 2020.

Racial and Ethnic Breakdown of Participants Enrolled in NIH-Funded Phase III Clinical Trials at U.S. Sites

Figures 43 and 44 summarize enrollment data for self-reported race and ethnicity of research participants enrolled in NIH-defined Phase III clinical trials at U.S. sites.

Figure 43 illustrates that in FY 2019 and FY 2020, Whites constituted 73.2% and 62.8% of enrollees in NIH-defined

Figure 43. Enrollment for All NIH-Defined Phase III Clinical Trials at U.S. Sites Racial Categories FY 2019 and FY 2020



Phase III clinical trials, respectively. Except for American Indians/Alaska Natives, all minority individuals' participation increased in FY 2020. Specifically, the rate of enrollment of Black/African American participants increased from 18.1% in FY 2019 to 19.3% in FY 2020. In addition, the percentage of enrollees who self-reported as more than one race increased by 4.2 points. The magnitudes of change for Asians, Native Hawaiians, and Pacific Islanders are negligible.

Figure 44 shows that Hispanic/Latino enrollment increased from 8.7% in FY 2019 to 17.3% in FY 2020. The rate of enrollment of people of unknown Hispanic/Latino identity increased from 2.9% in FY 2019 to 4.1% in FY 2020.

Valid Analysis Requirement for NIH-Defined Phase III Trials

In response to GAO's 2015 report titled *Better Oversight Needed to Help Ensure Continued Progress Including Women in Health Research* (GAO 16–13) and the associated recommendations, NIH has been committed to assessing the extent to which NIH-funded studies include analyses of potential differences between men and women. To this end, NIH added questions regarding required valid analysis for NIH-defined Phase III clinical trials beginning in FY 2016. Below is information on NIH-defined Phase III clinical trials that require valid analysis plans by sex/gender, race, and ethnicity.

Figure 45 and **Table 5 in Appendix E** summarize valid analysis requirements for NIH-defined Phase III clinical trials between FY 2019 and FY 2020, focusing on studies supported by the Extramural Research Program. "Valid analyses" refers to stratified analyses by sex/gender and racial and ethnic groups. Valid analyses enable researchers to explore the intervention effects across these demographic categories. Over the course of 2 years, the total number of IERs for NIH-defined Phase III clinical trials increased from 664 to 907. Among those submitted IERs, 94.1% and 88.2% in FY 2019 and FY 2020, respectively, were required to justify a plan for sex–gender valid analysis. As for the proportion of race–ethnicity valid analysis, it was about 94% in both years.

Figure 44. Enrollment for All NIH-Defined Phase III Clinical Trials at U.S. Sites Ethnic Categories for FY 2019 and FY 2020

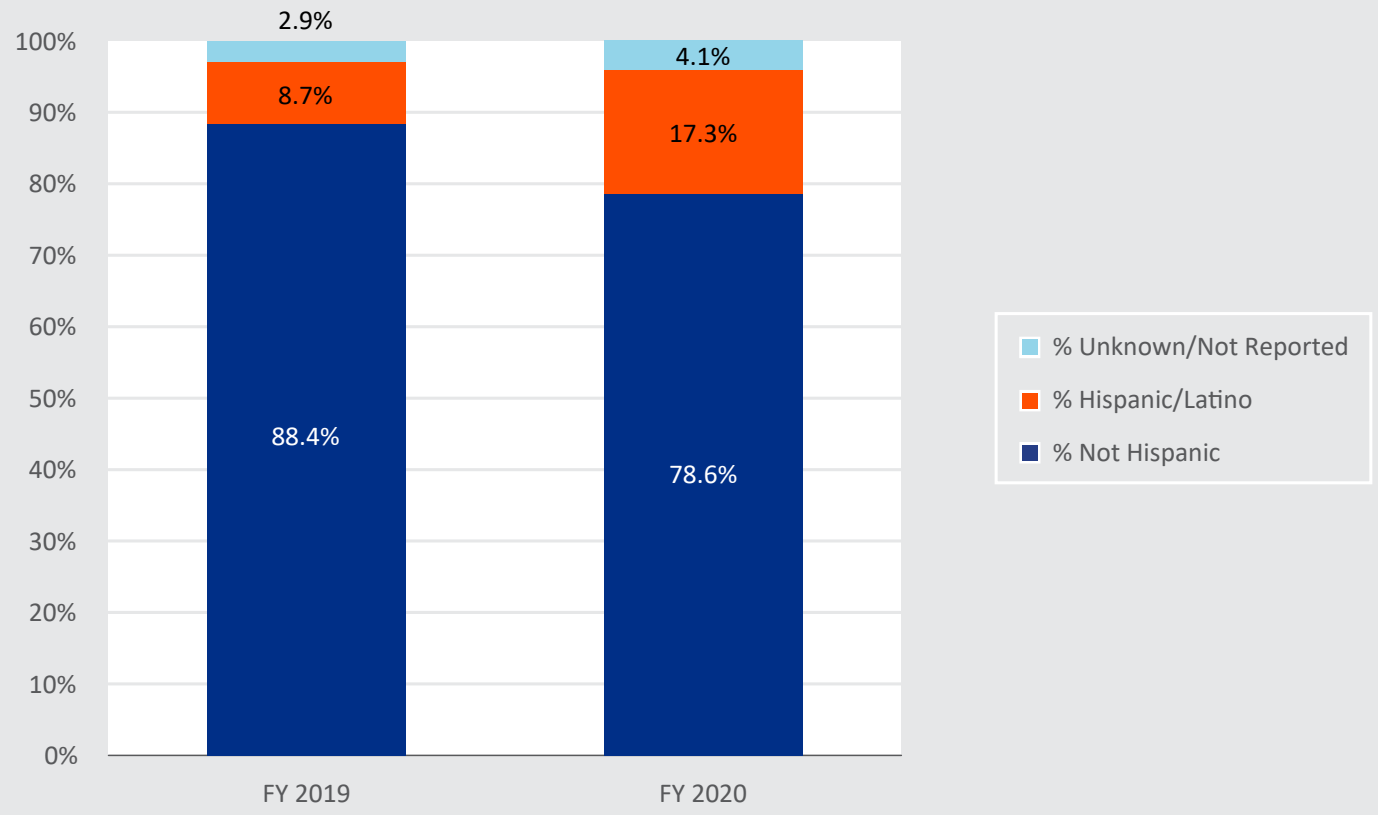
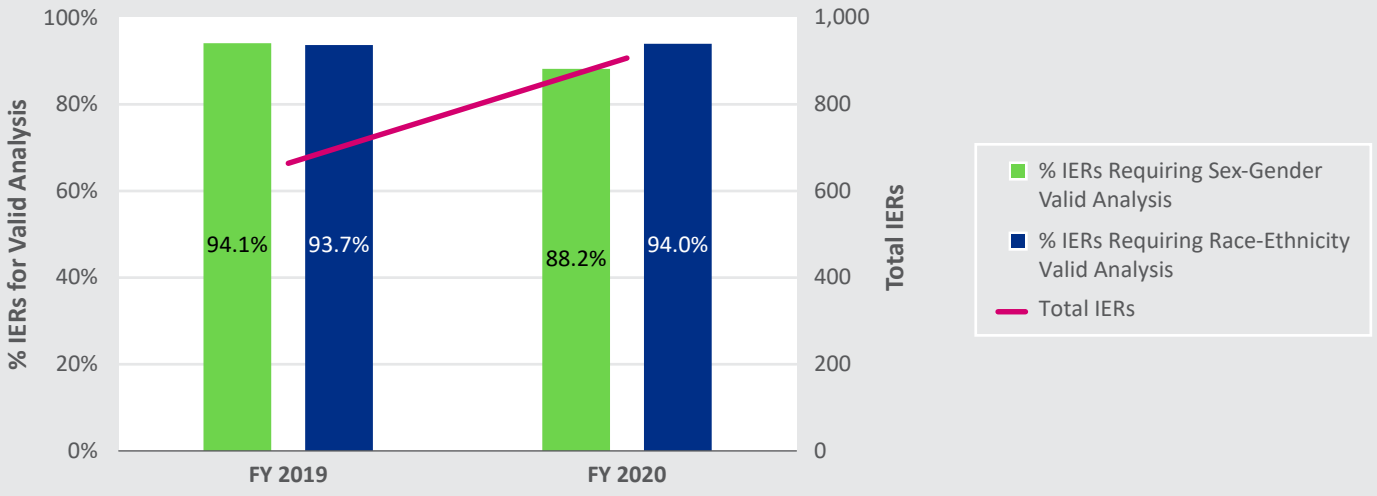


Figure 45. Valid Analysis Requirements for NIH-Defined Phase III Extramural Grants Reported for FY 2019 and FY 2020



Note: Plans for valid analysis methodologies specified in the project application are reported for all IERs, including IERs that have no reported actual enrollment at the time of reporting.

Summary

NIH uses several measures to address the inclusion of women and minorities in clinical research. During the peer review process for grant applications, the inclusion plan for clinical research is examined. NIH-defined Phase III clinical trials are required to have inclusion plans to inform enrollment targets. Peer reviewers assess the inclusion plans, and prior to each advisory council meeting, program directors examine the reviewers' comments on unacceptable inclusion goals and resolve issues with the investigators in writing. Program directors also review enrollment data submitted in the annual progress reports and determine whether the enrollment targets for inclusion are scientifically appropriate.

In summary, the aggregate enrollment data for the reporting period provide an overview of NIH clinical research participation and clearly show substantial inclusion of women and minorities in clinical research projects and NIH-defined Phase III clinical trials. The NIH HSS allows access to clinical inclusion records and cumulative reports and enables program staff members to monitor enrollment data. Overall trends in the data suggest a consistent pattern of 47.2% or greater enrollment of women in NIH-funded clinical research since 2010, with most of these years exceeding 52% **(Appendix E, Table 1A)**. Minority enrollment for NIH-defined Phase III clinical trials at U.S. sites was 30.6% in FY 2019 and 44.5% in FY 2020 **(Appendix E, Table 3B)**. The percentage of Hispanic/Latino participants in all clinical research and NIH-defined Phase III clinical trials also increased during the reporting period **(Appendix E, Tables 2F, 2H, 3F, and 3H)**.

VI. NIH Budget for Women's Health Research

NIH Budgetary Expenditures for Research on Women's Health, Fiscal Years 2017–2019

National Institutes of Health (NIH) funding of research during fiscal years (FYs) 2017 to 2019 is presented in this budget summary, which focuses on diseases and conditions relevant to women. Budget officials at each NIH Institute and Center (IC) and the NIH Office of Budget provided the data presented in this chapter.

Budget data for FY 2020 were not available at the time of publication and will be included in the next report. For comparison purposes, FY 2017 and FY 2018 data are included in this section.

"Women's health conditions," as defined in section 141 of the NIH Revitalization Act of 1993 (42 U.S.C. § 287d), include all diseases, disorders, and conditions:

1. That are unique to, more serious in, or more prevalent in women;
2. For which the factors of medical risk or types of medical intervention are different for women or for which it is unknown whether such factors or types are different for women;
3. With respect to which there has been insufficient clinical research involving women as subjects or insufficient clinical data on women.

Research on women's health conditions includes research on preventing such conditions and applies to women of all ages and racial and ethnic groups.

In collaboration with the U.S. Department of Health and Human Services (HHS) Coordinating Committee on Women's Health (CCWH), the NIH Office of Research on Women's Health (ORWH) reports the budgetary expenditures on women's health research throughout NIH. The reporting effort is coordinated by the HHS Office on Women's Health in the Office of the Assistant Secretary for Health. Other women's health offices and programs across HHS agencies and the HHS Office of the Assistant Secretary for Financial Resources contribute to the effort.

A variety of spending categories for diseases or disorders relevant to women are used for data collection and budgetary reporting on women's health research. The spending categories are periodically updated to reflect (1) new disease categories, (2) new methods to standardize the proportion of the budget accounted for by women's health research when enrollment data are not available, and (3) the inclusion of men for comparison with women's health categories in which both men and women may be affected. In this case, the data collection process has evolved to account for studies in which men and women are both included and reported on. For example, in some reports prior to FY 2003, the budgetary reporting on women's health research expenditures focused on single-gender studies, studies to evaluate sex/gender differences, and studies of diseases, disorders, and conditions unique to women. Previous reporting also used prevalence data as part of the reporting criteria and included research on diseases, disorders, and conditions that are not unique to one sex but for which there is documented evidence of greater prevalence in one sex by a ratio of at least 2-to-1 or for which a specific gender-related consideration exists.

For this report, budgetary expenditures are categorized as one of the following: (1) inseparably combined, (2) supporting research on women's health only, or (3) supporting research on men's health only. As a result of discussions with the CCWH and the NIH Coordinating Committee on Research on Women's Health, uniform procedures for determining the appropriate categorical allocations were established. The guidelines for budget calculations are:

1. All funding for projects that focus primarily on women—such as the Nurses' Health Study, the Mammography Quality Standards Act, and the Women's Health Initiative—should be categorized as supporting women's health.

2. For FY 2017 and FY 2018, research, studies, services, or projects that include both men and women, the recommended methods to calculate the proportion of funds spent on women's health research were:

    a. If target or accrual enrollment data are available, multiply the expenditure by the proportion of female subjects included in the program. For example, if 50% of the subjects enrolled in a trial, study, service, or treatment program are women, then 50% of the funds spent for that program should be counted as supporting women's health research.

    b. Where both males and females are included, as may be the case for many basic scientific research projects, multiply the expenditure by 50%.

3. The reporting method described above uses the percentages of females and males included in the research activities to estimate annual spending. However, this particular approach does not necessarily align with NIH's mission and potentially lacks scientific robustness. Starting in FY 2018, NIH convened a series of scientific meetings to develop a new method for classifying and prorating women's health–related investments. This science-based coding scheme was incorporated into a data platform, the Manual Categorization System-Women's Health (MCS-WH) reporting module, and officially used for reporting NIH's women's health research budgets in FY 2019. Because of methodology changes, please interpret the funding trends with caution.

ORWH, with its advisory and coordinating committees, monitors the methodology used by the ICs for collecting budget data and provides input to the methods of the CCWH to optimize budget data collection methods.

Table 7 lists the overall NIH research expenditures from FY 2017 to FY 2019 for specific diseases, disorders, and conditions by women only, by men only, and for both women and men. The health categories and subcategories in this table were developed to accommodate all HHS agencies. The table shows dashes across all columns for subcategories that had nothing to report for the fiscal year. Because the table is additive, dashes may be shown for relevant subcategories. Even though a budget expenditure can apply to more than one subcategory, funding must be applied to a single primary subcategory. When a budget expenditure overlaps multiple subcategories, the IC assigns the expenditure to the most scientifically appropriate subcategory. Because no overlap in reporting is allowed by the prescribed method of data collection for this report, the amount listed for each topic area may be understated or overstated.

Table 8 shows the dollar amounts and percentages of the NIH research budget from FY 2017 to FY 2019 for women and for men only, as well as for research including both women and men. The portion of the research budget supporting women only remained constant, at 14%, in FY 2017 and FY 2018; however, it declined to 11% in FY 2019. This decline does not necessarily mean that there was a decrease in the overall spending for women-only research. As mentioned, the downward trend is more likely explained by the change in coding methodology for FY 2019.

Table 9 lists the percentage of the NIH women's health research budget for each disease, disorder, or special initiative from FY 2017 to FY 2019. Generally, there was no major fluctuation from year to year, with the exception of research on aging, which went from 15% in FY 2017 and FY 2018 to 7% in FY 2019. Research on cancer received the highest portion of the women's health budget, followed by research on cardiovascular and pulmonary conditions as the second-highest in FY 2019. Research on infectious diseases and research on reproductive and maternal/child/adolescent health tied for third in FY 2019, both experiencing an increase of 2 to 3 percentage points over the previous fiscal year. These top four research areas encompass many of the high-priority topics and strategic goals for ORWH.

Table 10 shows the dollar amounts and percentages of change in the NIH research budget between FY 2017 and FY 2018 and between FY 2018 and FY 2019. Overall, the budget increased by 7% between FY 2017 and FY 2018 and by 8% between FY 2018 and FY 2019.

During this period, several high-priority research topics in women's health had a significant funding increase. Funding for research on vaginal, uterine, and other reproductive cancers increased over the 3 years, with a 32% increase between FY 2018 and FY 2019. Funding for research on pregnancy, pregnancy prevention, and maternal health also increased by 12%. Investment for the substance abuse category had a remarkable upsurge over time. From FY 2017 to FY 2018, the magnitude of increase was approximately 5%. Between FY 2018 and FY 2019, the percentage of spending escalated by 34%. Funding for the mental health category increased by 9% between FY 2018 and FY 2019. The improvement in funding can be explained by new initiatives, projects, and opportunities initiated by NIH, including the Implementing a Maternal health and PRegnancy Outcomes Vision for Everyone (IMPROVE) initiative and the NIH Helping to End Addiction Long-term℠—or HEAL—Initiative. The increased investment in these research areas demonstrates NIH's commitment to advancing research on women's health.

At the same time, there was also a decline in spending in a few high-priority research areas in women's health. Spending for menopause research declined in the reporting period, with a 7% drop from FY 2017 to FY 2018 and a 61% drop from FY 2018 to FY 2019. There was also a decline of 4% in funding for research on cervical cancer from FY 2018 to FY 2019, as well as a decline of 15% in hysterectomy research funding and a decline of 31% in funding for breastfeeding research, despite an increase of 1,308% the year before. The above categories are important topics of research for women's health, and efforts need to be made to bring increased focus to these high-priority topics.

Reference

NIH Reform Act of 2006, H.R. 6164, 109th Congress. (2004)

Table 7. **NIH Research Budget for Women's and Men's Health by Disease, Condition, and Special Initiatives, FY 2017 to FY 2019 (Dollars in Thousands)**

Disease, Condition, or Initiative	FY17 Women	FY17 Men	FY17 Both	FY17 Total	FY18 Women	FY18 Men	FY18 Both	FY18 Total	FY19 Women	FY19 Men	FY19 Both	FY19 Total
I. Cancer												
Breast cancer (including mammography & other services)	720,986	89	3,755	724,830	697,033	179	4,425	701,637	675,220	-	14,730	689,950
Reproductive cancers:												
Cervical	92,508	1,598	7,478	101,584	103,225	1,086	7,726	112,037	97,821	1,426	7,908	107,155
Ovarian	139,785	87	48	139,920	155,022	179	507	155,708	152,314	-	3,674	155,988
Vaginal, uterine, and other	27,065	23	38	27,126	28,924	23	1	28,948	38,118	-	53	38,171
Lung cancer	204,498	223	131,689	336,410	223,275	465	161,524	385,264	95,405	-	294,850	390,255
Colorectal cancer	120,373	1,260	140,317	261,950	144,804	1,091	150,504	296,399	79,305	2,311	201,300	282,916
Other neoplasms	9,659	13,861	4,463,904	4,487,424	110,674	14,376	4,628,219	4,753,269	119,203	11,597	4,764,426	4,895,227
Subtotal	1,314,874	17,141	4,747,229	6,079,244	1,462,957	17,399	4,952,906	6,433,262	1,257,385	15,335	5,286,942	6,559,662
II. Cardiovascular/Pulmonary												
Blood diseases	66,459	77,346	465,957	609,762	69,192	73,404	457,584	600,180	49,885	78,002	449,207	577,094
Heart disease	164,217	181,213	749,117	1,094,547	169,742	171,047	810,360	1,151,149	164,172	177,769	860,859	1,202,799
Stroke	23,398	240	237,460	261,098	16,631	-	265,394	282,025	18,910	1,175	261,433	281,518
Other cardiovascular diseases/disorders	94,680	67,736	872,610	1,035,026	123,101	73,078	902,444	1,098,623	118,446	80,769	958,920	1,158,135
Pulmonary diseases	127,566	115,303	371,013	613,882	127,441	107,452	415,844	650,737	126,174	112,970	488,101	727,244
Asthma	56,804	44,381	134,969	236,154	58,765	49,676	151,706	260,147	54,549	47,102	157,550	259,202
Other	2,684	468	388,448	391,600	2,884	754	398,112	401,750	1,264	381	406,117	407,762
Subtotal	535,808	486,687	3,219,574	4,242,069	567,756	475,411	3,401,444	4,444,611	533,400	498,168	3,582,187	4,613,754
III. Reproductive & Maternal/Child/Adolescent Health												
Contraception	15,242	6,420	84,546	106,208	30,136	6,399	95,229	131,764	68,233	10,975	52,636	131,844
Infertility	4,231	-	12,833	17,064	3,581	-	14,377	17,958	1,410	-	20,224	21,634
Female reproductive physiology	70,024	178	251	70,453	74,912	254	-	75,166	74,991	-	196	75,187
Hysterectomy	603	-	-	603	1,150	-	-	1,150	977	-	-	977
Endometriosis/ leiomyomas (fibroids)	8,612	-	396	9,008	8,745	-	396	9,141	3,648	-	-	3,648
Pregnancy/ pregnancy prevention/maternal health	230,716	1,390	598	232,704	254,205	1,443	15,878	271,526	269,283	167	33,879	303,329
Diseases related to DES exposure	-	-	-	-	-	-	-	-	-	-	-	-
Female genital cutting	-	-	-	-	-	-	-	-	-	-	-	-
Pelvic floor disorders	650	-	-	650	154	-	-	154	275	-	-	275
Other	17,601	11,325	519,402	548,328	5,783	11,317	658,830	675,930	10,235	8,957	718,313	737,505
Subtotal	347,679	19,313	618,026	985,018	378,666	19,413	784,710	1,182,789	429,052	20,100	825,248	1,274,400

Disease, Condition, or Initiative	FY17 Women	FY17 Men	FY17 Both	FY17 Total	FY18 Women	FY18 Men	FY18 Both	FY18 Total	FY19 Women	FY19 Men	FY19 Both	FY19 Total
IV. Aging												
Menopause	23,905	-	-	23,905	22,235	-	-	22,235	8,716	-	-	8,716
Menopausal hormone/non-hormone therapy	11,126	-	-	11,126	8,721	-	-	8,721	7,191	-	-	7,191
Alzheimer's disease	327,194	254,929	732,256	1,314,379	405,601	328,660	592,633	1,326,894	81,305	56,528	1,770,924	1,908,757
Malnutrition in the elderly	68	45	-	113	-	-	-	-	-	-	-	-
Osteoarthritis	55,169	4,864	58,621	118,654	52,128	5,726	52,411	110,265	16,823	3,690	55,181	75,694
Osteoporosis (including fractures)	74,623	7,277	18,955	100,855	79,262	9,819	9,736	98,817	80,241	4,789	7,614	92,644
Women's Health Initiative	-	-	-	-	200	-	-	200	-	-	-	-
Demography of aging	32,685	30,718	12,899	76,302	28,459	27,712	297	56,468	6,431	4,681	46,192	57,304
Aging economics	14,746	14,669	9,655	39,070	14,760	14,994	11,857	41,611	6,923	7,054	58,501	72,479
Other	158,672	139,494	509,648	807,814	169,700	148,648	1,028,877	1,347,225	111,529	64,493	1,086,131	1,262,153
Subtotal	698,188	451,996	1,342,034	2,492,218	781,066	535,559	1,695,811	3,012,436	319,160	141,235	3,024,543	3,484,938
V. Metabolism/Endocrinology/Gastrointestinal												
Diabetes	177,574	119,859	220,454	517,887	141,276	80,111	191,088	412,475	123,249	106,168	230,441	459,857
Obesity	202,228	91,674	114,100	408,002	211,153	96,497	136,684	444,334	174,646	142,567	155,743	472,957
Hepatobiliary diseases	1,495	2,613	237,904	242,012	1,821	2,457	284,036	288,314	1,524	1,832	302,621	305,977
Thyroid diseases/ conditions	11,307	2,839	631	14,777	10,586	2,630	40	13,256	8,627	2,072	69	10,768
Fecal incontinence	1,404	936	-	2,340	2,639	1,760	-	4,399	3,151	2,100	-	5,251
Irritable bowel syndrome	3,896	1,212	-	5,108	5,056	2,167	1,018	8,241	7,339	2,935	1,524	11,798
Other	699	668	138,938	140,305	2,139	1,480	156,008	159,627	1,257	582	168,998	170,837
Subtotal	398,603	219,801	712,027	1,330,431	374,670	187,102	768,874	1,330,646	319,793	258,255	859,395	1,437,444
VI. Substance Abuse												
Etiology (unspecified)	9,640	10,371	97,458	117,469	9,677	10,871	93,507	114,055	12,817	14,520	88,132	115,469
Epidemiology (unspecified)	29,288	31,297	51,271	111,856	29,291	32,164	49,502	110,957	16,265	15,212	79,747	111,224
Prevention (unspecified)	26,767	28,885	40,408	96,060	27,723	30,061	45,003	102,787	19,198	17,769	89,589	126,556
Treatment (unspecified)	82,449	93,234	147,373	323,056	81,063	91,151	143,024	315,238	76,951	72,057	399,515	548,523
Alcohol	20,084	23,293	121,682	165,059	22,573	24,620	115,467	162,660	23,112	24,361	122,306	169,779
Illegal drugs	118,699	128,623	214,221	461,543	119,366	133,128	226,353	478,847	81,410	75,102	468,783	625,295
Prescription drugs	16,100	17,768	29,296	63,164	27,708	31,086	52,530	111,324	25,334	23,058	146,979	195,371
Tobacco products	24,685	24,929	57,539	107,153	23,951	25,705	65,410	115,066	15,751	14,512	106,987	137,250
Other substances	1,686	1,634	12,003	15,323	1,651	2,097	13,992	17,740	1,374	1,894	21,027	24,295
Co-occurring substance abuse & mental disorders	2,038	1,232	4,256	7,526	1,463	1,271	5,589	8,323	1,677	1,345	5,949	8,971
Subtotal	331,436	361,266	775,507	1,468,209	344,465	382,154	810,377	1,536,996	273,888	259,830	1,529,014	2,062,731

Disease, Condition, or Initiative	FY17 Women	FY17 Men	FY17 Both	FY17 Total	FY18 Women	FY18 Men	FY18 Both	FY18 Total	FY19 Women	FY19 Men	FY19 Both	FY19 Total
VII. Behavioral Studies/Programs												
Violence (including domestic, abused women, spousal abuse, elder abuse, trafficking, bullying)	3,503	1,851	14,615	19,969	4,387	2,105	15,056	21,548	6,853	2,249	20,185	29,287
Tobacco use cessation	393	83	1,800	2,276	393	220	1,946	2,559	595	159	862	1,616
Physical activity/ exercise/nutrition (promoting healthy behavior)	2,072	1,014	256,454	259,540	5,768	1,811	293,896	301,475	6,449	232	311,729	318,411
Other behavior change/risk modification	14,545	13,946	519,262	547,753	15,597	11,928	542,919	570,444	24,733	8,801	524,138	557,671
Caregiving	185	159	20,775	21,119	258	158	16,351	16,767	1,149	-	11,801	12,950
Other	10,351	5,410	588,806	604,567	12,262	3,029	697,275	712,566	19,380	3,962	779,392	802,734
Subtotal	31,049	22,463	1,401,712	1,455,224	38,665	19,251	1,567,443	1,625,359	59,160	15,403	1,648,106	1,722,669
VIII. Mental Health												
Etiology (unspecified)	632	915	34,379	35,926	1,992	2,377	42,292	46,661	982	102	42,209	43,293
Epidemiology (unspecified)	-	-	507	507	199	-	1,626	1,825	423	-	1,016	1,439
Prevention (unspecified)	127	126	125	378	180	158	67	405	56	33	1	90
Treatment (unspecified)	259	223	3,791	4,273	365	297	3,209	3,871	1,132	169	2,162	3,463
Depression/mood disorders	17,651	585	129,688	147,924	14,468	510	136,161	151,139	24,263	542	184,668	209,473
Suicide	2,307	247	33,883	36,437	2,284	214	50,447	52,945	7,433	228	54,033	61,695
Schizophrenia	1,597	109	112,614	114,320	1,202	43	121,067	122,312	3,478	-	120,102	123,580
Anxiety disorders	3,950	1,214	46,620	51,784	3,388	393	48,980	52,761	5,661	378	42,012	48,051
Eating disorders	9,990	1,060	5,351	16,401	11,958	1,277	3,702	16,937	12,473	1,826	7,559	21,857
Psychosocial stress	5,048	759	24,913	30,720	7,464	1,475	28,458	37,397	11,860	1,493	33,797	47,149
Post-traumatic stress disorder (PTSD)	4,098	607	20,394	25,099	3,940	826	25,643	30,409	6,608	1,014	24,447	32,069
Other mental disorders (excluding Alzheimer's)	28,584	3,830	860,074	892,488	31,727	4,043	855,113	890,883	57,517	3,498	903,209	964,224
Autism	4,818	38,506	99,270	142,594	6,810	37,741	131,418	175,969	5,031	38,952	133,243	177,226
Subtotal	79,061	48,181	1,371,609	1,498,851	85,977	49,354	1,448,183	1,583,514	136,917	48,235	1,548,458	1,733,609
IX. Infectious Diseases												
HIV/AIDS	183,814	68,519	2,270,939	2,523,272	205,866	122,231	2,275,765	2,603,862	226,061	61,816	2,321,095	2,608,972
Tuberculosis	14,871	37,306	161,181	213,358	16,525	40,003	207,183	263,711	61,262	69,117	321,688	452,067
Sexually transmitted diseases (STDs)	26,280	22,592	126,592	175,464	31,680	25,099	110,944	167,723	76,546	27,223	103,733	207,502
Topical microbicides	89,615	-	3,134	92,749	72,425	-	2,671	75,096	4,248	-	75,353	79,601
Toxic shock syndrome	-	-	-	-	281	-	-	281	224	-	-	224

Disease, Condition, or Initiative	FY17 Women	FY17 Men	FY17 Both	FY17 Total	FY18 Women	FY18 Men	FY18 Both	FY18 Total	FY19 Women	FY19 Men	FY19 Both	FY19 Total
IX. Infectious Diseases *(Continued)*												
Tropical diseases (including malaria)	37,372	42,655	555,468	635,495	41,182	39,561	622,745	703,488	63,252	46,072	562,477	671,801
Other	1,624	665	600,880	603,169	4,121	2,002	595,643	601,766	1,528	1,254	604,936	607,718
Subtotal	353,576	171,737	3,718,194	4,243,507	372,079	228,896	3,814,951	4,415,926	433,120	205,483	3,989,283	4,627,886
X. Immune Disorders												
Rheumatoid arthritis	46,482	2,195	151,725	200,402	33,424	2,323	123,297	159,044	50,329	2,122	109,501	161,952
Lupus erythematosus	62,914	4,017	25,676	92,607	81,767	5,250	33,143	120,160	76,606	3,460	31,052	111,118
Multiple sclerosis	26,116	2,329	64,962	93,407	5,783	2,204	87,150	95,137	34,056	4,822	62,967	101,846
Myasthenia gravis	597	223	3,621	4,441	283	223	3,366	3,872	303	88	4,442	4,833
Scleroderma	9,368	369	1,111	10,848	11,198	631	997	12,826	13,024	122	1,037	14,183
Sjögren's syndrome	22,385	-	490	22,875	20,485	-	669	21,154	23,896	411	1,002	25,309
Takayasu disease	-	-	-	-	-	-	-	-	-	-	-	-
Other	3,182	2,893	193,798	199,873	3,758	3,303	152,405	159,466	1,419	866	162,030	164,316
Subtotal	171,044	12,026	441,383	624,453	156,698	13,934	401,027	571,659	199,635	11,891	372,031	583,557
XI. Neurologic, Muscular, & Bone												
Trauma research:												
Brain	16,134	-	253,392	269,526	10,161	245	295,331	305,737	12,600	-	271,448	284,048
Other neurologic trauma	-	-	19,483	19,483	-	-	18,840	18,840	-	-	17,546	17,546
Bone-fracture (non-osteoporotic) and muscle injury	142	160	24,247	24,549	597	155	23,335	24,087	565	155	37,239	37,959
Muscular dystrophy	1,750	35,969	30,108	67,827	1,605	39,601	28,393	69,599	1,242	36,155	29,603	67,001
Chronic pain conditions	14,418	138	138,298	152,854	11,396	376	148,039	159,811	20,248	696	474,495	495,439
Temporomandibular disorders	11,286	-	268	11,554	11,253	-	268	11,521	9,829	964	161	10,954
Vulvodynia	1,002	-	-	1,002	1,696	-	-	1,696	1,883	-	-	1,883
Fibromyalgia & eosinophilic myalgia	5,348	-	-	5,348	4,242	-	196	4,438	2,859	-	429	3,288
Migraine	8,095	-	5,201	13,296	4,587	-	9,302	13,889	7,909	-	13,221	21,129
Sleep disorders	3,720	647	56,581	60,948	4,035	777	82,519	87,331	4,179	638	28,667	33,484
Paget's disease	-	-	854	854	-	-	1,146	1,146	-	-	1,149	1,149
Parkinson's disease	7,949	827	125,847	134,623	6,103	656	135,065	141,824	6,108	-	143,424	149,532
Seizure disorders	6,980	113	113,153	120,246	6,745	113	133,222	140,080	8,764	108	129,298	138,170
Other	22,466	2,886	1,193,334	1,218,686	66,759	11,579	1,146,524	1,224,862	16,527	17,692	1,465,072	1,499,290
Subtotal	99,290	40,740	1,960,766	2,100,796	129,179	53,502	2,022,180	2,204,861	92,714	56,408	2,611,752	2,760,873
XII. Kidney and Urologic												
Urinary tract infections (cystitis, pyelonephritis)	10,584	3,099	28,348	42,031	11,631	3,512	22,821	37,964	8,601	1,947	14,884	25,432
ESRD/ transplantation	8,389	12,432	109,616	130,437	9,780	15,199	113,207	138,186	6,664	9,973	105,953	122,590
Urinary incontinence	10,286	-	-	10,286	10,762	-	-	10,762	12,953	-	4,164	17,117
Painful bladder, interstitial cystitis	10,653	1,117	588	12,358	9,407	1,023	835	11,265	5,334	1,820	1,810	8,964

Disease, Condition, or Initiative	FY17 Women	FY17 Men	FY17 Both	FY17 Total	FY18 Women	FY18 Men	FY18 Both	FY18 Total	FY19 Women	FY19 Men	FY19 Both	FY19 Total
XII. Kidney and Urologic *(Continued)*												
Other	659	4,042	440,975	445,676	1,183	3,893	436,452	441,528	522	4,640	456,982	462,144
Subtotal	40,571	20,690	579,527	640,788	42,763	23,627	573,315	639,705	34,074	18,380	583,793	636,247
XIII. Ophthalmic, Otolaryngologic, and Oral Health												
Eye diseases & disorders	26,096	9,977	709,540	745,613	23,425	12,559	743,483	779,467	20,782	13,930	756,875	791,587
Ear diseases & disorders	15,934	1	198,506	214,441	18,313	1	197,055	215,369	22,318	-	211,864	234,182
Dental and oral health	4,614	-	368,583	373,197	9,161	-	383,110	392,271	13,140	-	396,379	409,519
Other	684	590	2,502	3,776	709	609	2,773	4,091	799	94	2,811	3,704
Subtotal	47,328	10,568	1,279,131	1,337,027	51,608	13,169	1,326,421	1,391,198	57,039	14,024	1,367,929	1,438,992
XIV. Health Effects of the Environment												
Environmental estrogens	17,479	-	4,448	21,927	18,510	982	3,097	22,589	10,599	453	1,683	12,735
Health effects of toxic exposure (excluding cancer)	1,292	-	108,640	109,932	1,494	-	111,469	112,963	1,771	683	121,178	123,632
Toxicological research & testing program	-	-	103,828	103,828	31	31	102,778	102,840	31	-	106,489	106,520
Chemical/biological warfare agents	-	-	7,304	7,304	-	-	6,569	6,569	-	-	813	813
Other	446	19	8,929	9,394	1,238	87	7,521	8,846	1,204	107	8,012	9,323
Subtotal	19,217	19	233,149	252,385	21,273	1,100	231,434	253,807	13,606	1,243	238,175	253,024
XV. Cross-Cutting Categories and Special Initiatives												
Treatment, prevention, & services	7,528	18,191	465,994	491,713	8,996	9,499	527,433	545,928	12,863	12,768	471,633	497,264
Access to health care & financing	1,118	712	7,509	9,339	2,107	1,055	10,246	13,408	3,813	781	9,835	14,429
Education & training for health care providers	1,008	912	94,151	96,071	4,362	1,858	82,940	89,160	6,548	12,060	73,380	91,988
Health literacy & bilingual information	465	100	31,273	31,838	799	808	33,493	35,100	833	442	32,776	34,051
Cultural influences	2,669	1,851	84,153	88,673	2,243	2,267	84,023	88,533	4,605	5,282	79,607	89,494
Disability research & services	659	1,422	104,555	106,636	52	1,045	109,079	110,176	365	2,145	122,315	124,825
Homelessness	15	231	13	259	172	310	9	491	242	304	47	593
Chronic fatigue syndrome	4,015	1,419	6,670	12,104	2,824	1,720	8,497	13,041	5,983	1,395	6,102	13,481
Breastfeeding	430	45	-	475	4,141	-	2,547	6,688	2,622	-	2,001	4,623
Organ donation	-	-	-	-	-	-	402	402	132	-	1,201	1,333
Genetic services/ counseling	15,151	11,766	12,659	39,576	17,548	15,489	37,160	70,197	11,221	7,868	210,585	229,675
Unintentional injury	17	266	56,268	56,551	25	133	47,763	47,921	513	137	46,509	47,160
Alternative & complementary therapies	38,809	35,937	136,699	211,445	42,309	34,115	148,669	225,093	29,023	30,011	156,768	215,802
Health statistics & data collection	2,394	2,078	250,067	254,539	2,360	1,060	113,809	117,229	3,819	840	51,406	56,065

Disease, Condition, or Initiative	FY17 Women	FY17 Men	FY17 Both	FY17 Total	FY18 Women	FY18 Men	FY18 Both	FY18 Total	FY19 Women	FY19 Men	FY19 Both	FY19 Total
XV. Cross-Cutting Categories and Special Initiatives *(Continued)*												
Programs/offices on women's health	197,785	16,148	1,747,784	1,961,717	120,031	22,730	2,035,981	2,178,742	99,768	20,515	2,246,206	2,366,489
Global health	27,490	111,796	1,820,710	1,959,996	31,121	120,112	1,996,396	2,147,629	125,677	142,756	1,962,407	2,230,839
Drug metabolism (sex differences, pregnancy, etc.)	1,276	518	4,435	6,229	1,210	835	4,050	6,095	1,850	1,263	3,696	6,809
Subtotal	300,829	203,392	4,822,940	5,327,161	240,300	213,036	5,242,497	5,695,833	309,878	238,567	5,476,474	6,024,919
TOTAL	4,768,553	2,086,020	27,222,808	34,077,381	5,048,123	2,232,907	29,041,573	36,322,602	4,468,821	1,802,556	32,943,328	39,214,705

Table 8. FY 2017 to FY 2019 Summary: NIH Research Budget by Sex (Dollars in Thousands)

Category	FY17 ($)	FY17 (%)	FY18 ($)	FY18 (%)	FY19 ($)	FY19 (%)
Women	4,768,553	14%	5,048,123	14%	4,468,821	11%
Men	2,086,020	6%	2,232,907	6%	1,802,556	5%
Both	27,222,808	80%	29,041,573	80%	32,943,328	84%
Total	34,077,381	100%	36,322,602	100%	39,214,705	100%

Table 9. Proportion of Women's Health Research Budget in Relation to the Overall NIH Research Spending by Disease, Condition, and Special Initiative: FY 2017 to FY 2019 (Dollars in Thousands)

Diseases, Disorder, or Condition	FY17 ($)	FY17 (%)	FY18 ($)	FY18 (%)	FY19 ($)	FY19 (%)
Cancer	$1,314,874	28%	$1,462,957	29%	$1,257,385	28%
Cardiovascular/Pulmonary	$535,808	11%	$567,756	11%	$533,400	12%
Infectious Diseases	$353,576	7%	$372,079	7%	$433,120	10%
Reproductive & Maternal/Child/Adolescent Health	$347,679	7%	$378,666	8%	$429,052	10%
Metabolism/Endocrinology/Gastrointestinal	$398,603	8%	$374,670	7%	$319,793	7%
Aging	$698,188	15%	$781,066	15%	$319,160	7%
Cross-Cutting Categories and Special Initiatives	$300,829	6%	$240,300	5%	$309,878	7%
Substance Abuse	$331,436	7%	$344,465	7%	$273,888	6%
Immune Disorders	$171,044	4%	$156,698	3%	$199,635	4%
Mental Health	$79,061	2%	$85,977	2%	$136,917	3%
Neurologic, Muscular, & Bone	$99,290	2%	$129,179	3%	$92,714	2%
Behavioral Studies/Programs	$31,049	1%	$38,665	1%	$59,160	1%
Ophthalmic, Otolaryngologic, and Oral Health	$47,328	1%	$51,608	1%	$57,039	1%
Kidney and Urologic	$40,571	1%	$42,763	1%	$34,074	1%
Health Effects of the Environment	$19,217	0%	$21,273	0%	$13,606	0%
Total	$4,768,553	100%	$5,048,123	100%	$4,468,821	100%

Table 10. FY 2017 to FY 2019: Change from Year to Year by Disease, Condition, and Special Initiatives (Dollars in Thousands)

	$ Change (FY17 to FY18)	% Change (FY17 to FY18)	$ Change (FY18 to FY19)	% Change (FY18 to FY19)
I. Cancer				
Breast cancer (including mammography & other services)	$(23,193.00)	-3%	$(11,686.60)	-2%
Reproductive cancers:				
Cervical	$10,453.00	10%	$(4,882.00)	-4%
Ovarian	$15,788.00	11%	$280.00	0%
Vaginal, uterine, and other	$1,822.00	7%	$9,223.00	32%
Lung cancer	$48,854.00	15%	$4,991.07	1%
Colorectal cancer	$34,449.00	13%	$(13,483.17)	-5%
Other neoplasms	$265,844.64	6%	$141,958.17	3%
Subtotal	$354,017.64	6%	$126,400.48	2%
II. Cardiovascular/Pulmonary				
Blood diseases	$(9,582.00)	-2%	$(23,085.74)	-4%
Heart disease	$56,602.00	5%	$51,650.37	4%
Stroke	$20,927.00	8%	$(506.77)	-0%
Other cardiovascular diseases/disorders	$63,597.00	6%	$59,511.78	5%
Pulmonary diseases	$36,855.00	6%	$76,507.33	12%
Asthma	$23,993.00	10%	$(945.40)	-0%
Other	$10,150.00	3%	$6,011.90	1%
Subtotal	$202,542.00	5%	$169,143.48	4%
III. Reproductive & Maternal/Child/Adolescent Health				
Contraception	$25,556.00	24%	$80.04	0%
Infertility	$894.00	5%	$3,676.00	20%
Female reproductive physiology	$4,713.00	7%	$21.30	0%
Hysterectomy	$547.00	91%	$(173.37)	-15%
Endometriosis/leiomyomas (fibroids)	$133.00	1%	$(5,493.00)	-60%
Pregnancy/pregnancy prevention/maternal health	$38,822.00	17%	$31,803.16	12%
Diseases related to DES exposure	$-	N/A	$-	N/A
Female genital cutting	$-	N/A	$-	N/A
Pelvic floor disorders	$(496.00)	-76%	$121.00	79%
Other	$127,602.00	23%	$61,575.38	9%
Subtotal	$197,771.00	20%	$91,610.50	8%
IV. Aging				
Menopause	$(1,670.00)	-7%	$(13,519.00)	-61%
Menopausal hormone/non-hormone therapy	$(2,405.00)	-22%	$(1,529.53)	-18%
Alzheimer's disease	$12,515.00	1%	$581,862.66	44%
Malnutrition in the elderly	$(113.00)	-100%	$-	0%
Osteoarthritis	$(8,389.00)	-7%	$(34,570.84)	-31%
Osteoporosis (including fractures)	$(2,038.00)	-2%	$(6,173.18)	-6%
Women's Health Initiative	$200.00	N/A	$(200.00)	-100%
Demography of aging	$(19,834.00)	-26%	$836.00	1%
Aging economics	$2,541.00	7%	$30,867.64	74%
Other	$539,411.00	67%	$(85,071.52)	-6%
Subtotal	$520,218.00	21%	$472,502.23	16%

	$ Change (FY17 to FY18)	% Change (FY17 to FY18)	$ Change (FY18 to FY19)	% Change (FY18 to FY19)
V. Metabolism/Endocrinology/Gastrointestinal				
Diabetes	$(105,412.00)	-20%	$47,381.85	11%
Obesity	$36,332.00	9%	$28,622.92	6%
Hepatobiliary diseases	$46,302.00	19%	$17,662.55	6%
Thyroid diseases/conditions	$(1,521.00)	-10%	$(2,488.00)	-19%
Fecal incontinence	$2,059.00	88%	$852.00	19%
Irritable bowel syndrome	$3,133.00	61%	$3,556.78	43%
Other	$19,322.00	14%	$11,209.52	7%
Subtotal	$215.00	0%	$106,797.62	8%
VI. Substance Abuse				
Etiology (unspecified)	$(3,414.00)	-3%	$1,413.79	1%
Epidemiology (unspecified)	$(899.00)	-1%	$266.69	0%
Prevention (unspecified)	$6,727.00	7%	$23,768.91	23%
Treatment (unspecified)	$(7,817.84)	-2%	$233,284.58	74%
Alcohol	$(2,399.47)	-1%	$7,119.78	4%
Illegal drugs	$17,303.58	4%	$146,448.34	31%
Prescription drugs	$48,160.00	76%	$84,046.55	75%
Tobacco products	$7,912.54	7%	$22,184.07	19%
Other substances	$2,417.13	16%	$6,555.14	37%
Co-occurring substance abuse & mental disorders	$797.11	11%	$647.59	8%
Subtotal	$68,787.04	5%	$525,735.45	34%
VII. Behavioral Studies/Programs				
Violence (including domestic, abused women, spousal abuse, elder abuse, trafficking, bullying)	$1,579.00	8%	$7,739.38	36%
Tobacco use cessation	$283.00	12%	$(942.86)	-37%
Physical activity/exercise/nutrition (promoting healthy behavior)	$41,935.00	16%	$16,935.87	6%
Other behavior change/risk modification	$22,691.07	4%	$(12,772.82)	-2%
Caregiving	$(4,352.04)	-21%	$(3,817.50)	-23%
Other	$107,999.00	18%	$90,168.20	13%
Subtotal	$170,135.04	12%	$97,310.27	6%
VIII. Mental Health				
Etiology (unspecified)	$10,735.00	30%	$(3,368.48)	-7%
Epidemiology (unspecified)	$1,318.30	260%	$(385.84)	-21%
Prevention (unspecified)	$27.00	7%	$(315.45)	-78%
Treatment (unspecified)	$(402.00)	-9%	$(407.55)	-11%
Depression/mood disorders	$3,215.21	2%	$58,334.23	39%
Suicide	$16,508.00	45%	$8,749.75	17%
Schizophrenia	$7,992.00	7%	$1,268.12	1%
Anxiety disorders	$977.00	2%	$(4,710.19)	-9%
Eating disorders	$536.00	3%	$4,920.35	29%
Psychosocial stress	$6,677.00	22%	$9,752.46	26%
Post-traumatic stress disorder (PTSD)	$5,309.79	21%	$1,659.78	5%
Other mental disorders (excluding Alzheimer's)	$(1,605.33)	-0%	$73,341.24	8%
Autism	$33,375.44	23%	$1,256.56	1%
Subtotal	$84,663.42	6%	$150,094.98	9%

	$ Change (FY17 to FY18)	% Change (FY17 to FY18)	$ Change (FY18 to FY19)	% Change (FY18 to FY19)
IX. Infectious Diseases				
HIV/AIDS	$80,589.67	3%	$5,110.04	0%
Tuberculosis	$50,353.00	24%	$188,356.22	71%
Sexually transmitted diseases (STDs)	$(7,741.00)	-4%	$39,779.35	24%
Topical microbicides	$(17,653.00)	-19%	$4,505.00	6%
Toxic shock syndrome	$281.00	N/A	$(57.00)	-20%
Tropical diseases (including malaria)	$67,992.94	11%	$(31,686.94)	-5%
Other	$(1,403.27)	-0%	$5,952.57	1%
Subtotal	$172,419.33	4%	$211,959.24	5%
X. Immune Disorders				
Rheumatoid arthritis	$(41,358.00)	-21%	$2,907.92	2%
Lupus erythematosus	$27,553.00	30%	$(9,041.72)	-8%
Multiple sclerosis	$1,730.00	2%	$6,708.82	7%
Myasthenia gravis	$(569.00)	-13%	$960.73	25%
Scleroderma	$1,978.00	18%	$1,357.46	11%
Sjögren's syndrome	$(1,721.00)	-8%	$4,154.70	20%
Takayasu disease	$-	N/A	$-	N/A
Other	$(40,406.71)	-20%	$4,849.60	3%
Subtotal	$(52,793.71)	-8%	$11,897.51	2%
XI. Neurologic, Muscular, & Bone				
Trauma research:				
Brain	$36,211.00	13%	$(21,688.72)	-7%
Other neurologic trauma	$(643.00)	-3%	$(1,294.00)	-7%
Bone-fracture (non-osteoporotic) and muscle injury	$(461.75)	-2%	$13,871.62	58%
Muscular dystrophy	$1,772.00	3%	$(2,597.91)	-4%
Chronic pain conditions	$6,957.00	5%	$335,627.87	210%
Temporomandibular disorders	$(33.00)	-0%	$(567.00)	-5%
Vulvodynia	$694.00	69%	$187.00	11%
Fibromyalgia & eosinophilic myalgia	$(910.00)	-17%	$(1,149.74)	-26%
Migraine	$593.00	4%	$7,240.33	52%
Sleep disorders	$26,382.60	43%	$(53,846.74)	-62%
Paget's disease	$292.00	34%	$2.71	0%
Parkinson's disease	$7,201.00	5%	$7,708.45	5%
Seizure disorders	$19,834.00	16%	$(1,909.65)	-1%
Other	$6,176.42	1%	$274,427.37	22%
Subtotal	$104,065.26	5%	$556,011.59	25%
XII. Kidney and Urologic				
Urinary tract infections (cystitis, pyelonephritis)	$(4,067.00)	-10%	$(12,532.00)	-33%
ESRD/transplantation	$7,749.00	6%	$(15,596.21)	-11%
Urinary incontinence	$476.00	5%	$6,355.00	59%
Painful bladder, interstitial cystitis	$(1,093.00)	-9%	$(2,301.00)	-20%
Other	$(4,148.45)	-1%	$20,616.78	5%
Subtotal	$(1,083.45)	-0%	$(3,457.43)	-1%

	$ Change (FY17 to FY18)	% Change (FY17 to FY18)	$ Change (FY18 to FY19)	% Change (FY18 to FY19)
XIII. Ophthalmic, Otolaryngologic, and Oral Health				
Eye diseases & disorders	$33,854.00	5%	$12,120.00	2%
Ear diseases & disorders	$928.00	0%	$18,813.00	9%
Dental and oral health	$19,074.00	5%	$17,247.77	4%
Other	$315.05	8%	$(386.58)	-9%
Subtotal	$54,171.05	4%	$47,794.18	3%
XIV. Health Effects of the Environment				
Environmental estrogens	$662.00	3%	$(9,854.00)	-44%
Health effects of toxic exposure (excluding cancer)	$3,031.00	3%	$10,669.20	9%
Toxicological research & testing program	$(988.00)	-1%	$3,680.00	4%
Chemical/biological warfare agents	$(735.00)	-10%	$(5,756.00)	-88%
Other	$(548.00)	-6%	$477.50	5%
Subtotal	$1,422.00	1%	$(783.30)	-0%
XV. Cross-Cutting Categories and Special Initiatives				
Treatment, prevention, & services	$54,215.00	11%	$(48,663.66)	-9%
Access to health care & financing	$4,069.00	44%	$1,021.24	8%
Education & training for health care providers	$(6,911.00)	-7%	$2,827.65	3%
Health literacy & bilingual information	$3,262.00	10%	$(1,048.67)	-3%
Cultural influences	$(140.00)	-0%	$961.31	1%
Disability research & services	$3,540.00	3%	$14,649.00	13%
Homelessness	$232.00	90%	$101.83	21%
Chronic fatigue syndrome	$937.00	8%	$439.81	3%
Breastfeeding	$6,213.00	1308%	$(2,065.27)	-31%
Organ donation	$402.00	N/A	$930.68	232%
Genetic services/counseling	$30,621.00	77%	$159,477.65	227%
Unintentional injury	$(8,630.00)	-15%	$(761.18)	-2%
Alternative & complementary therapies	$13,648.00	6%	$(9,291.05)	-4%
Health statistics & data collection	$(137,310.00)	-54%	$(61,163.83)	-52%
Programs/offices on women's health	$217,025.00	11%	$187,746.57	9%
Global health	$187,633.00	10%	$83,210.36	4%
Drug metabolism (sex differences, pregnancy, etc.)	$(134.00)	-2%	$713.77	12%
Subtotal	$368,672.00	7%	$329,086.19	6%
TOTAL	**$2,245,221.63**	**7%**	**$2,892,102.98**	**8%**

Report of the NIH Institutes, Centers, and Offices

Fogarty International Center

I. Executive Summary

The Fogarty International Center (FIC) seeks to advance the mission of the National Institutes of Health (NIH) by supporting and facilitating global health research conducted by U.S. and international investigators, building partnerships between health research institutions in the United States and abroad, and training the next generation of scientists to address global health needs. The Office of Research on Women's Health (ORWH) is among the many NIH Institutes, Centers, and Offices (ICOs) that collaborate with FIC to support this mission. Although FIC does not have any programs with a focus specifically and only on women's health issues, FIC's strategic plan demonstrates a commitment to the health of the most vulnerable and a focus on reducing health disparities, as outlined in the 21st Century Cures Act. Several FIC efforts support research and research training related to conditions that disproportionately or exclusively affect women or girls. FIC programs also enhance understanding of sex as a biological variable and gender differences. Scientific areas of focus include violence against women, mental health—including antenatal and postpartum depression and post-traumatic stress disorder—breast and cervical cancers, HIV/AIDS, pregnancy, and other reproductive health/contraception issues.

FIC accomplishments and activities particularly relevant to women's health and highlighted in this report include the following:

- The International Research Scientist Development Award (IRSDA) supports early-career U.S. scientists to pursue independent research careers in global health.
- The Fogarty Emerging Global Leader Award provides research support and protected time for career development activities to scientists from low- and middle-income countries (LMICs) who hold an academic junior faculty position or research scientist appointment at an LMIC academic or research institution.
- The Mobile Health: Technology and Outcomes in Low and Middle Income Countries (mHealth) program funds exploratory research studies on the development or adaptation of innovative mHealth technology specifically suited for use in LMICs and health-related outcomes.
- The HIV-associated Noncommunicable Diseases Research at Low and Middle Income Country Institutions program supports locally relevant research to enhance research capacity and build a network of researchers to address this critical burden.
- The Clean Cooking Implementation Science Network advances the science of uptake and scale-up of clean cooking technology in the developing world.
- The Adolescent HIV Prevention and Treatment Implementation Science Alliance aims to enhance the effective use of evidence and help overcome implementation challenges related to HIV among adolescents in sub-Saharan Africa.
- The Health Professional Education Partnership Initiative complements and enhances the training of a workforce to meet the biomedical, behavioral, and clinical research needs in high HIV-burden countries in Africa.
- The Global Health Program for Fellows and Scholars supports 1-year mentored clinical research experiences for postdoctorates, medical students, or graduate students in the health sciences at 27 LMIC research sites.
- The Fogarty HIV Research Training program strengthens the ability of LMIC institutions to conduct research on HIV in their country and to provide training in infrastructure development.
- Reducing Stigma to Improve HIV/AIDS Prevention, Treatment and Care in Low and Middle Income Countries seeks to stimulate new and impactful research on stigma reduction interventions leading to better outcomes for the prevention and treatment of HIV/AIDS.

II. Scientific Advances

In an ongoing effort to reduce sexual harassment in science, FIC has awarded funds to 10 LMIC institutions to shore up relevant policies, conduct training sessions, and create awareness of the processes to report sexual harassment. These 1-year supplemental awards are funded through the NIH Office of AIDS Research. During a recent virtual network meeting hosted by FIC, awardees discussed how their institutions are dealing with the problem and shared strategies on how to make improvements. Although grantees reported most organizations have anti-harassment policies in place, many said they were not well publicized, and reporting processes and follow-up procedures were not clearly defined. The conversation was intended to encourage collaboration in developing models to combat harassment that can be shared broadly.

FIC invests in building current and future leaders in global health research and encourages trainees to consider how they can advance the development of women's careers. Former Fogarty trainees and current grantees led and took part in the 2019 Women Leaders in Global Health Conference in Rwanda. Dr. Patty Garcia, a former Fogarty trainee and Peru's Minister of Health from 2016 to 2017, was part of the conference planning committee. During her 15 months in office, Garcia successfully pushed to allow contraception from the age of 14 to tackle Peru's teen pregnancy problem and changed the way Peru screens for cervical cancer. "We now have molecular testing and self-testing so women can be empowered taking their own samples," Garcia told the conference. But change didn't come without a struggle. "I got into a big fight with male physicians. They didn't want empowerment," said Garcia. The Bill & Melinda Gates Foundation's Dr. Anita Zaidi, who is also the principal investigator on a Fogarty-supported project on children's health, was also on the conference planning committee. She said, "To pursue a common mission that's higher than yourself and the people you're trying to lead," all leaders, male and female, need to be able to inspire others.

Dr. Lisa Bebell leveraged her two FIC fellowships in sub-Saharan Africa to successfully compete for a 5-year research career development grant from NIH's National Institute of Allergy and Infectious Diseases. In her 2005 fellowship, Bebell traveled to the Centre for the AIDS Programme of Research in South Africa (CAPRISA) for her first fellowship, to study mucosal immunity among women living with HIV. In a 2014 fellowship, Bebell conducted research at Mbarara University of Science and Technology in western Uganda, studying the postpartum risk for women with HIV to develop other infections after delivering their babies in a semi-rural hospital. The findings she published in conjunction with her partners showed there were fewer infections than expected but those that did exist—mainly urinary tract infections—were highly resistant to antibiotics. Her current career development grant is allowing her to test her hypothesis that placental inflammation may contribute to poor health outcomes for children who were HIV-exposed but uninfected (HEU). Now with dual appointments at Harvard Medical School and Massachusetts General Hospital, she's passing on what she learned during her Fogarty fellowships as she mentors the next generation of global health leaders.

Fogarty has provided over 25 years of support to HIV research through two HIV research training programs: the AIDS International Training and Research Program (AITRP) and the International Clinical, Operations and Health Services Research Training Award for AIDS and Tuberculosis program (IICOHRTA AIDS TB). In 2013, Fogarty consolidated these two programs into the new Fogarty HIV Research Training Program. This program seeks to strengthen the capacity of LMIC investigators and their institutions to conduct HIV-related research on the evolving HIV-related epidemics in their countries and to compete independently for research funding. Mentored research training projects conducted under this program include addressing AIDS-related cervical cancer (screening, exploring disease mechanisms, and identifying treatment strategies) and the treatment as prevention and prevention of mother-to-child transmission (PMTCT) of HIV. Dr. Carla Chibwesha, a HIV Research Training Program grantee, is building capacity around the intersection of HIV and women's reproductive health in Zambia. Her project leverages the connections between the University of North Carolina at Chapel Hill, the University of Zambia (UNZA), and the University of the Witwatersrand. It supports both doctoral and postdoctoral training for Zambian investigators and professional development of current faculty at the University of Zambia in order to develop a cadre of UNZA faculty researchers who are independently funded to conduct collaborative, multidisciplinary research in HIV and women's reproductive health. In addition, Dr. Chibwesha

also recently received an R21 from FIC to use an implementation science approach to address multilevel barriers to cancer screening among women living with HIV in South Africa (R21TW011715).

Fogarty's Reducing Stigma to Improve HIV/AIDS Prevention, Treatment and Care in Low and Middle Income Countries program seeks to support research on novel stigma reduction interventions, reducing the impact of stigma on adolescent or youth health, strategies to cope with stigmatization, and improved stigma measurement. Proposed collaborative exploratory research is expected to help build the capacity for full research programs by improving the research environment and strengthening LMIC individual and institutional research capabilities in the proposed research areas. Areas of study particularly focused on women include peer support to mitigate impact of stigma in HIV-positive pregnant women in South Africa, stigma reduction at time of entry into antenatal care to improve PMTCT services in Tanzania, and reducing intersectional stigma through increased social participation among transwomen in Nepal. Dr. Jill Owczarzak evaluated the role of layered stigma, the multiple stigmas that women often face because of having an HIV-positive status, drug use, and gender, among others, on engagement in care among HIV-positive women who use drugs in Ukraine (R21TW011060). Her study uses latent class analysis and in-depth interviews to empirically characterize patterns of HIV, drug use, and gender-based stigma among women living with HIV who use drugs in order to provide a more sophisticated perspective on the intersection between layered stigmas, mental health, and engagement in HIV care. The analysis revealed that requirements for internal passports and residency permits exposed these women to new forms of stigma and exclusion, such as reduced opportunities for employment and losing custody of children (Owczarzak et al., 2021).

III. Promotion of Women's Health Research

The FIC portfolio includes a variety of programs and projects related to research that disproportionately or exclusively affects women and/or girls. Several of these are in areas of expressed congressional interest, including neuroscience, cardiovascular disease and stroke, and inclusion of women in clinical research. FIC's programs fall under several of the Trans-NIH Strategic Plan for Women's Health Research's strategic goals, primarily Goal 1, "Advance rigorous research that is relevant to the health of women"; Goal 2, "Develop methods and leverage data sources to consider sex and gender influences that enhance research for the health of women"; and Goal 3, "Enhance dissemination and implementation of evidence to improve the health of women." A number of FIC's programs are training and fellowships so contributions to women's health are more aligned with creating opportunities for women scientists and promoting women's advancement and leadership in health research more globally. Highlights of these programs and projects are provided below.

FIC Programs in Support of Goal 1:

FIC's International Research Scientist Development Award (IRSDA) supports U.S. postdoctoral biomedical, epidemiologic, clinical, social, and behavioral scientists in the formative stages of their careers in pursuing careers in research on global health and preparing them for independent research by engaging in a mentored career development experience. Current IRSDA investigators are studying bone loss among people living with HIV in China, family smoking cessation starting with pregnant women in Romania, risk factors for sub-optimal breastfeeding among working mothers in Kenya, and mental health and understanding pre-exposure prophylaxis cascade in pregnant women and breastfeeding women in South Africa. With support from IRSDA, Dr. Tomi Akinyemiju is researching metabolic syndrome (MetS) and epigenetic markers of breast cancer in Nigerian women (Akinyemiju et al., 2017). In the past 40 years, Nigeria has seen a threefold increase in breast cancer incidence, and Nigerian women diagnosed with breast cancer are also more likely to present at younger ages, with highly aggressive, hormone receptor–negative tumors, associated with higher mortality. In response, Dr. Akinyemiju is examining the association between MetS and breast cancer overall and by subtype in Nigeria using newly diagnosed breast cancer cases and age-matched healthy controls. In addition, she will identify genome-wide DNA methylation differences between breast cancer tumor and adjacent normal tissue among women with and without MetS. This work, originally funded in 2016, expands research on female-specific conditions and diseases, as outlined in the Trans-NIH Strategic Plan

for Women's Health Research's Objective 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health").

The purpose of the FIC Emerging Global Leader Award is to provide 3 to 5 years of research support and protected time for career development activities to an early-career research scientist from an LMIC who holds a junior faculty position at an LMIC academic or research institution. Along with other ICs signed on to the funding opportunity announcement, including ORWH, FIC expects this intensive, mentored research career development experience to lead to an independently funded research career at an LMIC institution. FIC emerging leaders are advancing women's health research by studying the effect of hypertensive disorders in pregnancy and HIV infection on maternal, birth, and infant outcomes in South Africa, promoting physical activity and healthy eating in faith-based settings in Nigeria, and evaluating HIV self-testing as a means to empower prevention choices in Ugandan sex workers. Dr. Lola Kola is understanding the influence of sex and gender on the connection between the mind and body, the Trans-NIH Strategic Plan for Women's Health Research's Objective 1.4 ("Promote research that explores the influence of sex and gender on the connection between the mind and body, and its impact on health and disease") is being addressed by exploring the challenges of perinatal depression in Nigerian adolescents with patient-centered mobile health (K43TW011046). A combination of self-stigma and perceived stigma from health care workers exacerbate feelings of ostracization in adolescent mothers, who are less likely to attend treatment sessions and have children with poorer outcomes despite availability of effective treatment. In response, Dr. Kola will utilize a user-centered approach to design, develop, and refine the mHealth system for the treatment of adolescent perinatal depression within routine care and develop a roadmap to scale the application using implementation research approaches.

FIC Programs in Support of Goal 2:

The Fogarty Mobile Health: Technology and Outcomes in Low and Middle Income Countries (mHealth) program funds exploratory research studies on the development or adaptation of innovative mHealth technology specifically suited for use in LMICs and health-related outcomes associated with implementation of the technology. The overall goal of the program is to contribute to the evidence base for the use of mobile technology to improve clinical outcomes and public health. mHealth researchers are developing and testing mobile phone interventions that provide breastfeeding education support in India and management of gestational diabetes in Nepal. In response to the high number of cervical cancer deaths in Peru, one mHealth grantee is evaluating the efficacy of an mHealth-supported telecolposcopy approach in communities within Lima province, Peru (R21TW011223). During the study, originally funded in 2018, midwives conducting community-based screening are acquiring cervical images using a low-cost ultraportable colposcope and receive remote feedback from expert colposcopists using a mobile device. The central hypothesis is that access to expert colposcopists using an mHealth-supported telecolposcopy approach will improve the quality and timeliness of patient triage in community-based settings, increasing the proportion of women who receive a diagnosis and adhere to treatment. In support of the Trans-NIH Strategic Plan for Women's Health Research's Objective 2.2 ("Develop and adapt reliable and valid measures relevant to the health of women"), the study will use telemedicine to allow women to receive colposcopic evaluations in the communities where they live, precluding need for additional and distant clinical visits for diagnosis of cervical lesions.

FIC Programs in Support of Goal 3:

The HIV-associated Noncommunicable Diseases Research at Low and Middle Income Country Institutions program supports locally relevant research in critical areas of HIV-associated non-communicable diseases (NCDs) at LMIC institutions, to enhance research capacity and build a network of researchers both within and across LMICs to address this critical burden. Current investigators are addressing the dual burden of HIV and NCDs in pregnancy and assessing the cardiometabolic outcomes, mechanisms, and approach to prevention of dolutegravir-associated weight gain in South Africa. One project in South Africa is using an implementation science approach to address multilevel barriers to cancer screening among women living with HIV (R21TW011715). Dr. Carla Chibwesha is using a sequential mixed-methods design consisting of focus groups, a discrete choice experiment, and in-depth interviews to study multilevel drivers of cancer screening and determine women's preferences

for cancer screening services. She is then developing an intervention package with patients, providers, and policymakers and assessing its acceptability and collecting data to inform larger-scale implementation trials to promote uptake and improve retention in care. This study, funded in 2020, supports the Trans-NIH Strategic Plan for Women's Health Research's Objective 3.1 to design and test approaches to promote the adoption, adaptation, and integration of evidence-based interventions in public health, clinical practice, and community settings.

In addition to funding programs, FIC hosts two implementation science alliances that directly support the Trans-NIH Strategic Plan for Women's Health Research's Objective 3.2 ("Identify collaborative opportunities and leverage partnerships to disseminate research that improves the health of women"). FIC launched the Clean Cooking Implementation Science Network (ISN), which aims to advance collaborative efforts and understanding among researchers and implementers to accelerate adoption and use of clean cooking technologies. In many cultures, women traditionally do most of the cooking and, therefore, are disproportionately affected by the exposure to particulate matter and noxious gases from elemental stoves. The primary goal of the ISN is to develop an implementation science platform to advance the understanding of how to improve the uptake and sustained use of evidence-based clean cooking interventions to maximize their benefits on the health and longevity of populations in LMICs. In addition, FIC runs the Adolescent HIV Prevention and Treatment Implementation Science Alliance (AHISA), which convenes a forum that enables the exchange of ideas and experiences in understanding factors that drive uptake and adherence to adolescent HIV prevention and treatment strategies. Comprising program implementers, policymakers, and NIH-funded scientists, the group aims to enhance the use of evidence and help overcome implementation challenges related to prevention, screening, and treatment of HIV among adolescents in sub-Saharan Africa. Members' research addresses topics such as HIV treatment targeting adolescent girls in Zambia, cost-effective scale-up of cervical cancer prevention in sub-Saharan Africa, and gender-based violence and HIV risk.

IV. Advancement of Women in Biomedical Careers

Based on 25 years of experience in global health research training, FIC will continue to invest in building current and future leaders in global health research, strengthen the long-term capacity of research institutions to be sustainable platforms for cutting-edge science, and catalyze meaningful collaborations among institutions, as outlined in Goal 1 of FIC's strategic plan. FIC's research training portfolio generally addresses Goal 4 of the Trans-NIH Strategic Plan for Women's Health Research ("Promote training and careers to develop a well-trained, diverse, and robust workforce to advance science for the health of women") by supporting U.S. and LMIC women scientists' career development. All of FIC's research training grants involve a significant mentorship or capacity building component. Specifically, FIC's Health Professional Education Partnership Initiative (HEPI) and Global Health Program for Scholars and Fellows address Objective 4.2 ("Develop the next generation of researchers to advance science on the health of women"), 4.3 ("Enhance and develop programs to recruit, support, retain, and advance women at all stages of their research careers, from early career to leadership positions"), and 4.4. ("Promote and support policies, mentoring and networks, collaborations, and infrastructure to retain and advance women in their careers").

HEPI complements and enhances the training of a workforce to meet the biomedical, behavioral, and clinical research needs in low-resource, high HIV–burden countries in Africa, including Ethiopia, Kenya, Malawi, Mozambique, Tanzania, Uganda, Zambia, and Zimbabwe. The program leverages the achievements and lessons learned from the Medical Education Partnership Initiative (MEPI), MEPI Junior Faculty Research Training and Nursing Education Partnership Initiative. HEPI and MEPI Junior Faculty fund foreign institutions in sub-Saharan African countries to strengthen their capacity to carry out locally relevant research that contributes to improved human health and to foster the next generation of faculty researchers in Africa. The Limited Competition: Research Training for Career Development of Junior Faculty in MEPI Institutions states, "Support for increased engagement of female junior faculty and mentors in research activities in any relevant health area is also highly

desired." It is expected that increased research opportunities can add to the sustainability and quality of the HEPI program to strengthen medical education, promote faculty retention, and lead to the acquisition of new knowledge that contributes to improved human health.

FIC also promotes the careers of emerging young global health leaders through the Global Health Program for Scholars and Fellows. Fellows and Scholars, in partnership with NIH ICOs including ORWH, supports 1-year mentored clinical research experiences for postdoctorates, medical students, or graduate students in the health sciences at LMIC sites; more than half of the trainees are women. Following their year abroad, many female scholars and fellows successfully compete for a FIC IRSDA career development or Emerging Global Leader awards and acquire a faculty position at an academic institution and compete successfully for independent research funding (e.g., NIH R01). The most recent gender-focused clinical research from the program includes topics such as assessing maternal to fetal HIV transmission rates in Botswana, breast cancer diagnostic technology in Rwanda, training obstetric staff in the screening and assessment of antenatal depressive symptoms in India, and understanding how household air pollution affects pregnancy and child development outcomes in Guatemala. In response to high postpartum hemorrhaging (PPH) rates in Zimbabwe, one Fogarty Fellow is assessing the effectiveness of tranexamic acid in preventing PPH after cesarean delivery. Dr. Chipo Gwanzura is using her time as a Fogarty Scholar to prevent and decrease morbidity and mortality caused by PPH, the second-most common cause of maternal death in Zimbabwe, by building on her preliminary work that showed that the use of tranexamic acid was an efficacious prophylaxis for elective cesarean section.

V. Implementation of the NIH Policy on Sex as a Biological Variable (SABV)

Along with including the NIH policy in funding opportunity announcements and considering compliance during Research Performance Progress Reports, FIC shares NIH's policy with applicants and grantees and raises awareness of the policy through its research and training programs.

VI. Inclusion of Women in Clinical Research

FIC has incorporated the following language in its research training announcements to encourage research training activities related to sex and gender differences: "Where appropriate, the design of training-related research projects should take into account potential sex and gender differences that may affect the questions asked and the analyses performed. These might include different responses to and impacts of health interventions, differences in physiology, and different behavioral bases for disease prevention strategies."

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National Center for Advancing Translational Sciences

I. Executive Summary

The National Center for Advancing Translational Sciences (NCATS) catalyzes intervention development to bring more treatments to more patients more quickly. Translation is the process of turning observations in the laboratory, clinic, and community into interventions that improve the public's health. Translational science is the field of investigation focused on understanding the scientific and operational principles underlying each step of the translational process to speed therapy development that will benefit public health, including women's health.

NCATS' efforts are designed to complement and empower the research efforts of others. NCATS develops and disseminates translational science knowledge, technologies, expertise, and collaborative networks that allow researchers working on different diseases, including those affecting women, to advance their research. NCATS programs highlighted below often support research projects to improve women's health.

The NCATS Clinical and Translational Science Awards (CTSA) Program supports a national network of research institutions that work together to improve the translational research process. CTSA support enables research teams—including scientists, patient advocacy organizations, and community members—to tackle systemwide scientific and operational problems in clinical and translational research. CTSA awards provide support for pilot projects, training awards, biostatistics, and informatics infrastructure to investigators.

The Office of Rare Diseases Research coordinates and supports rare diseases research and provides information on rare diseases, including those exclusively or disproportionately affecting girls and women. It supports training of rare diseases investigators, a rare diseases clinical research network, and other scientific opportunities.

The Division of Preclinical Innovation plans and conducts collaborative research projects across the preclinical phases of the translational science spectrum to speed development of new potential therapies to test in future clinical studies. This could include new therapies to improve women's health.

The Office of Strategic Initiatives supports research programs such as tissue chips from both sexes to screen drugs for toxicities and possible therapeutic benefit.

II. Scientific Advances

The Impact of Systemic Lupus Erythematosus on the Clinical Phenotype of Antiphospholipid Antibody Positive Patients

Although systemic lupus erythematosus (SLE), a disease nine times more prevalent in women, is the most common autoimmune disease associated with antiphospholipid antibodies (aPL), limited data exist on the impact of SLE on the clinical phenotype of aPL-positive patients. The primary objective of this study (Unlu et al., 2019) was to compare the clinical, laboratory, and treatment characteristics of aPL-positive patients with or without SLE using a secure web-based data capture system that stores patient demographics and aPL-related clinical and laboratory characteristics. Inclusion criteria included aPL positivity according to the Updated Sapporo Classification Criteria. Patients fulfilling the SLE Classification Criteria and those with no other autoimmune diseases were included in the analysis.

The study included 672 aPL-positive patients recruited from 24 international centers; 426 had no autoimmune diseases, and 197 had SLE. The aPL with SLE group had higher rates of thrombocytopenia, hemolytic anemia, low complement levels, and IgA anti-β2 glycoprotein-I antibodies ($a\beta_2GPI$), whereas the aPL only group had higher rates of cognitive dysfunction and IgG $a\beta_2GPI$. The frequency of arterial and venous thromboses (including recurrent) as well as the pregnancy morbidity were similar between the groups. The prevalence of cardiovascular disease risk factors at the registry entry

did not differ between the two groups, except current smoking, which was more frequent in the aPL with SLE group.

The conclusions were that the frequencies of thrombosis and pregnancy morbidity are similar between aPL-positive patients with or without SLE. However, the diagnosis of SLE in persistently aPL-positive patients is associated with an increased frequency of thrombocytopenia, hemolytic anemia, low complement levels, and IgA aβ_2GPI positivity.

This clinical study relates to Goal 1 of the Trans-NIH Strategic Plan for Women's Health Research ("Advance rigorous research that is relevant to the health of women").

Optimizing Perioperative Pain Control After Ambulatory Urogynecologic Surgery

This study (Winkelman et al., 2020) aimed to determine the impact of a multimodal protocol on opiate use and postoperative pain after ambulatory urogynecologic surgery. This was a retrospective cohort study comparing ambulatory urogynecologic surgery patients treated under a standard perioperative pain protocol with those treated under a multimodal perioperative pain protocol. The multimodal protocol consisted of preoperative gabapentin and acetaminophen and postoperative scheduled doses of acetaminophen and nonsteroidal anti-inflammatory drugs. Pain scores were obtained from nursing records and assessed on the Numeric Rating Scale 11 per hospital protocol. All opioid dosages were converted into morphine milligram equivalents using standardized conversion tables.

One hundred nine patients were treated under the standard protocol and 112 under the multimodal protocol. Patients had similar baseline characteristics. Overall, a minority of patients (39%) used postoperative opioids; this was similar in the 2 groups (P=0.45). The two groups also were similar regarding total postoperative morphine milligram equivalents (P=0.35). Postoperatively, patients treated under the standard protocol had higher mean pain scores (2.2 versus 1.4, P=0.002). Patients treated under the standard protocol were also significantly more likely to report postoperative pain (69%) than those treated under the multimodal protocol (52%; P=0.01), and the multimodal protocol was associated with a 25% lower risk of postoperative pain (risk ratio, 0.75; 95% confidence interval, 0.60–0.94) than the standard protocol.

The study concluded that patients infrequently use opiates after ambulatory urogynecologic surgery. The use of a multimodal pain protocol was associated with lower pain scores, and patients in a multimodal pain protocol were more likely to report no pain.

This clinical study relates to Goal 1 of the Trans-NIH Strategic Plan for Women's Health Research ("Advance rigorous research that is relevant to the health of women").

Sex Differences in Perioperative Outcomes After Complex Abdominal Aortic Aneurysm Repair

Female sex is associated with worse outcomes after infrarenal abdominal aortic aneurysm (AAA) repair. However, the impact of female sex on complex AAA repair is poorly characterized. The investigators in this study (de Guerre et al., 2020) compared outcomes between female and male patients after open and endovascular treatment of complex AAA by identifying all patients who underwent complex aneurysm repair between 2011 and 2017 in the American College of Surgeons National Surgical Quality Improvement Program's targeted vascular module. Complex repairs were defined as those for juxtarenal, pararenal, or suprarenal aneurysms. They compared rates of perioperative adverse events between female and male patients stratified by open AAA repair and endovascular aneurysm repair (EVAR). Propensity scores were calculated, with inverse probability-weighted logistic regression to identify independent associations between female sex and outcomes.

Investigators identified 2,270 complex aneurysm repairs, of which 1,260 were EVARs (21.4% female) and 1,010 were open repairs (30.7% female). After EVAR, female patients had higher rates of perioperative mortality (6.3% versus 2.4%; P=0.001) and major complications (15.9% versus 7.6%; P<0.001) compared with male patients. In contrast, after open repair, perioperative mortality was not significantly different (7.4% versus 5.6%; P=0.3), and the rate of major complications was similar (29.4% versus 27.4%; P=0.53) between female and male patients. Furthermore, even though perioperative mortality was significantly lower after EVAR compared with open repair for male patients

(2.4% versus 5.6%; *P*=0.001), this difference was not significant for women (6.3% versus 7.4%; *P*=0.60). On multivariable analysis, female sex remained independently associated with higher perioperative mortality (odds ratio [OR], 2.5; 95% confidence interval [CI], 1.3–4.9; *P*=0.007) and major complications (OR, 2.0; 95% CI, 1.3–3.2; *P*=0.002) in patients treated with EVAR but showed no significant association with mortality (OR, 0.9; 95% CI, 0.5–1.6; *P*=0.69) or major complications (OR, 1.1; 95% CI, 0.8–1.5; *P*=0.74) after open repair. However, the association of female sex with higher perioperative mortality in patients undergoing complex EVAR was attenuated when diameter was replaced with aortic size index in the multivariable analysis (OR, 1.9; 95% CI, 0.9–3.9; *P*=0.091).

The authors concluded that female sex is associated with higher perioperative mortality and more major complications than for male patients after complex EVAR but not after complex open repair. Continuous efforts are warranted to improve the sex discrepancies in patients undergoing endovascular repair of complex AAA.

This clinical study relates to Objective 1.2 of the Trans-NIH Strategic Plan for Women's Health Research ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes").

Affordable Care Act State-Specific Medicaid Expansion: Impact on Health Insurance Coverage and Breast Cancer Screening Rate

Under the Affordable Care Act, States were given the option to expand Medicaid in 2014. By the end of 2014, 32 States had opted to expand Medicaid and 19 had not. Previous quasi-experimental studies took advantage of this State-specific policy implementation and found increased insurance coverage in expansion compared with nonexpansion States. With longer-term data now available, these investigators studied the effect of Medicaid expansion on changes in insurance coverage and mammography rates in expansion and nonexpansion States.

Seven States that expanded Medicaid eligibility in 2014 and 6 nonexpansion States were selected based on available data. The U.S. Census American Community Survey was queried for insurance coverage from 2011 to 2016, and the CDC Behavioral Risk Factor Surveillance System from 2010 to 2018 was used. Difference-in-difference linear mixed models were used to estimate and compare insurance coverage and screening mammogram rates between expansion and nonexpansion States before and after 2014.

Investigators found the increase in insurance rates for all people covered by some type of health insurance after Medicaid expansion was significantly different in expansion than nonexpansion States (*P*=0.001). The increase in Medicaid coverage was significant in expansion compared with nonexpansion states (*P*<0.001). A similar trend was seen in screening mammogram rates among women from low-income households in expansion versus nonexpansion States (Yoshiko et al., 2020) (*P*=0.049).

This study concluded that Medicaid expansion States saw greater improvement in total insurance and Medicaid coverage and in mammogram rates in lower-income women compared with nonexpansion States after Medicaid legislation was passed. This demonstrates that people do take advantage of expanded eligibility by acquiring insurance, which can improve access to preventive measures such as screening mammography.

This clinical study relates to Goal 3 of the Trans-NIH Strategic Plan for Women's Health Research ("Enhance dissemination and implementation of evidence to improve the health of women").

Exposure to Trichloroethylene Metabolite S-(1,2-Dichlorovinyl)-L-cysteine Causes Compensatory Changes to Macronutrient Utilization and Energy Metabolism in Placental HTR-8/SVneo Cells (Elkin et al., 2020)

Trichloroethylene (TCE) is a widespread environmental contaminant following decades of use as an industrial solvent, improper disposal, and remediation challenges. Consequently, TCE exposure continues to constitute a risk to human health. Despite epidemiological evidence associating exposure with adverse birth outcomes, the effects of TCE and its metabolite S-(1, 2-dichlorovinyl)-L-cysteine (DCVC) on the placenta remain undetermined.

Flexible and efficient macronutrient and energy metabolism pathway utilization is essential for placental cell physiological adaptability. Because DCVC is known to compromise cellular energy status and disrupt energy metabolism in renal proximal tubular cells, this study investigated the effects of DCVC on cellular energy status and energy metabolism pathways in placental cells.

Human extravillous trophoblast cells, HTR-8/SVneo, were exposed to 5-20 µM DCVC for 6 or 12 h. After establishing concentration and exposure duration thresholds for DCVC-induced cytotoxicity, targeted metabolomics was used to evaluate overall energy status and metabolite concentrations from energy metabolism pathways.

The data revealed glucose metabolism perturbations including a time-dependent accumulation of glucose-6-phosphate+frutose-6-phosphate (G6P+F6P) as well as independent shunting of glucose intermediates that diminished with time, with modest energy status decline but in the absence of significant changes in ATP concentrations. Furthermore, metabolic profiling suggested that DCVC stimulated compensatory utilization of glycerol, lipid, and amino acid metabolism to provide intermediate substrates entering downstream in the glycolytic pathway or the tricarboxylic acid cycle. Lastly, amino acid deprivation increased susceptibility to DCVC-induced cytotoxicity. Taken together, these results suggest that DCVC caused metabolic perturbations necessitating adaptations in macronutrient and energy metabolism pathway utilization to maintain adequate ATP levels.

This basic science research relates to Objective 1.3 of the Trans-NIH Strategic Plan for Women's Health Research ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes").

III. Promotion of Women's Health Research

National COVID Cohort Collaborative

During public health emergencies like COVID-19, science—and the process of turning observations into new therapies—must be translated faster than ever. Vast amounts of clinical data are being generated that could be used to advance research efforts focused on COVID-19. These datasets often become too large to share and the networks for data management are so dissimilar that they cannot be combined easily, creating roadblocks along the path to developing new treatments. With no standardized way to collect and harmonize all these data being generated, there is an urgent need for a COVID-19 analytics platform that can turn all these data into new knowledge that can speed research efforts across the country. Making data more meaningful, open, and accessible is a key goal in NCATS' efforts to improve translational science and advance research across many diseases. An effort called the National COVID Cohort Collaborative, or N3C, built a centralized national data resource—the NCATS N3C Data Enclave—in 2020 that the research community uses to study COVID-19 and identify potential treatments as the pandemic continues to evolve. Specifically, the N3C enables the rapid collection and analysis of clinical, laboratory, and diagnostic data from hospitals and health care plans. This approach will likely be applicable to other research questions and may serve as a model for addressing future public health emergencies. The N3C data enclave is open and available for the research community. Currently, N3C Domain Teams are forming (or have formed) to connect researchers with shared interests so they can analyze data within the N3C Data Enclave and collaborate more efficiently. The Pregnancy Clinical Domain Team aims to leverage N3C data to gain insights into pressing COVID-19 questions around pregnancy. The goal is to understand incidence, timing, and severity of COVID-19 in pregnant women, associated maternal and infant outcomes, and related characteristics (clinical, demographic, environmental).

Maternal Mortality

As part of the trans-NIH initiative Implementing a Maternal health and PRegnancy Outcomes Vision for Everyone (IMPROVE) to support research to address the rising U.S. rates of maternal mortality, NCATS in 2020 fully funded or co-funded eleven Clinical and Translational Science Awards (CTSA) Program administrative supplement applications that responded to NOT-OD-20-104. These awards will address the maternal mortality disparity affecting African American, rural, and underserved populations and focus on mostly common preventable causes of maternal deaths, including cardiovascular and hemorrhage, through application of translational science.

The Issuance of Notice of Special Interest (NOT-TR-20-007): Research through NCATS' Clinical and Translational Science Award (CTSA) Program: Collaborative Innovation Awards (U01 and R21) highlighted NCATS' interest in receiving grant applications focused on racial and ethnic disparities in maternal mortality.

Tissue Chips for Drug Screening

Approximately 30% of promising medications fail in human clinical trials because of toxicities, despite promising preclinical animal studies. To address this problem, NCATS' Tissue Chip program funds tissue chip devices designed to be accurate models of human organ structure and function. Tissue chips—small 3D bioengineered devices using human tissues from both sexes—could improve drug testing and development by predicting more accurately how safe and effective drugs are before they are tested in people.

Tissue chips also allow modeling of maternal morbidity and mortality and the influence of sex on health and disease. In 2020, NCATS—with co-funding from NIAMS, NCI, and NICHD—issued 10 "Clinical Trials" on a Chip (CToC) awards to develop tissue chips to inform clinical trial design, patient exclusion criteria, patient stratification, and selection of clinically relevant biomarkers. One CToC award issued to Drs. Arum Han and Ramkumar Menon at Texas A&M University and the University of Texas will develop a maternal–fetal interface on a chip to study both infection and inflammation-induced pre-term birth (PTB). To study the interface and its response to infection and inflammation, the team will develop a maternal–fetal interface on a chip. A candidate anti-inflammatory drug will be delivered to evaluate its effectiveness in reducing PTB risk (funded by NCATS and NICHD).

Another tissue chip project, led by Dr. Julie Kim at Northwestern University, is "Polycystic Ovary Syndrome (PCOS) and Androgen-Related Disease Modeling and Drug Testing in Multi-Organ Integrated Microfluidic Reproductive Platform." The team created a next-generation platform to support the translation from mouse-to-human models of the female reproductive system (ovaries, fallopian tubes, uterus, cervix, adipose, liver, and pancreas). Previously, this human model demonstrated capability of mimicking a 28-day menstrual cycle and is being used to screen drugs to treat PCOS (funded by NCATS and NIEHS).

Clinical and Translational Science Awards (CTSA) Program

The NCATS Clinical and Translational Science Awards (CTSA) Program strengthens and supports clinical and translational research from scientific discovery to improved patient care and leverages the expertise and resources from a network of high-performing biomedical research institutions across the United States. A nationwide network of biomedical research hubs forms the backbone of the program in addressing important roadblocks in clinical translation by working locally, regionally, and nationally on research and training in translation. Hubs can support research of special interest to their institutions, such as women's health, and issues such as novel approaches to the recruitment of women, minorities, and individuals living in rural areas, who are often underrepresented in clinical research and clinical trials.

Programs within the individual CTSA program hubs support aspects of women's health research. Examples include:

- The Women's Health Practice-Based Research Network (WHPBRN), which promotes collaboration between practitioners and clinical investigators to improve women's health. This network is part of Magee-Womens Research Institute and the University of Pittsburgh CTSI.
- Women's Health Research Pilot Grant Program. The Purdue Women's Global Health Institute (WGHI) and Indiana Clinical and Translational Sciences Institute (CTSI) have teamed up to fund translational research of women's health issues focusing on prevention and early detection of disease.

CTSA hubs fund over 300 clinical pilot projects per year through the hub award. In FY 2019, at least 38 were focused on women's health research. Topics included the role of endocrine aging on brain metabolism and mitochondrial function, preterm birth, health disparities in breast cancer care, the impact of menopause on sleep, risk stratification in benign breast disease, and maternal morbidity and mortality. Pilot projects may generate sufficient findings to answer the scientific questions of the project, or data may be used to inform a larger, more robust study of the topic.

CTSA Program Trial Innovation Network: Recruitment Innovation Center

The Trial Innovation Network (TIN) is a collaborative program started in 2016 with three key partners: three Trial Innovation Centers, a Recruitment Innovation Center (RIC), and the CTSA Program hubs. NCATS' vision for the TIN is to address critical roadblocks in clinical trials and accelerate the translation of interventions into beneficial therapies.

The Recruitment Innovation Center at Vanderbilt University leverages expertise in clinical informatics and patient and community engagement to accelerate recruitment and enhance retention in clinical trials. This includes increasing the number of underrepresented minorities, including women of color, enrolled in clinical research studies. The RIC pairs informatics expertise with engagement expertise to create customized engagement and recruitment materials. RIC researchers and their collaborators publish peer-reviewed manuscripts, create videos, and provide other resources that promote evidence-based strategies to enhance engagement, recruitment, and retention of disenfranchised people in research studies. The RIC has provided more than 100 consultations to investigators seeking assistance with their clinical studies. In FYs 2019 and 2020, this included investigators planning studies or trials to treat diseases that disproportionately affect women. Examples include clinical trials to treat postpartum cardiac complications, ongoing trials to prevent Alzheimer's disease, heart disease in those over 75 years of age, and community-based weight loss programs. They also developed generalized recruitment materials for use in COVID-19 trials to reach communities of color.

RIC investigators also reach out directly to patients through Trials Today, a portal where patients can learn more about trials and register to be contacted. Another RIC resource is Faster Together, a web-based course for investigators to enhance recruitment of minorities in clinical trials.

IV. Advancement of Women in Biomedical Careers

Training & Career Development

The CTSA Program supports two types of formal clinical research training awards at CTSA Program hubs. These training programs, imbedded within the CTSA Program for over 10 years, have been very successful at training women, including those from underrepresented minorities, for careers in biomedical research (Sweeney et al., 2017). Both programs combine formal course work with direct research experience, and many institutions' programs offer opportunities to pursue additional advanced degrees. The institutional awards (known as KL2s) support mentored research career development for clinical investigators who have recently completed professional training and who are commencing basic, translational, and/or clinical research. The CTSA Program hub selects candidates, providing them with a rich career development experience in a multidisciplinary setting. These appointees—referred to as Clinical Research KL2 Scholars—come from a variety of fields (e.g., medicine, dentistry, nursing, the behavioral sciences, biostatistics, and epidemiology) and can receive up to 5 years of career development support.

KL2 Scholars and TL1 Trainee Awardees Female Representation

- In FY 2019, 339 scholars were funded by the CTSA KL2 Scholars program. Of these, 56% identified as female. Data from FY 2020 is not complete, as these data are extracted manually from annual progress reports.
- In FY 2020, 335 predoctoral trainees and 184 postdoctoral trainees were funded by NCATS. Of these, 57.6% identified as female.

In addition to training awards, individual CTSAs may offer programs to advance the biomedical careers of women. Two examples are:

- ***Mayo Clinic Center for Clinical and Translational Science (CCaTS)***
  Mayo CCaTS, WE-SPARK has monthly invited guest lectures focused on female entrepreneurship in the life sciences and health that is funded and co-led by the Office of Entrepreneurship.

» ***National Research Mentoring Network (NRMN)*** The National Research Mentoring Network (NRMN) Strategic Empowerment Tailored for Health Equity Investigators recruits underrepresented minority (URM) early-stage investigators and women for a virtual grant writing and coaching intervention. The primary sponsor is the NIH's National Institute of General Medical Sciences (NIGMS). The Georgia Clinical and Translational Science Award (CTSA) supports NRMN with research mentors and access to institutional resources.

V. Implementation of the NIH Policy on Sex as a Biological Variable (SABV)

All new scientific staff attend the NIH Core Curriculum. NCATS Program Officials participate in training about NIH's policy to consider sex as a biological variable (SABV) in research design, analysis, and reporting. NCATS expects that SABV will be factored into research designs, analyses, and reporting in vertebrate animal and human studies in grant applications and awarded studies. Strong justification from the scientific literature, preliminary data, or other relevant considerations must be provided for applications proposing to study only one sex. Reviewers of grant applications are asked to consider whether the applicants have presented adequate plans to address relevant biological variables, such as sex, for studies in vertebrate animals or human subjects. Unacceptable plans for either animal or human studies must be reflected in the priority score of the application and documented in the Summary Statement. Applications with unacceptable SABV plans receive a bar to funding; an award is not issued until an acceptable resolution is received that is considered appropriate by the NCATS Program Officer.

Intramural investigators are required to consider SABV in all experimental research design and studies. When purchasing and/or acquiring human or animal cells, investigators are required to purchase and/or acquire both male and female cells, if possible, unless the disease is primarily prevalent in males or females. However, there are situations in which cells are immortalized and have gone through so many passages that the sex is no longer known. For animal studies, investigators are required to plan a study with 50% male and 50% females unless the disease is primarily in one sex of the affected human population. All toxicology and toxicokinetic studies will have both male and female animals in a protocol. In addition, mixed male and female liver microsomes and cytosols are used for *in vitro* absorption, distribution, metabolism, and excretion (ADME) studies.

VI. Inclusion of Women in Clinical Research

CTSA Program Trial Innovation Network: Recruitment Innovation Center

The Recruitment Innovation Center (RIC) at Vanderbilt University leverages expertise in clinical informatics and patient and community engagement to accelerate recruitment and enhance retention in clinical trials. This includes increasing the number of underrepresented minorities, including women of color, enrolled in clinical research studies. RIC researchers and their collaborators have created a tool kit of peer-reviewed manuscripts, videos, and other resources for researchers to use to enhance engagement and recruitment of participants.

NCATS Program

The NCATS program development process involves several strategies to support the inclusion of a diverse population in clinical studies and workforce development. Funding announcements contain language requiring that women and minorities be included in all clinical research studies as appropriate for the scientific goals of the work proposed. The current CTSA funding announcement (PAR-18-940) states that the application review and award decisions will include consideration of efforts to include special populations such as children, the elderly, rural populations, minorities, pregnant women, people with disabilities, and hard-to-reach populations. NCATS ensures that all applicants, peer reviewers, NCATS Scientific Review Officers, Program Officers, and Grants Management Officers are aware of the NIH policies on inclusion on the basis of sex/gender, race, ethnicity, and age in clinical research. Internet resources are available for NCATS staff to learn about including diverse populations in clinical research.

For proposed research projects, inclusion is first addressed in peer review. After provided with guidance on reviewing inclusion on the basis of sex/gender, race, ethnicity, and age, reviewers evaluate applications for the appropriateness of the proposed plan for inclusion. Unacceptable inclusion plans must be reflected in the priority score of the application and documented in the Summary Statement. Applications with unacceptable inclusion plans receive a bar to funding; an award is not issued until an acceptable resolution is received that is considered appropriate by the NCATS Inclusion Policy Officer.

Prior to award, program staff are responsible for reviewing inclusion information in the application and Summary Statement and indicating whether plans are scientifically appropriate. Program staff monitor actual enrollment progress in annual progress reports and consult with investigators when necessary. Grants management staff ensure that appropriate terms and conditions of award are included in Notices of Award and information is documented in the official grant file.

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National Center for Complementary and Integrative Health

I. Executive Summary

The National Center for Complementary and Integrative Health (NCCIH) is the lead Federal agency for scientific research on the fundamental science, usefulness, and safety of complementary and integrative treatments and practices. To address the need for objective evidence on the safety and efficacy of these approaches, NCCIH supports rigorous scientific investigation to better understand how these interventions impact health, for whom, and the optimal methods of practice and delivery.

NCCIH supports research on a diverse group of health practices encompassing dietary, psychological, and physical approaches that may have originated outside of conventional medicine and includes natural products, such as dietary supplements, plant-based products, and probiotics, as well as mind and body approaches, such as yoga, massage therapy, meditation, mindfulness-based stress reduction, spinal/joint manipulation, and acupuncture. In clinical practice, these approaches are often combined into multimodal therapeutic systems—such as traditional Chinese medicine, Ayurveda, and naturopathy—that have an underlying diagnostic and theoretical framework that may be different from that of conventional medicine. These practices and systems are considered complementary because they are used in conjunction with conventional medicine. Integrative health care seeks to bring conventional and complementary approaches together in a safe, coordinated way with the goal of improving clinical care for patients, health restoration, resilience, health promotion, and disease prevention.

II. Scientific Advances

Sex Differences in Interactions Between Intervertebral Disc Degeneration and Pain Demonstrated by New Animal Study

The interactions between intervertebral disc degeneration (IVD) and pain differ between the sexes, according to the findings of an NCCIH-funded study in an *in vivo* rat model. The study, conducted at Icahn School of Medicine at Mount Sinai, was published in *Scientific Reports*.

Forty-eight Sprague-Dawley rats underwent lumbar IVD puncture or sham surgery; IVD degeneration and pain were assessed 6 weeks later. In both sexes, lumbar puncture induced structural IVD degeneration, but females and males had distinct differences in pain as assessed by dorsal root ganglia expression of the pain-related genes *Calca* and *Tac1* and by the von Frey assay for mechanical allodynia. (Mechanical allodynia is a condition caused by injury in which gentle, harmless touches become painful; it's why putting on a lightweight shirt hurts when your shoulders are sunburned.) Injury was associated with the measures of pain in male rats but not in females.

Both low-back pain and IVD degeneration are extremely common medical problems. IVD degeneration is highly associated with low-back pain, but the relationship between them is complicated, and pain often doesn't correlate with imaging findings. The results of this study add to the understanding of the complex nature of the relationship between IVD injury and pain, provide additional evidence for the relevance of the experimental model used in this study, and highlight the importance of sex as a major source of variance. (Mosley et al., 2020)

Cannabis Use, But Not Tobacco Smoking, Has Increased Among New Mothers

Cannabis use has approximately doubled among new mothers in the United States in recent years, but the proportion of new mothers who smoke tobacco has not changed, according to an analysis of data from the U.S. National Health and Nutrition Examination Survey (NHANES). The new NCCIH-supported analysis, conducted by researchers from Michigan State University, was published in the journal *Addiction*.

NHANES is designed to be nationally representative of the noninstitutionalized U.S. civilian population. The data collected include serum cotinine levels (an indicator of exposure to tobacco smoke) and self-reports of tobacco use for the entire period analyzed (2001–2018). Data on self-reported cannabis use were available for the years 2005–2018. For the purposes of this analysis, women within 2 years of childbirth were considered new mothers.

From 2005 to 2018, 10.6% of new mothers reported having used cannabis at least once in the 30 days prior to the survey. The prevalence of cannabis use rose over time, from 9% in 2005–2006 to 19.5% in 2017–2018. From 2001 to 2018, 20.9% of the new mothers were tobacco smokers. There was no significant change in the prevalence of tobacco smoking over time.

Exposure to maternal tobacco smoking is linked with adverse health outcomes in infants, and concerns have been raised about the health effects of exposure to cannabis as well. The researchers who conducted this study concluded that the increase in cannabis use prevalence among new mothers is alarming. The results of this analysis can guide clinicians' efforts to screen and counsel new mothers on cannabis use. (Alshaarawy et al., 2021)

Study Explores Online Yoga to Reduce Psychological Distress in Women After Stillbirth

Online yoga may be an effective and feasible strategy to reduce depressive symptoms, perinatal grief, and symptoms of post-traumatic stress disorder (PTSD) in mothers who have experienced stillbirth, according to a preliminary study funded by NCCIH. The study—from Arizona State University, Colorado School of Public Health, and University of Michigan Medical School—was published in the journal *BMC Complementary Medicine and Therapies.*

Mothers who have lost babies to stillbirth have increased risks of PTSD, clinical depression, and anxiety disorders. These effects may be long-lasting and may even have an impact on the health of the mother and child in later pregnancies. Yoga has been reported to reduce symptoms of PTSD, anxiety, and depression in several populations. This study evaluated the feasibility and preliminary efficacy of a yoga intervention in women who have lost a baby to stillbirth.

Ninety women who had experienced stillbirth within the previous 2 years and who had post-traumatic stress symptoms were recruited nationally and randomly assigned to 12 weeks of either a low- or moderate-dose yoga intervention or a control stretch-and-tone exercise intervention. The programs were delivered online. More than half of the participants completed the intervention, and most reported satisfaction and enjoyment. Participants in both yoga groups showed significant decreases in symptoms of PTSD and depression, as well as improvements in self-rated health, after the intervention. Participants in the moderate-dose yoga group reported that the 150 prescribed minutes of yoga per week was too much.

The authors concluded that the results of this study were promising enough to warrant further investigation of yoga as an intervention for mothers after stillbirth. (Huberty et al., 2020)

New Tools Can Assess Women's Self-Efficacy and Observed Success in the Practice of Therapeutic Yoga

Although yoga has been evaluated for many therapeutic uses, few studies have measured participants' self-efficacy regarding the performance of yoga postures (whether they believe they can do them) and their success in performing them (whether they can actually do them). In this new NCCIH-supported study from the University of California, San Francisco and the San Francisco Veterans Affairs Health Care System, tools to evaluate self-efficacy and observed success in practicing yoga were developed and piloted in the context of a trial of a yoga intervention for urinary incontinence in women. The study was published in *BMC Complementary Medicine and Therapies.*

This study involved 27 women who were participating in a randomized trial to assess the feasibility, tolerability, acceptability, and preliminary efficacy of an Iyengar-based yoga program for urinary incontinence in middle-aged and older women. A self-assessment instrument, in which the women rated their confidence in performing each of 15 yoga postures on a 5-point scale, was developed for use at the end of the 12-week program. The participants were also asked to rate their self-efficacy in being able to adhere to regular yoga practice. An expert consultant visited each class during the 12th week and assessed individual participants'

competency in performing the yoga postures on a 5-point scale.

The new measures may help advance yoga research by describing specific components of yoga interventions and by making it possible to assess whether study participants can learn physical aspects of yoga and maintain a yoga practice over time. They may help inform instructors about participants who may need extra assistance, and they may be useful in studies that assess the effects of yoga on specific health outcomes. (Nicosia et al., 2020)

Greater Mindfulness Is Linked to Lower Pain, Fatigue, and Psychological Distress in Women with Metastatic Breast Cancer

Higher levels of mindfulness were associated with lower levels of symptoms—including pain, fatigue, anxiety, depression, and sleep disturbance—in women with metastatic breast cancer, according to an NCCIH-funded study conducted at Duke University Medical Center and cooperating institutions, published in *Psychooncology*.

Women with metastatic breast cancer report high levels of symptoms such as pain, fatigue, psychological distress, and sleep disturbance. Mindfulness might be helpful for these symptoms, but little research on it has been done in this population. This study reports results from a questionnaire on mindfulness (the Five Facet Mindfulness Questionnaire-Short Form) completed by 64 women with metastatic breast cancer before they participated in a trial of a mindful yoga intervention. The questionnaire includes five mindfulness subscales: observing, describing, acting with awareness, nonjudging, and nonreactivity. Symptoms were assessed using self-report measures of pain, fatigue, sleep quality, and psychological distress.

Overall, higher mindfulness was associated with lower symptom levels. Higher scores on each of the five facets were associated with lower scores for at least one symptom, and none of the facets of mindfulness was associated with higher symptom scores. Nonreactivity, nonjudging, and describing showed the most frequent and strongest associations with symptoms. The authors of the study suggested that assessing mindfulness in patients with metastatic cancer may help identify those who are at risk for experiencing greater symptoms. Such patients might benefit from education on mindfulness skills to improve symptom management. (Zimmaro et al., 2020)

III. Promotion of Women's Health Research

Goal 1 of the Trans-NIH Strategic Plan for Women's Health Research: Advance rigorous research that is relevant to the health of women.

Feasibility of a Yoga Intervention in Sedentary African American Women

Decreasing sedentary behavior has numerous health benefits. Yoga is an emerging activity that has the potential to decrease sedentary behavior in adults and reduce risk factors such as high blood pressure and stress. Although yoga has the reputation of attracting college-educated, non-Hispanic White populations and is sometimes viewed as exclusionary to those outside that community, it has become increasingly popular among African Americans with the growth of Afrocentric (i.e., focusing on Black or African culture) yoga, the establishment of Black yoga organizations, and the expansion of social media presence of African American yoga practitioners. The literature suggests that yoga could be an effective strategy to address adverse health outcomes by decreasing sedentary behavior in African Americans; however, this has not been examined in African American women. This research will test the feasibility, acceptability, safety and targeted outcomes of a 3-month hatha (which involves breath, body, and mind, and classes are usually 45 minutes to 90 minutes of breathing, yoga poses, and meditation) and restorative yoga intervention to decrease sedentary behavior (primary outcome), stress, and blood pressure in 60 sedentary (less than 30 minutes of moderate-to-vigorous physical activity per week) African American women. This intervention could have broad public health impact in the future, as it will be ultimately grounded in feasibility, generalizability, and efficacy and targets a population with a high level of sedentary behavior and chronic disease comorbidities.

Prebiotic Activity of Tart Cherry and the Immunoregulation of Bone Homeostasis

Worldwide, an estimated 1 in 3 women over the age of 50 experience an osteoporotic fracture. In the U.S. alone, the impact on the health care system is $19 billion annually, but with our aging population and poor compliance with existing pharmacological options, these costs are expected to escalate. Consequently, the search has continued for alternative strategies to prevent and treat osteoporosis. Recent reports targeting the gut–bone axis have provided renewed interest in the role of nutritional interventions. Compelling evidence has shown that probiotics increase short chain fatty acids (SCFAs), which in turn promote the differentiation of T regulatory (TREG) cells that mediate osteoprotective effects. The bone-protective benefits of classic prebiotics (i.e., fibers) have been attributed to a SCFA-induced increase in intestinal calcium uptake; however, insights gained more recently from studies of probiotics raise the question of whether prebiotics target gut commensal microbiota and alter bone homeostasis by similar immunoregulatory mechanisms. The recent adoption of a more comprehensive definition of prebiotics has revealed that natural products such as tart cherries provide an excellent source of fructo-oligosaccharide, anthocyanin and phenolic acid, each with notable prebiotic activity. This project will investigate the extent to which the prebiotic activity of tart cherry is responsible for its potent bone protective effects. These findings will provide new insights into the potential of using natural prebiotics targeting the gut microbiota as a novel therapeutic strategy for osteoporosis.

Reducing Maternal Stress to Improve Obesity-related Parenting Practices

Maternal stress is associated with children's risk for obesity controlling for socioeconomic status, yet standard of care child obesity prevention programs have not focused on maternal stress reduction. The association between maternal stress and child obesity is particularly strong in Latino families, whose children also have the highest rates of obesity in the United States. A mindful parenting program might reduce Latina mothers' psychological stress and lead to improved parenting practices and ability to create a healthier environment. This research will evaluate the feasibility and acceptability of an intervention that integrates mindfulness-based stress reduction and mindful parenting in a population whose children are at highest risk for obesity: Latina mothers. Phase 1 of the research involves developing and refining an integrative intervention manual, titled ATIENDE (Awareness Training to Influence Eating, Nutrition, Decision-making, and Exercise) and translating it into Spanish. Phase 2 involves conducting a randomized clinical trial comparing the ATIENDE intervention to an active control condition in 50 Latina mothers of elementary school–age children. Completion of this project will inform the development of a full-scale efficacy trial.

A Feasibility Trial of a Group Based Yoga Intervention for Chronic Pelvic Pain in Women

One in 10 U.S. women suffer from chronic pelvic pain, a condition that can lead to depression, social isolation, sexual dysfunction, physical inactivity, and dependence on or abuse of pain medications. Unfortunately, most medications used to manage pelvic pain have problematic side effects or addictive potential, and other clinical therapies for this condition depend on costly one-on-one visits with specialized health care practitioners. As a result, many women with chronic pelvic pain are eager to identify alternative treatment strategies that are not only effective but also better tolerated and more accessible. Yoga is a set of complementary physical and mental practices with the potential to improve chronic pelvic pain through multiple mechanisms. When practiced in a way that emphasizes careful anatomic alignment, mindful awareness of bodily structures, and deep breathing during the practice of yoga postures, yoga can be used to improve pelvic floor dysfunction, correct maladaptive postural and physical behaviors, and decrease comorbid anxiety and perceived stress. As a result, regular practice of yoga has the potential to improve multiple factors that can precipitate and exacerbate pelvic pain or worsen pain-related disability. This project will evaluate the feasibility of conducting a rigorous randomized trial of an 8-week yoga program. This research addresses the urgent need for more effective, accessible, and patient-centered treatment strategies for chronic pelvic pain as a common and debilitating pain syndrome in women. If successful, this research may pave the way for women suffering from chronic

pelvic pain to use yoga to improve their pain-related functioning in community settings while also gaining other potential benefits for their long-term health.

IV. Advancement of Women in Biomedical Careers

Researchers from many different biomedical and behavioral disciplines are key to further advancing basic, mechanistic, translational, and clinical research in complementary approaches and their integration into health care. Over the years, NCCIH has also targeted resources to attract well-trained and experienced scientists and clinicians into complementary and integrative health research supporting their development as scientific leaders in the field. NCCIH will continue to promote strategies to enhance diversity of the workforce, enhance the clinician scientist pathway at both the individual and institutional level, and enhance the transition of Research Career Development (K) Awardees to an independent research career.

NCCIH supports research training and career development programs to increase the number and diversity of well-trained scientists to conduct rigorous complementary and integrative health research. We have special opportunities for individuals from groups who are underrepresented in scientific research (e.g., racial and ethnic minority populations) throughout the continuum from high school to faculty. In addition, we support workshops at NIH and at scientific conferences to help students and fellows connect to NIH funding opportunities, understand how to interact with NIH staff to develop research proposals, navigate the NIH peer review process successfully, develop resilience to overcome career roadblocks, and develop plans for a successful research career.

V. Implementation of the NIH Policy on Sex as a Biological Variable (SABV)

The 2017 National Health Interview Survey showed that women were more than twice as likely to use yoga compared with men (19.8% versus 8.6%). Women were also more likely than men to use meditation (16.3% versus 11.8%) and see a chiropractor (11.1% versus 9.4%). Women may also use natural products to improve their health during the lifespan, including during pregnancy and lactation.

NCCIH will continue to further research on women's health and sex as a biological variable by:

- Developing and testing interventions using complementary health approaches for managing symptoms such as perinatal and postpartum depression, stress, anxiety, pain, and sleep disturbance and assess their impact on maternal health outcomes.
- Supporting research on the use of complementary health approaches to support pregnant and parenting women with opioid use disorder.
- Supporting research on the contributions of sex, gender, and the intersection of sex and gender on the mechanisms of action of complex interventions, including various mind and body approaches and natural products.
- Conducting research that investigates the influence of sex and gender on utilization of complementary health approaches to improve health outcomes among diverse populations, including gender-diverse populations.

VI. Inclusion of Women in Clinical Research

Applications submitted to NCCIH for funding consideration are evaluated for inclusion (or exclusion) of individuals on the basis of sex/gender, race, and ethnicity, as well as the inclusion (or exclusion) of children to determine whether it is justified in terms of the scientific goals and research strategy proposed. In addition, NCCIH requires that all efficacy, effectiveness, or pragmatic trials be conducted at multiple sites because this increases the likelihood that results can be generalized, increases the diversity of the population to meet NIH policy and guidelines on the inclusion of women and minorities as subjects in clinical research, and demonstrates that the intervention can be delivered with fidelity at more than one location.

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National Cancer Institute

I. Executive Summary

The mission of the National Cancer Institute (NCI) is to lead, conduct, and support cancer research across the Nation to advance scientific knowledge and help all people live longer, healthier lives. NCI implements the Trans-NIH Strategic Plan for Women's Health Research by supporting research to increase our basic understanding of all cancers and to advance cancer prevention, detection, and treatment for women. Over the past 2 years, NCI-supported researchers have made strides in advancing understanding and treatment of a variety of cancers specific to or primarily affecting women and identifying sex differences in cancer-related areas. For example, work highlighted herein describes sex differences in response to treatment for glioblastoma and provides insight into why females have poorer responses to immune checkpoint inhibitor therapy. Advances were also made in the treatment of breast and ovarian cancers and in the detection of cervical cancer. It is well known that NCI scientists played a critical role in the development of a human papillomavirus (HPV) vaccine to prevent cervical cancer. NCI continues to support research to improve vaccination rates in the United States, particularly in underserved and high-risk populations. NCI also supports numerous research initiatives and activities to reduce cancer disparities. Three new ovarian cancer projects in Black/African American women are described. These projects seek to determine why this group of women with ovarian cancer do worse than others. In 2020, NCI established an Equity and Inclusion Program to ensure a workplace climate that promotes advancement of women and other underrepresented groups in biomedical careers and to strengthen efforts to address health disparities. Although far from comprehensive, the following highlights provide a sample of the accomplishments, initiatives, and activities of NCI related to women's health in fiscal years 2019 and 2020.

II. Scientific Advances

Novel, more accurate, and automated tests for cervical cancer – Each year, more than 500,000 women worldwide are diagnosed with cervical cancer. Almost all these cases are caused by infection of human papillomavirus (HPV). Of about 200 known HPV variants, or genotypes, only 12 can transform healthy cells of the cervix into precancerous lesions and eventually cancer. The traditional test to detect abnormal cervical cells, precancers, and cancer is the Pap test, in which the cervical cells are collected and analyzed by a pathologist. In lower-resource settings, visual inspections are used. However, HPV genotyping is now recommended for primary screening. All these methods have limitations. The sensitivity, or ability to identify true positives, of Pap and visual tests is about 70%. Likewise, commercial assays for HPV genotyping are slow and expensive. National Cancer Institute (NCI) researchers made advances in all three areas. They developed a computer algorithm based on artificial intelligence (AI) that analyzes cervical images and identifies precancerous changes more accurately than standard tests (Hu et al., 2019). This screening tool can be used in low-resource settings. For HPV genotyping, NCI researchers developed TypeSeq, a high-throughput, low-cost HPV test, which is already employed as a gold standard in some regulatory trials (Wagner et al., 2019). When suspicious cervical lesions are found, a woman is usually referred for a biopsy. Because most lesions can be cleared by the immune system, many biopsies are performed unnecessarily. NCI researchers developed a dual-stain test that helps to reduce unnecessary biopsies, which predicts more accurately than a Pap test whether an HPV-positive woman with a suspicious lesion would develop cervical precancer (Clarke et al., 2018). Because this test still requires visual interpretation, which is subjective and costly, researchers developed an AI-based automated testing platform. The resulting test reduces referral to biopsy by one-third (Wentzensen et al., 2020). Overall, NCI researchers made significant advances in cervical cancer prevention, some of which have already began to benefit women.

This translational work relates to Objective 1.5 of the Trans-NIH Strategic Plan for Women's Health Research ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health") and the health of women overall.

Treatment Advances for Ovarian Cancer – Ovarian cancer is the leading cause of death from gynecologic cancers, with high-grade serous ovarian cancer (HGSOC) the most common histologic subtype of ovarian cancer. HGSOC has been shown to have numerous alterations that result in replication stress when ovarian cancer cells copy their DNA to prepare to divide and grow. The cellular response to replication stress includes activation of the ATR protein. A National Cancer Institute (NCI) Experimental Therapeutics Clinical Trial Network randomized Phase II trial tested the ATR inhibitor berzosertib in combination with the chemotherapy drug gemcitabine for patients with platinum-resistant HGSOC (Konstantinopoulos et al., 2020). The results from this study showed that the addition of the ATR inhibitor to gemcitabine extended progression-free survival without increasing treatment-related toxicity. This was the first randomized trial of an ATR inhibitor, and the promising results warrant further evaluation of this drug combination in HGSOC. In addition, an NCI National Clinical Trials Network randomized Phase II/III trial for women with recurrent low-grade serous ovarian cancer (LGSOC) or peritoneal cancer investigated the use of a novel molecularly targeted therapy (ESMO Congress 2019). This study compared treatment with the MEK protein inhibitor trametinib to the physician's choice of standard of care treatment. MEK is a key protein in a cell signaling pathway (MAPK pathway) that is dysregulated in approximately one-third of all cancers. Results of this trial indicate that trametinib was able to significantly improve progression-free survival and objective response rate. Improvements in response duration and overall survival were also observed. The findings of this study suggest that trametinib represents a new standard of care treatment option for women with recurrent LGSOC. These are two examples of molecularly targeted therapies improving the treatment options for women with serous ovarian cancer.

This clinical work relates to Objective 1.5 of the Trans-NIH Strategic Plan for Women's Health Research ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health") and the health of women overall.

Standard Therapy for Glioblastoma Appears to Be More Effective in Female Patients – Glioblastoma multiforme (GBM) is an aggressive type of brain cancer with a median survival time of only 15 months for patients undergoing standard-of-care therapy: surgery, chemotherapy, and focal irradiation. GBM occurs more frequently in males than in females. Recent studies suggest that female GBM patients also survive longer than males. In this study, the authors demonstrate that standard-of-care therapy for glioblastoma may benefit female patients more than male patients (Yang et al., 2019). The authors analyzed MRI images of tumors from male and female GBM patients treated with standard-of-care therapy. Specifically, they measured the velocity at which tumors expanded over time. Upon therapy, the velocity decreased substantially only for females. Also, the decreases in the velocity correlated with longer survival times only in female patients and not in males. In the past, The Cancer Genome Atlas Research Network (TCGA) compiled a list of genomic abnormalities that underlie glioblastoma tumorigenesis and proposed a classification of GBM into four subtypes. In three of the subtypes, the incidence is twice smaller for females. Lower incidence of GBM in females occurs at all stages of life, suggesting that action of female sex hormones cannot fully explain the difference in incidence between sexes. To uncover molecular bases for the differences in incidence and response to treatment, the authors analyzed the TCGA data, defining sex-specific molecular clusters of GBM, five for each sex. Comparison of clusters with best outcome to other clusters revealed that survival in different sexes likely depends on different molecular pathways. Although these pathways need to be further validated, this study suggests that different therapies may be needed for female versus male patients and that glioblastoma patients may be better stratified with sex-specific subtyping. This research team recently received new NCI funding to better delineate sex-specific mechanisms that drive GBM, which may be used for future therapies.

This translational work relates to Objective 1.2 of the Trans-NIH Strategic Plan for Women's Health Research ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes").

Uncovering Why Young and Female Patients Respond Poorly to Immunotherapy – During the past 10 years, immune checkpoint inhibitor therapy has shown impressive responses for certain cancers and in certain patients. Recent studies have shown that females have poorer responses to this type of immunotherapy. Immune checkpoint inhibitor drugs work by reversing

blocks that immune cells activate to stop the body from recognizing and destroying cancer cells. By analyzing genomic information from nearly 10,000 tumors from The Cancer Genome Atlas data and validating their finding in an independent cohort of over 300 tumors, researchers determined that young age and female sex are predictors of immune selection in tumors and help to explain the different outcomes observed for checkpoint inhibitor therapy (Castro et al., 2020). First, the researchers showed there were no age- or sex-related differences in the function of the immune system complex (major histocompatibility complex [MHC]) that presents tumor cells to immune cells. Instead, they found that tumor cells in younger and female patients tend to amass cancer-causing mutations that are less able to be recognized by the MHC. In summary, young individuals and females, and thus young females, tend to have a robust initial response to tumor cells triggering the immune system to eliminate them. However, the tumor cells that are not eliminated by the immune system in this initial response persist, grow, and are poor targets for immune system destruction. This is true even when immune checkpoint inhibitor therapies remove immune cell blocks to recognizing tumor cells. Overall, age and sex differences in immune system function and response are well documented, including that females are more susceptible to autoimmune diseases and that the immune system tends to weaken with age. All of this information taken together can be used to personalize treatment decisions and could help to develop predictive models to determine an individual's response to immune checkpoint inhibitor therapy.

This basic work relates to Objective 1.2 of the Trans-NIH Strategic Plan for Women's Health Research ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes").

Sparing Women with the Most Common Type of Breast Cancer from Chemotherapy – Endocrine (hormone) therapy with or without chemotherapy is standard

treatment for women with the most common type of breast cancer—estrogen receptor–positive, HER2-negative (ER+/HER2-) disease. Previous research has shown that the addition of chemotherapy benefits these women to different extents. We must move away from a one-size-fits-all treatment approach and use evidence to determine the best treatment. A recently completed NCI-supported clinical trial, called TAILORx, examined women with ER+/HER2- breast cancer that had not spread to the lymph nodes. This trial compared women receiving endocrine therapy alone with women receiving both endocrine and chemotherapy. The trial used a genetic test to assign a risk of recurrence score (RS). Findings showed that the majority of women with a low-to-intermediate RS did not derive any additional benefit from chemotherapy, saving thousands of women from unnecessary chemotherapy and onerous side effects (Sparano et al., 2018). Further analysis of TAILORx data revealed that women with a high RS do benefit from the addition of chemotherapy (Sparano et al., 2020). The RxPONDER trial then examined women with ER+/HER2- breast cancer who had a low recurrence test score but are at high risk of a recurrence because of the presence of regional lymph node disease. RxPONDER showed that postmenopausal women in this group do not reap additional benefit from chemotherapy and therefore may skip it (Kalinsky et al., 2020). Overall, these NCI-supported trials provide evidence for chemotherapy de-escalation in defined subsets of ER+/HER2- breast cancer patients and, therefore, will enable doctors to better prescribe treatments for these women.

This clinical work relates to Objective 1.5 of the Trans-NIH Strategic Plan for Women's Health Research ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health").

III. Promotion of Women's Health Research

Ovarian Cancer Studies to Understand Disparities and Improve Outcomes – The National Cancer Institute (NCI) supports a robust research program in women's cancers, including research aimed at addressing disparities for women from certain racial and ethnic and underserved populations. It is well documented that African American women with ovarian cancer do not survive as long as non-Hispanic White women with the disease. Studies suggest that multiple factors, including access to care and socioeconomic factors, result in the disparity. In 2019 and 2020, three new separate but complementary studies were launched to better understand why certain groups of patients with ovarian cancer do worse than others (NCI, 2020). One of the studies uses a comprehensive approach to examine the interplay among patient, health care, socio-contextual, and biological factors from data collected on approximately 4,500 women to understand racial disparities in ovarian cancer survival (1R01CA243188-01A1). Similarly, a second study is focusing on factors that contribute to poor ovarian cancer survival in African American women (1R01CA237318-01A1). This study will recruit 350 newly diagnosed African American women and integrate information from their social and physical environments with data on inflammation-related exposures and inflammatory markers in samples from their tumor tissues. The third study is surveying women who recently completed initial treatment for ovarian cancer to determine barriers to access to quality cancer care (5R37CA233777-03). The study will investigate five dimensions of health care: access, affordability, availability, accommodation, and acceptability. Together these new studies, along with existing NCI-funded studies such as the African American Cancer Epidemiology, will increase understanding of why certain groups of women with ovarian cancer do worse than others and help develop new strategies to improve cancer and outcomes for all ovarian cancer patients.

These studies relate to Objective 1.5 of the Trans-NIH Strategic Plan for Women's Health Research ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health") and the health of women overall.

Traceback Approach to Identify Women At Risk of Breast and Ovarian Cancer – Women with pathogenic mutations in the *BRCA1/2* gene have an increased risk for developing breast and ovarian cancers. However, research shows only a small percentage of women at risk of carrying these mutations undergo genetic testing, particularly women diagnosed with ovarian cancer, despite recommended guidelines (Kurian et al., 2019). The NCI previously released a funding opportunity announcement titled "Traceback Testing: Increasing Identification and Genetic Counseling of Mutation Carries Through Family-based Outreach" and in 2020

funded the first three collaborative pilot projects. "Traceback" testing is a framework for identifying and genetically testing previously diagnosed but unreferred patients with ovarian cancer and other unrecognized mutation carriers to improve the detection of families at risk for breast or ovarian cancer. The NCI projects are using this traceback approach to contact family members of women with a personal or family history of ovarian cancer to identify unaffected individuals who are at increased risk for cancer (1U01CA240747-01A1, 1U01CA244323-01, 1U01CA240581-01A1). These projects specifically address the ethical, legal, and societal implications of genetic testing related to communication, consent, return of results, and community engagement. One of the funded projects will enlist community partners as citizen scientists to help develop messaging and outreach interventions. The Traceback initiative complements research on identifying and caring for individuals with inherited cancer syndromes supported by the Cancer Moonshot. Identifying individuals with hereditary cancer syndromes will allow delivery of evidence-based genetic counseling, preventive and early detection services, and ongoing surveillance through public health programs to lessen the burden of cancer on women and their families.

These studies relate to Goal 1 ("Advance rigorous research that is relevant to the health of women") and Objective 3.1 ("Design and test approaches to promote the adoption, adaptation, and integration of evidence-based interventions in public health, clinical practice, and community settings") of the Trans-NIH Strategic Plan for Women's Health Research.

Working to Prevent Cervical Cancer – Human papillomavirus (HPV) is a major cause of cervical cancer. NCI researchers developed the technology used to create an HPV vaccine to prevent cervical cancer. However, adoption and dissemination of the HPV vaccine is problematic, especially in low- and middle-income countries, where most cervical cancer cases and deaths occur. To improve cancer prevention through vaccination, NCI researchers, in collaboration with investigators in Costa Rica, studied HPV vaccine efficacy. The HPV Vaccine Trial in Costa Rica was a blinded, randomized Phase III clinical trial of the bivalent HPV-16/18 vaccine developed by investigators at NCI and other institutions and manufactured by GlaxoSmithKline. For 4 years, trial staff followed more than 7,000 women who were randomized to receive three doses of the HPV vaccine or Havrix (hepatitis A) vaccine. In addition to strong evidence for vaccine safety and efficacy, data from the trial demonstrated that three doses of the HPV vaccine may not be necessary (Kreimer et al., 2018; Kreimer et al., 2020). In the United States, Cervarix and GARDASIL-9 are currently approved for two doses in younger recipients. Researchers are now conducting the ESCUDDO study to determine whether one dose of the HPV vaccines works as well as giving two doses to young women. Using a single dose of the vaccine would reduce challenges to vaccine uptake in many parts of the world, including cost and lack of medical infrastructure for multiple vaccination visits. ESCUDDO has two components: a randomized, double-blinded non-inferiority trial to compare one-dose to two-dose vaccination and a concurrent epidemiologic survey for HPV infection status among unvaccinated women. The trial is enrolling and following 2,000 young women in Costa Rica. If one dose of an HPV vaccine is found to be sufficient to reduce cervical cancer burden, NCI would expect widespread vaccine uptake in the United States, and around the world, with lower-cost vaccination programs.

This work relates to Objective 1.5 of the Trans-NIH Strategic Plan for Women's Health Research ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health") and the health of women overall.

Sharing Proteogenomics Data to Enable Research – The NCI-supported Clinical Proteomic Tumor Analysis Consortium (CPTAC) is a collaborative effort among academic institutions, industry, and several Federal agencies. CPTAC's goal is to measure the entire complement of proteins in tumors in a rapid and large-scale manner and combine this information with genomic, imaging, and clinical data to enable a more complete understanding of a patient's tumor that will inform diagnosis and treatment and improve outcomes. CPTAC has also developed robust and reproducible analytical methods for comprehensive and targeted protein measurements from tumors and methodologies for open-access data sharing of large-scale proteomics data with researchers around the globe. Thus far, scientists supported by CPTAC and its collaborators have completed proteogenomic characterizations for 11 tumor types, including breast (Mertins et al., 2016), ovarian (Zhang et al., 2016), and uterine cancers (Dou et al., 2020). In combination with the methods developed

by the consortium, these data sets are publicly available so that scientists can use them for discovery research. With these data, NCI has developed some of the world's largest public, open-access repositories of data. These repositories include DNA, RNA, protein, and imaging data on many cancer types, and the list is growing. These data are housed in the NCI Cancer Research Data Commons, a virtual platform for secure data storage and public data sharing.

This activity and the data that are shared relate to Objective 2.3 of the Trans-NIH Strategic Plan for Women's Health Research ("Leverage secondary data sources for research on the health of women through a big data enterprise that includes data sharing and analytic strategies").

Identifying Research Opportunities in Gynecologic Cancer Disease Progression – The NCI and the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) explored research opportunities into the progression of benign gynecologic conditions to cancers through a collaborative workshop in April 2019. Currently, NICHD funds research on benign gynecologic conditions such as endometriosis and uterine fibroids, while NCI funds research on women's cancers. The workshop sought to bridge the two research areas and identify gaps in the biologic, epidemiologic, and clinical understanding of progression from benign conditions to cancer. The workshop addressed three gynecologic disease types: (1) endometriosis or endometrial cancer and endometrial-associated ovarian cancer, (2) uterine fibroids (leiomyoma) or leiomyosarcoma, and (3) adenomyosis or adenocarcinoma. Working groups were formed for each disease type, and key questions and current challenges that emerged from the discussions, along with potential research opportunities to advance understanding of progression of gynecologic benign conditions to cancer, were published (Samimi et al., 2020). Specific research questions and gaps were identified in all three focus areas, and several cross-cutting topics emerged. There is a need for natural history studies to characterize disease progression and identify risk factors. Biorepositories of well-characterized samples of benign, precancerous, and cancerous lesions are needed from patients. And increased communication and collaboration between the benign conditions and the oncology research communities is critical to advance knowledge across the spectrum of diseases.

This collaborative activity relates to Objective 1.5 of the Trans-NIH Strategic Plan for Women's Health Research ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health").

IV. Advancement of Women in Biomedical Careers

NCI is committed to activities that advance women in biomedical careers and conducted several activities that are germane to retaining and advancing women in cancer research. During the past several years, specific NCI activities have included "speed dating" events in honor of Women and Girls in Science Month in 2019 and 2020, a conversation on the National Academy of Sciences' Report on Sexual Harassment in 2019, and four listening sessions on caregiving during COVID-19 in 2020 to identify and address the difficulties women scientists at NCI faced and their concerns due to the COVID-19 pandemic. Also in 2020, NCI participated in "Women Leaders in Biotech and Pharma Seminar Series," which featured female executives from MiraDx, Merck, and other organizations. To recognize outstanding women in science, the NCI Women Scientists Advisors (WSA) sponsor the Rosalind E. Franklin Award and Lecture at the annual NCI Intramural Retreat and the WSA Mentoring and Leadership Award, which recognizes men and women scientists in the NCI community who have shown strong support, scientific leadership, and/or direct mentoring to women scientists leading to professional scientific and career achievement of women scientists at the NCI. Through these activities, NCI works to represent the interests of women scientists, raise awareness of issues facing women scientists, and improve women's representation in the NIH faculty at all levels. To ensure a workplace climate that promotes advancement of women and other underrepresented groups in biomedical careers, in 2020, NCI established an Equity and Inclusion Program to increase the diversity of its intramural and extramural workforce, increase equity and energize efforts to address health disparities. This effort involves a steering committee, the NCI Equity Council, and five working groups. Approaches include an emphasis on work–home

balance, implicit bias training for search committees and principal investigators, and promotion and compliance of NIH anti–sexual harassment training initiatives.

V. Implementation of the NIH Policy on Sex as a Biological Variable (SABV)

NCI ensures the research it supports is in alignment with NIH's SABV policy. In the NCI scientific review process, peer reviewers evaluate the SABV policy's elements in grant applications as one element of the policy on rigor and reproducibility. For awarded grants, NCI program staff members evaluate compliance with the SABV policy when reviewing and approving yearly progress reports. NCI participates in the Trans-NIH SABV Working Group, which informs SABV policy development and implementation. In addition, NCI encourages and supports investigator-initiated research that focuses on sex differences in the incidence, treatment, and mortality of cancers, such as the two research studies highlighted in section II above that describe the results of studies on sex differences in the response to (1) treatment for glioblastoma and (2) immunotherapy.

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National Eye Institute

I. Executive Summary

Worldwide, the prevalence of moderate to severe visual impairment and blindness is 285 million people, with 65% of visually impaired and 82% of blind people being 50 years or older. Many eye diseases and conditions affect women disproportionately or in unique ways. Clinical analyses indicate that 2 in 3 blind people are women, a gender discrepancy that holds true for both developed and developing countries (Zetterberg, 2016). This gender difference may be explained in part by the longevity of women; however, there are sex-dependent biological differences across the lifespan, which may affect symptoms, conditions, and risks associated with this vision loss.

For example, estrogen levels significantly decrease during menopause and in postmenopausal women, and a decrease in estrogen levels is known to correlate with an increased risk of glaucoma, wet (neovascular) and dry age-related macular degeneration (AMD), cataracts, dry eye disease (DED), low vision, and other ocular functions. Hormone replacement therapy (HRT) in women and estrogen (E2) treatment in animal models have been shown to reduce intraocular pressure (IOP) associated with glaucoma; however, despite this, the mechanisms are not known (Dewundara et al., 2016). Women also have higher rates of autoimmune diseases, such as lupus, rheumatoid arthritis, and multiple sclerosis. These conditions often have serious effects on the eyes, causing vision loss, and the rates of these diseases are increasing as the population ages, especially among women.

Many of the National Eye Institute's (NEI) strategic planning efforts are germane to women's health. NEI has a diverse portfolio of both basic and clinical research directed at advancing our understanding of sex/gender differences in ocular diseases and conditions. These include diseases such as DED and Sjögren's, AMD, glaucoma, corneal dystrophies, myopia, cataracts, infectious diseases, and other eye conditions affecting aging women and the role of dietary supplements in eye health. Other areas of research include sex-related effects linked to basic developmental retinal processes, population-based studies to understand the prevalence of these diseases and its impact on women, as well as epidemiological studies to determine the efficacy, toxicity, and safety of drugs to treat these conditions. In addition, an NEI representative serves as a Women's Health Liaison to the Office of Research on Women's Health (ORWH) and works to coordinate efforts across the institute and ORWH to encourage input and/or partnerships in areas of joint interest.

II. Scientific Advances

Coronavirus: Recent data demonstrate that the severity of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, which causes coronavirus disease 2019 (COVID-19), is greater in men than in women and that men are dying at a higher rate than women (approximately 1.70 times greater) in certain global regions (Rossman, 2020). This may be caused by the presence of chronic diseases such as heart disease, diabetes, and cancer, which are generally more common in men, and/or hormonal differences.

Sex hormones have been shown to play an important role as determinants of susceptibility to nearsightedness or myopia and dry eye, both of which are significantly more prevalent in women (Rudnicka et al., 2016). Although COVID-19 appears to be greater in men, women are reporting that symptoms of myopia and dry eye are worsening because of the COVID-19 crisis. As a result, large numbers of people have been schooling/working from home, increasing their exposure to a visual display terminal (VDT), which is having a negative impact on the health of their ocular surface. Of the 200 students selected at the University Magna Graecia in Italy, a significant percentage of the students experienced worsened myopia and ocular discomfort caused by rapid evaporation of tear fluid. The percentage of women who developed myopia and DED or experienced an increase in symptoms was 76.5% higher than among men (Pellegrini et al., 2020; Giannaccare et al., 2020; Objective 2.1 ["Expand and develop advanced and innovative approaches for study design, data collection, and analysis to optimize data quality and the ability to detect the influences of sex and gender on health and disease"] of the Trans-NIH Strategic Plan for Women's Health Research). In addition, data suggest that dry eye may precede

COVID-19 symptoms; however, further analysis needs to be done to determine whether dry eye can increase susceptibility to infections such as COVID-19. These issues were recently discussed at the Fifth Annual Dry Eye Awareness Month Congressional Hearing on July 8, 2020 (Global Health 50/50, 2020).

Evidence also suggests that SARS-CoV-2 may cause ocular pain and conjunctivitis, or "pink eye," and that infectious viral particles might be present in the tears of COVID-19 patients (Xia et al., 2020). Even though transmission occurs mainly through respiratory droplets, other routes such as ocular secretions/fluids are currently being investigated (Colavita et al., 2020). Data supporting this hypothesis were recently published by researchers from Johns Hopkins University. They demonstrated that the ACE2 receptor, a key factor responsible for binding with the virus and allowing entry of SARS-CoV-2 into the host cell, and TMPRSS2, a cell surface protease that facilitates viral entry are expressed on the ocular surface, including the conjunctival epithelium, limbus, and corneal epithelium. These results show that eye surfaces could be a portal of entry/infection as well as a reservoir for person-to-person transmission of this virus (Zhou et al., 2020).

These studies address Objectives 1.1 ("Discover basic biological differences between females and males"), 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes"), 2.1 ("Expand and develop advanced and innovative approaches for study design, data collection, and analysis to optimize data quality and the ability to detect the influences of sex and gender on health and disease"), and 2.3 ("Leverage secondary data sources for research on the health of women through a big data enterprise that includes data sharing and analytic strategies") of the Trans-NIH Strategic Plan for Women's Health Research.

Herpes zoster ophthalmicus (HZO): HZO is a complication of herpes zoster (HZ) or shingles affecting the eye, which is a common and serious disease caused by reactivation of the chickenpox virus that can result in chronic eye disease and incapacitating pain. Population-based studies show that the prevalence of HZ is about twice as common in women than men and that female patients with HZ may suffer from ocular complications more frequently than men.

Epidemiological studies show that sex, age, and race may be risk factors for ocular herpes and associated postherpetic trigeminal neuralgia/eye pain (Borkar et al., 2013; Yawn & Gilden, 2013). The NEI and ORWH recently co-funded a grant to study the effects of the HZ vaccine on the incidence and severity of HZO and evaluate differences based on these factors. Secondary analysis of data obtained from the electronic medical records of patients with HZO in four multi-national, multi-ethnic databases revealed that in men the incidence rate ratio (IRR) of HZO is 0.74 as compared with women, which means that women are at greater risk of getting ocular herpes when they have shingles. Compared with White patients, the IRRs were 0.70, 0.75, and 0.64 for Asian, Black, and Hispanic patients, respectively (Cohen, 2020; Kong et al., 2020; Thompson et al., 2020). Further analysis of additional databases to evaluate the effectiveness of the new Shingrix vaccine as compared with the first Zostavax vaccine in women are needed.

NEI is also funding a clinical trial to determine whether prolonged treatment with a low dose of the antiviral valacyclovir is different in men versus women and whether the effectiveness of antivirals treatments improve outcomes by reducing eye disease and/or chronic pain in HZO patients. This study is currently recruiting patients (Objectives 1.2 ["Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes"] and 2.3 ["Leverage secondary data sources for research on the health of women through a big data enterprise that includes data sharing and analytic strategies"] of the Trans-NIH Strategic Plan for Women's Health Research).

Sjögren's syndrome: A recent genetic study showed that complement component 4 (C4) genes, C4A and C4B, contribute sex-biased vulnerability in several disorders, including Sjögren's syndrome, which affects nine times more women than men. Evidence showed that the same variations of the C4 genes increase risk for schizophrenia and reduce risk for systemic lupus erythematosus (SLE) and Sjögren's syndrome. In all three cases, C4 alleles act more strongly in men than in women. Specifically, a 31-fold variation in risk for Sjögren's among men was observed as compared with 15-fold in women. Likewise, C4 and C3 proteins levels in the cerebrospinal fluid and plasma were more greatly elevated in men than in women between the ages of 20

and 50 years. Therefore, sex differences in complement protein levels may explain, in part, why women are at increased risk of SLE and Sjögren's and men are at greater vulnerability to schizophrenia. The NEI and ORWH are interested in studies aimed at investigating how this sexual dimorphism in the levels of complement protein alters vulnerability to these illnesses (European-Ancestry Sjögren's Syndrome Cohort; Kamitaki et al., 2020; Objective 1.2 ["Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes"] of the Trans-NIH Strategic Plan for Women's Health Research).

Retinopathy of prematurity (ROP): ROP causes abnormal blood vessel growth in the retina and is a leading cause of vision loss in children worldwide. Common risk factors for ROP include preterm birth, low birth weight, multiple-gestation pregnancies and pregnancy complications. Early diagnosis and treatment give infants with severe ROP the best chance of having healthy vision. However, early diagnosis of ROP in infants is difficult, partly because of the extensive time and training required to perform these specialized ophthalmic examinations and the lack of access to screening. Therefore, treatment is often delayed, increasing the risk of progression. Using artificial intelligence algorithms, NEI-funded researchers have developed a deep learning retinal imaging system (i-ROP DL) that automatically recognizes and evaluates images and has been shown to diagnose ROP with nearly perfect accuracy. This device has been granted breakthrough status by the Food and Drug Administration (FDA), a program that facilitates and enables the development and assessment of medical devices by speeding up the review process (Redd et al., 2019). It is worth noting that women who experience preterm birth complications (e.g., brain, heart, vision problems, etc.) are at increased risk of ill health and negative feelings about their infant in the early months after birth. They make less use of postnatal services and support than other women. Therefore, the development of this innovative technology is expected to improve health and well-being of both mothers and infants.

The NEI is actively funding multiple grants to the Oregon Health & Science University (OHSU) and Massachusetts General Hospital (MGH) to further access this system, and for clinical evaluation, and to develop a commercialization plan for this technology in order to receive FDA approval. This research program address Objectives 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health"), 2.1 ("Expand and develop advanced and innovative approaches for study design, data collection, and analysis to optimize data quality and the ability to detect the influences of sex and gender on health and disease"), and 2.2 ("Develop and adapt reliable and valid measures relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

Vernal keratoconjunctivitis (VKC): VKC is a chronic allergic disease mostly affecting young boys in their first decade of life. In particular, boys are two to four times more likely to develop the disease. Symptoms include inflammation at the ocular surface, leading to ocular scaring and vision loss if not properly treated. Studies demonstrate a significant increase of conjunctival estrogen and progesterone receptors in children with VKC as compared with healthy subjects. These findings, together with the higher disease prevalence in boys, suggest an influence of sex hormones on VKC development and/or activity. Recent data highlight that the endocrine system, particularly an altered balance in the androgen pathway, along with the immune system, contribute to increased inflammation. Determining the mechanisms of the inflammations and fibrosis requires further investigation (Di Zazzo et al., 2020; Sacchetti et al., 2015; Objective 1.2 ["Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes"] of the Trans-NIH Strategic Plan for Women's Health Research).

Glaucoma: Since the 1970s, evidence has suggested that medical marijuana helps patients manage symptoms of glaucoma. Studies supported by the NEI have shown that when marijuana is taken orally or via inhalation, it can lower intraocular pressure (IOP). Recently, a study demonstrated in mice that two components of marijuana, cannabidiol (CBD) and δ-tetrahydrocannabinol (THC), have opposite effects (Miller et al., 2018). The data showed that CBD raises intraocular pressure (IOP) whereas THC lowers ocular pressure and that cannabinoid regulation of IOP associated with glaucoma is sex-dependent. In other words, THC has a modest effect or no effect in lowering IOP among females compared with males in the mice model (Straiker, 2019).

III. Promotion of Women's Health Research

Carotenoids and pregnancy: Carotenoids are dietary plant pigments, lutein (L) and zeaxanthin (Z), and the lutein metabolite meso-zeaxanthin that are located in the central retina and lens epithelium. There is a large body of evidence suggesting that these pigments can protect against damage that contributes to AMD and protect against UV light damage and oxidative stress, which are associated with cataract development. Data from the Second Carotenoids in Age-Related Eye Disease (CAREDS2) clinical trial, an ancillary study of the Women's Health Initiative (WHI), demonstrated that there is an increased risk of AMD and/or cataract development among women with low and high macular pigment optical density (MPOD), respectively (Lawler et al., 2017).

To expand on this finding, the NEI, in collaboration with ORWH and the NIH Office of Dietary Supplements (ODS), is currently funding an Exploratory/ Developmental Research grant proposing a small-scale prospective clinical trial study to determine whether prenatal and postnatal supplementation of lutein and zeaxanthin carotenoids have beneficial effects on maternal visual function and on infant visual and cognitive development in normal and high-risk pregnancies. If successful, this study will provide the necessary preliminary data to design and power future, larger-scale clinical trials aimed at optimizing formulations of carotenoid supplementation. The results may also provide evidence-based support to guide policy decisions about prenatal nutritional recommendations to enhance maternal and infant carotenoid status, especially in regions of the world at risk for malnutrition (Objectives 1.5 ["Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health"] and 2.3 ["Leverage secondary data sources for research on the health of women through a big data enterprise that includes data sharing and analytic strategies"] of the Trans-NIH Strategic Plan for Women's Health Research).

Anterior Segment Initiative (ASI): The anterior segment is the front of the eye and includes the cornea, iris, ciliary body, and ocular lens. Disruptions in the health of the anterior segment manifest in a variety of ways, including dry eye disease, ocular pain, Sjögren's syndrome, and uveitis, all of which are more prevalent in women and are experienced by an aging population. The NEI has been a longtime supporter of basic and clinical research in these areas, and significant progress has been made. Nonetheless, there are a number of knowledge gaps involving the anterior segment that present exciting research opportunities. The NEI is developing an initiative to address challenges in the anterior segment and released a request for information (RFI) to seek input from the scientific community. The scientific community identified diseases/conditions of the anterior segment where there are major gaps in knowledge, and therefore, NEI plans to collaborate with ORWH to develop funding opportunity announcements and workshops in these areas. The effects of sex hormones in each of these areas will be addressed (NOT-EY-20-001; Goals 1 ["Advance rigorous research that is relevant to the health of women"], 2 ["Develop methods and leveraging data sources to consider sex and gender influences that enhance research for the health of women"], and 5 ["Improve evaluation of research that is relevant to the health of women"] of the Trans-NIH Strategic Plan for Women's Health Research).

Initiatives:

- Identification and Development of New Biomarkers and Effective methods to Diagnose Dry Eye Disease (NOT-EY-21-007).
- Ocular Surface Innervation from Cell Types to Circuit Functions
  - Workshop: Immune System and Eye Health

Microbiome: The vision community identified the interaction of the human microbiome together with the immune system as an area that is not well understood. Many factors are known to influence the composition of the microbiome, including age, sex hormones, and the use of antibiotics. A recent article suggests that collectively, age and sex may influence the immune homeostasis of the ocular surface through changes in the conjunctival microbiome, which may in turn influence conditions such as DED and other eye diseases. In this study, the conjunctival microbiome of young male and female groups was indistinguishable; however, older females (approximately 67.1 years old),

i.e., after menopause, showed significant changes in the β diversity of the ocular surface microbiota (Wen et al., 2017).

A recent publication demonstrated that depletion and selective reconstitution of the maternal gut microbiome influences fetal neurodevelopment in mice, specifically the development of neurons in the thalamus. Thalamocortical axons are guided to the somatosensory cortex, where they mediate touch, smell, visual, and auditory signals for sensory processing. This study is of interest to the NEI because axonal development of retinal cells connects to nerve cells in the visual cortex. Data from embryos of antibiotic-treated and germ-free dams exhibited reduced brain expression of genes related to axonogenesis, deficient thalamocortical axons, and impaired outgrowth of thalamic axons in response to cell-extrinsic factors, and colonization with select bacteria prevented these abnormalities. In addition, metabolites secreted from the microbiota were shown to abrogate these abnormalities. Intriguingly, although depletion of the maternal gut microbiota during pregnancy impairs early fetal thalamocortical axonogenesis, no apparent differences are detected for visual sensory behavior of adult offspring, indicating that further studies are needed to address this question (Vuong et al., 2020).

The NEI is sponsoring a program to identify core constituents of the ocular microbiome and solicit applications proposing to assess the microbiome's role in ocular health and disease. This includes collaborating with ORWH to study the molecular underpinnings of sex hormones on the associations between microbial communities and eye diseases/conditions such as dry eye, Sjögren's syndrome, and Fuchs's dystrophy-conditions, all of which are more prevalent in females than males (Goals 1 ["Advance rigorous research that is relevant to the health of women"], 2 ["Develop methods and leveraging data sources to consider sex and gender influences that enhance research for the health of women"], and 5 ["Improve evaluation of research that is relevant to the health of women"] of the Trans-NIH Strategic Plan for Women's Health Research).

Women's Eye Health website: The NEI is sponsoring the development of a free public-accessible website (http://w-e-h.org) to provide information on the effects of aging, autoimmune conditions, and hormonal changes in women that often come with visual side effects. The mission of Women's Eye Health is to educate people regarding eye diseases that (1) are intrinsically more prevalent in women, (2) occur more often in women because women live longer than men, and (3) are exacerbated by nutritional habits, smoking, and/or environmental insults (Women's Eye Health, 2021; Objective 3.1 ["Design and test approaches to promote the adoption, adaptation, and integration of evidence-based interventions in public health, clinical practice, and community settings"] of the Trans-NIH Strategic Plan for Women's Health Research).

COVID-19: Both NEI and ORWH are currently participating in several NIH-wide COVID-19-related announcements and notices. The NEI will co-fund eye-relevant research studying ocular implications caused by COVID-19, as well as the development of diagnostics and treatments. These include studies to determine the rate of transmission through ocular fluids, as well as the impact of SARS-CoV-2 on the eye during pregnancy, telemedicine for diagnosing and treating ocular symptoms related to COVID-19, and mitigation strategies. NEI will also consider providing a supplement to an NIH Institute or Center to fund a grant on COVID-19-related research that contains a vision/eye component (PAR-20-237; PAR-20-243; NOT-MD-20-022; NOT-MH-20-053; NOT-MH-20-058; NOT-OD-20-119; NOT-OD-20-120; NOT-OD-20-121; RFA-OD-20-013).

IV. Advancement of Women in Biomedical Careers

The NEI recognizes the importance of training research scientists to study sex differences in all aspects of vision science and promotes training and career development of postdocs and scientists to get the research experience necessary to become highly competitive for positions as an independent scientist in vision science. Recent statistics show that women remain underrepresented in the science and engineering fields, and therefore, NEI is participating with other NIH Institutes and Centers to promote postdoctoral training of women in basic and clinical research.

In collaboration with ORWH, NEI is co-funding several research training grants and clinical scientist career development awards to encourage women to become independent vision scientists and, in particular, to focus

on conditions that disproportionately affect women's eye health, such as:

- Supporting a postdoctorate to study eye-related sex differences. Sex-related effects have also been linked to a retinal neuroprotective pathway associated with stressed photoreceptor damage (Hooper et al., 2018). Understanding these effects during development will lead to a better understanding of stem cell differentiation and subsequently improved *in vitro* protocols and transplantation methods of adult-, iPSC-, and ESC-derived retinal, corneal, and other ocular tissues.
- Funding an NIH fellowship to promote training in bioimaging technology in order to develop a sex-specific biomarker to detect differences in visual processing. Recent data show a difference in motion processing between males and females and demonstrate the importance of sex as a factor in the design and analysis of perceptual and cognitive research (Murray et al., 2018).

Recently, the NEI Intramural Research Program has recruited four tenure-track investigators—all women—doubling its number of women investigators from four to eight. Currently, women account for almost a third of NEI investigators (8 of 25), up substantially from 17% before the recent hires. One of the new hires has the prestigious Earl Stadtman designation. Two have been selected as prestigious Lasker Research Scholars. And three are part of the new NIH Distinguished Scholars Program.

NEI is committed to developing the next generation of researchers to advance science on the health of women, starting as early as high school. The NEI Diversity in Vision Research and Ophthalmology (DIVRO) hosts around 8–12 interns each year and offers hands-on training and mentoring for students from underrepresented groups in vision research. Participants work closely with leading NEI scientists and get experience working in an environment that will prepare them to continue their studies and advance their careers in basic and clinical research. Since 2011, the DIVRO program has hosted 71 interns, 63% of them female, 45% African American, and 42% Latino, with the remainder from Native American and multiracial populations. In 2015, the program expanded to include students with disabilities when the NEI hosted its first deaf student. Most of the students in the DIVRO program have been college students (48%), with 26% coming from medical school and the rest from high school or graduate school. DIVRO interns return to the program for multiple summers (28%); come back as postbaccalaureate fellows to the NEI and other ICs (seven to the NEI, two to the National Institute of Allergy and Infectious Diseases, and one to the National Heart, Lung, and Blood Institute); and have become postdoctoral fellows (three). Former interns have moved on to graduate, medical, and optometry programs. The DIVRO program continues its ninth successful year and recently expanded beyond college summer interns to include more experienced trainees and applied science researchers.

V. Implementation of the NIH Policy on Sex as a Biological Variable (SABV)

In December 2016, Congress passed the 21st Century Cures Act, which enjoins many important issues while conducting strategic planning for the NIH ICOs, including the expansion of research related to the health of racial, sexual, and gender minorities. This congressional mandate ensures that NEI research incorporates women and minorities and is focused on reducing health disparities. NEI-supported and conducted research receive objective and fair reviews to ensure that all applicable laws, regulations, and policies are followed, such as the inclusion of women, minority, and children in clinical research and the application of sex as a biological variable (SABV) in research design, analysis, and reporting.

In consultation and coordination with ORWH and external researchers and stakeholders, NEI incorporates methods and analyses aimed at understanding SABV in ocular conditions. NEI elucidates knowledge on the burden and impact of women's vision and eye-related issues and is actively involved in various working groups, including the NIH Sex as a Biological Variable Working Group, the Coordinating Committee on Research on Women's Health, and the Women Scientists Advisory Group.

NEI evaluates compliance with NIH's policy to consider SABV through several mechanisms. For example, NEI

routinely tracks and reports on categories of disease, condition, and research areas, including women's health, through the Research Condition and Disease Reporting (RCDC) process that informs the NIH RePORT website, which provides consistent and transparent information to the public. In FY 2019, over 4% of NEI research spending was associated with women's health as it relates to eye diseases and disorders of vision, such as ocular cicatricial pemphigoid, a rare autoimmune disease that can cause scarring in the inside membrane that covers the front of the eye and lines the inside of the eyelids; dry eye; and Graves' disease, an autoimmune disorder that causes overactive thyroid with common symptoms, including bulging eyes.

Recent efforts to capitalize on research opportunities at the front of the eye through the start of the NEI Anterior Segment Initiative will include further examination of conditions that disproportionately affect women, such as dry eye, Sjögren's syndrome, and ocular effects of migraines.

VI. Inclusion of Women in Clinical Research

The advancement of women's health depends on an integrative research approach across all health sectors, including vision. NEI works closely with several NIH offices that have a focus on women's health, including ORWH, the Sexual & Gender Minority Research Office (SGMRO), and the NIH Division of Intramural Research Women Scientists Advisors/NIH Equity Committee to ensure the inclusion and promotion of women and girls in clinical research.

In addition to the research activities listed in Section IV. Advancement of Women in Biomedical Careers, NEI is funding a research training grant to examine the association between estrogen exposure in women from the WHI and Medicare claims of Fuchs' endothelial corneal dystrophy (FECD). The results showed that the greatest sex disparity in FECD prevalence is seen in women who are between 50 and 59 years old, which represents the peri- and postmenopausal transition. Other risk factors—such as reproductive lifespan, height and weight, smoking, and diet—showed no significant differences. These findings support a hypothesized role for menopausal hormonal changes in FECD pathophysiology (Patel et al., 2019; Zoega et al., 2013). The role of estradiol and estrogen receptors on corneal health and the development Fuchs dystrophy is currently being studied.

NEI is also supporting a clinical scientist career development award to investigate the role of complement factors, cytokines, and estradiol levels at the ocular surface in postmenopausal women with Sjögren's syndrome (SS) and non-SS-DED. Sjögren's syndrome is a chronic autoimmune disease that occurs primarily in women (with female patients outnumbering males by a ratio of 9:1) and attacks the salivary and lacrimal glands resulting in severe dry eye. The complement cascade, though best known for its role in infection, is activated in autoimmune diseases such as primary SS.

Further exploration and incorporation of research methods and analyses aimed at addressing these and other conditions are important to improve women's health, as well as vision and eye health for all.

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National Human Genome Research Institute

I. Executive Summary

The origin of the National Human Genome Research Institute (NHGRI) dates back to 1989, when its preceding organizational entity (the National Center for Human Genome Research) was created to lead NIH's efforts in the Human Genome Project (HGP). Since the HGP's completion in 2003, NHGRI has funded and pursued genomics research to advance basic knowledge about how genomes function, discover the genomic underpinnings of health and disease, and facilitate the application of genomics to clinical care.

NHGRI is a pioneer in the development and dissemination of new genomic technologies, which has consistently catapulted the field forward and dramatically increased the accessibility of genomic approaches in biomedical research. NHGRI's focus on technology development has had a positive impact on the immediate field of genomics but also the many disease-specific research efforts inside and outside of NIH, including those specific to women.

NHGRI also funds research that positively affects women in a more targeted manner, and NHGRI-funded research in FY 2019 and FY 2020 has led to advances in disease areas specific to women's health (such as endometrial and breast cancers) and issues affecting maternal and child health (such as prenatal genetic testing). Women represent over half of the participants in NHGRI-funded human subjects research, and NHGRI ensures that male and female tissue, cell lines, and model organisms are included equally in all studies.

Women are often at the center of health-related decision-making in families and bear disproportionate psychosocial burdens associated with genetic testing and participation in genomics research. NHGRI has funded research and conducted outreach activities on the ethical and psychosocial aspects of participating in genomics research through activities in the NHGRI Ethical, Legal, and Social Implications (ELSI) research program and the intramural Social and Behavioral Research Branch.

Finally, NHGRI is committed to supporting the most qualified trainees and ensuring that its training programs are accessible to all. Approximately half of the NHGRI intramural and extramural trainees are women.

II. Scientific Advances

NHGRI contributes significantly to the **H3Africa Common Fund consortium**, which performs fundamental research into diseases in Africa while also developing infrastructure, resources, training, and ethical guidelines to support a sustainable African research enterprise. Several NHGRI-led or -co-funded projects within the H3Africa consortium are focused primarily on the health of African women. Research has shown that prevalence of obesity in women across Africa and in low- and middle-income countries elsewhere is much higher than is observed in men (Akpa et al., 2020). Previous work has also shown a link between obesity and cardiovascular risk and menopause, but this link has yet to be investigated in African women. This translational study (U54HG006938) seeks to investigate the contribution of menopausal transition to cardiovascular disease risk in midlife sub-Saharan African women. The African Female Breast Cancer Epidemiology (AFBRECANE) Study (U01HG009784) is an NHGRI-funded effort to utilize nutrition epidemiology and genomics epidemiology tools to study dietary intakes and breast cancer risk in African women. NHGRI also contributes to the Breast Milk Microbiota Influence on Infant Immunity and Growth (BEAMING) study, which investigates how the microbiota of breast milk affects infants gut bacteria and how this in turn affects infants' growth and their ability to respond to childhood vaccination (Ojo-Okunola et al., 2020). This effect is being examined in HIV-exposed but uninfected children, and the results are being compared with HIV-unexposed children. Together, these studies contribute to not only the research on female-specific conditions and women's health but also the reduction of global health disparities.

NHGRI's **Ethical, Legal and Social Implications (ELSI) Research Program** was established in 1990 as an integral part of the Human Genome Project (HGP). The program's primary mission is to foster basic and applied research on the ethical, legal, and social implications of genomic research and medicine for individuals, families, and communities. NHGRI dedicates at least 5% of its annual extramural research budget to support research focused on these issues, including ELSI issues related to the health of women. NHGRI is currently funding a number of projects that focus on factors influencing access and utilization of genetic prenatal care and ensuring patients informed access to noninvasive prenatal testing (NIPT). The NHGRI ELSI Research Program has made significant contributions in prenatal genetic testing and care scholarship over the past 2 years that will inform clinical practice and care. One qualitative interview study evaluating decision-making regarding prenatal genetic screens and tests at the first prenatal visit found that patients and providers have different priorities at the first prenatal visit and that these differences may interfere with shared decision-making (Farrell et al., 2020). Future research is critical to determine how to restructure the initiation of prenatal care in a way that best positions pregnant women to make informed decisions about prenatal genetic screens and tests. An NHGRI-funded commentary also explored preparation as a reason why women are increasingly choosing prenatal genetic testing and the need for a clearer definition of the term and what it means to parents, clinicians, and support groups (Michie, 2020). Supplemental funds were also dedicated to the critical examination of the effect of the COVID-19 pandemic on prenatal health care delivery, specifically patients' ability to access prenatal genetic screening and diagnostic tests (3R01HG010092-04S1). The work of the ESLI Research Program over the past 2 years has also contributed to the study of minority women's health and health disparities. In FY 2020, NHGRI-funded ELSI researchers published a review of the growing body of evidence implicating the role of social, structural, and environmental stressors associated with historic and present-day racism in adverse pregnancy outcomes among women of color (Riggan et al., 2021). A study out of the NHGRI-funded Utah Center of Excellence in ELSI Research (UCEER) revealed the limited use of U.S. residual newborn screening dried bloodspots for health disparity research (Riches et al., 2020).

Intramural researchers at NHGRI carry out research relevant to several areas of women's health, including reproductive cancers, maternal nutrition and reproductive health, perceptions and behaviors of women who are overweight, and prenatal genetic screening. One group of NHGRI intramural researchers has focused its research on understanding the genomic basis of endometrial (uterine) cancers. One study identified a novel therapeutic target for serous endometrial cancers, which are hard to treat and associated with poorer outcomes (Urick et al., 2020). The group published a review paper on the clinical actionability of molecular targets in endometrial cancer (Urick et al., 2019). The group also performed a genome-wide analysis of clear cell endometrial carcinomas for somatic copy number alterations using high-resolution SNP arrays (a type of DNA microarray that is used to detect polymorphisms within a population), adding to the current understanding of the molecular etiology of that subtype of endometrial cancer and laying the ground for future work (O'Hara et al., 2020). As noninvasive prenatal testing becomes more prevalent in the clinic, NHGRI intramural researchers are studying the best approach for clinical follow-up if the test results are suggestive of cancer in the pregnant woman, as cfDNA can detect maternal neoplasia. NHGRI researchers have also participated in social and behavioral research with women, particularly in the context of their role as caregivers for individuals affected with genetic disease. In the past 2 years, NHGRI-funded intramural investigators have published on primary caregivers to individuals affected by Alzheimer's disease and related dementia (ADRD) in a network context (Marcum et al., 2020) and assessing the dietary perceptions and practices of parental caregivers of children affected by propionic acidemia (Lea et al., 2019).

III. Promotion of Women's Health Research

NHGRI is committed to outreach and community involvement programs to engage a broad range of the public in understanding genomics and accompanying ethical, legal, and social issues, particularly via the Education and Community Involvement Branch (ECIB). ECIB has spearheaded several public outreach programs that particularly target or impact women, including

women from underserved groups. The following activities are aligned with Goal 5 of the Trans-NIH Strategic Plan for Women's Health Research ("Enhance dissemination and implementation of evidence to improve the health of women").

NHGRI has continued efforts from prior years to develop public resource webpages for patients and families, including guidance on collecting family health history information before visiting the doctor. Women are often at the center of health-related decision-making in families. Family health history is a key component to helping families and health care providers identify patterns of inheritance and risk factors.

NHGRI's ECIB collaborated with the Deaf Health Communication and Quality of Life Center at Gallaudet University to produce a short film in American Sign Language (ASL) on genetic testing for breast cancer. In the film, a deaf mother learns she has breast cancer. The film includes information on BRCA 1 and 2 variants. In addition, the film describes how to learn about the genetic conditions afflicting many breast cancer patients and potential proactive steps. The film was presented in 2019 at the American Public Health Association Annual Film Festival and at Deafopia hosted at Gallaudet University.

In addition, ECIB develops resources for educators on topics related to genomics and society. In 2020, a series of lesson plans about Henrietta Lacks was published. Henrietta Lacks was an African American woman whose cells were removed during a biopsy in 1951 and used for research without her consent. Although Mrs. Lacks died of an aggressive form of cervical cancer, her cells continued to grow and ultimately provided the foundation for innumerable advancements in biomedical research, including genomics. The lesson plan supports students in exploring our current understanding of the link between human papillomavirus (HPV) and cervical cancer, a disease that affects hundreds of thousands of women each year.

IV. Advancement of Women in Biomedical Careers

Ensuring diversity in genomics research goes hand in hand with championing a diverse genomics workforce. The promise of genomics cannot be fully achieved without attracting, developing, and retaining a diverse workforce comprising individuals from groups currently underrepresented in the genomics enterprise, including women. NHGRI has a strong record of funding diversity-enhancing programs, including the Diversity Action Plan (DAP) program (PAR-19-380), which has been in place since 2002 and seeks to expose students at the undergraduate, postbaccalaureate and graduate levels who are from diverse backgrounds, including those from underrepresented groups, to the foundational sciences relevant to genomics to enable them to pursue careers that span all areas of interest to NHGRI. In April 2019, NHGRI partnered with the American Society of Human Genetics to launch the Human Genetics Scholars Initiative (HGI), a program dedicated to achieving diversity and inclusion in the field of human genetics and genomics. The program provides crucial mentorship and funds to early-career scientists from underrepresented backgrounds. Five out of eight of the first cohort (2019–2021) of Human Genetics Scholars are women.

Most recently, NHGRI developed a 10-year "Building a Diverse Genomics Workforce: An NHGRI Action Agenda." The objectives of this "Action Agenda" include both reducing barriers to training opportunities in the field and supporting the development and career progression of female researchers and other researchers from underrepresented backgrounds (Bonham & Green, 2021). The specific goals outlined in the Action Agenda are: (1) Develop and support initiatives that provide early exposure and access to careers in genomics; (2) develop and support training programs and networks that connect undergraduate and graduate education to careers in genomics; (3) develop and support training, career development, and research transition programs that lead to independent research and clinical careers in genomics; and (4) evaluate progress toward achieving greater diversity in the genomics workforce. Each goal is supported by a series of objectives, implementation strategies, and indicators of success. NHGRI also supports several R25 initiatives (PAR-19-185, PAR-21-074, PAR-21-075) aimed at providing mentorship, training, and educational activities in specialty areas such as data science, particularly to underrepresented groups, including women.

V. Implementation of the NIH Policy on Sex as a Biological Variable (SABV)

NHGRI implements NIH's policy to consider sex as a biological variable (SABV) during the peer review process, when reviewers utilize the Reviewer Guidance to Evaluate Sex as a Biological Variable document (https://grants.nih.gov/grants/peer/guidelines_general/sabv_decision_tree_for_reviewers.pdf). If a reviewer raises a concern, the Program Director discusses that concern with the applicant, and the applicant is asked to devise an explicit plan for addressing the weakness. However, absent including information about NIH's SABV policy on the NIH checklists and FOA templates, there is no way to ensure complete compliance.

VI. Inclusion of Women in Clinical Research

Women represent over half of the participants in NHGRI-funded human subjects research, and NHGRI ensures that male and female tissue, cell lines, and model organisms are included equally in all studies. As a disease-agnostic institute, NHGRI has fostered a culture of open data sharing, resource development, and offering expertise and leadership, furthering not just its own mission but also the missions of other institutes and agencies. The current phase of the eMERGE Network, for example, is focused on compiling diverse datasets that will be used for studying common diseases in all patient populations, with the results returned to a diverse group of ethnic minority populations, underserved populations, or populations that experience poorer medical outcomes through their electronic medical records (EMRs). These efforts will shape the conversations about implementing genomics-based risk estimates in clinical care, as well as how and in what format to return genomics results to patients. NHGRI's support of the curation of diverse, representative, and accessible datasets and the resultant resource development drives genomic discoveries for all populations, including women. In order to achieve the promise of precision medicine tailored to every individual, a thorough understanding of the biology of the genomes of women is essential.

The Human Genome Reference Program (HGRP), co-funded by NHGRI and the NIH Office of Research on Women's Health, seeks to create a genome reference that is representative of all human genetic diversity. The HGRP has produced several publications over the past 2 years, including the first telomere-to-telomere assembly of a complete human X chromosome (Miga et al., 2020). Although the X and Y chromosomes will be underrepresented in human genome data compared with autosomes, the existence of high-quality, complete reference genomes will enable greater study of sex-based variation and its contribution to human health.

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National Heart, Lung, and Blood Institute

I. Executive Summary

The National Heart, Lung, and Blood Institute (NHLBI) supports research to better understand and promote heart, lung, blood, and sleep health to prevent and treat disease. The institute remains committed to funding studies on how sex and gender differences influence disease risk, disease expression and outcome, and response to interventions. As it has since its inception, with the launch of the Framingham Heart Study, NHLBI also remains committed to the inclusion of women in all aspects of research. Another large-scale study, the Women's Health Initiative has been continuously funded since 1993 and has been renewed through 2027. This long-term study focuses on preventing disability and death in postmenopausal women and continues to advance women's health research through ancillary and extension studies.

A key part of supporting women's health research includes promoting the NIH policy of incorporation of sex as a biological variable (SABV) into scientific research from basic science to clinical trials. NHLBI participates in funding opportunities specifically focused on understanding sex and gender influences on health and disease, as well as SABV education via publications and textbooks.

NHLBI supports research to promote the health of women and understand risk of disease across the life course, including, for many women, before, during, and after pregnancy. The changing demographic and health profile of pregnant women impacts their future risk of heart disease. Cardiovascular disease is the leading cause of pregnancy-related deaths. Addressing long-term cardiovascular risk in populations with high incidence of maternal morbidity and mortality, including preeclampsia, can have long-term benefits for the health of at-risk populations. NHLBI's new Maternal Health Community Implementation Project will support community-engaged implementation research to bring evidence-based maternal health interventions to underserved communities.

In line with the institute's Strategic Vision, the NHLBI is working to grow and retain women in the biomedical workforce. Leadership and program staff strive to find innovative approaches to recruit and retain women scientists in research. Funding opportunities are designed to help women advance from mentored career awards to independent investigators and to mitigate the potential career impact of life-changing events, for example, through supplemental grants to support re-entry into biomedical research.

II. Scientific Advances

NHLBI strives to support research for women's health, disease prevention, and treatment across a woman's entire lifespan; for many women, that includes the critical times before, during, and after pregnancy.

- The nuMoM2b Sleep Disordered Breathing (SDB) study found that 8.3% of women had SDB in mid-pregnancy, along with a higher risk of gestational hypertension and preeclampsia (Louis et al., 2018). This has led to a Phase III clinical trial to determine whether treating SDB with continuous positive airway pressure (CPAP) can reduce the risk of these cardiovascular conditions.

  This clinical research relates to Objective 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health" of the Trans-NIH Strategic Plan for Women's Health Research.

- Lymphangioleiomyomatosis (LAM) is a rare disease in which connective tissue cells grow out of control in certain organs—including the lungs, where the most severe damage occurs. It affects women almost exclusively and is exacerbated by pregnancy. Using single-cell gene expression analysis, an NHLBI-funded study identified a unique cell type, found only in LAM-affected lungs, that has properties of connective tissue and lung alveolar (air sac) cells. The study also defined the abnormal molecular pathway that gives rise to these cells, which may help to identify therapeutic targets and determine the origin of LAM (Obraztsova et al., 2020).

  This basic research relates to Objective 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes") of the Trans-NIH Strategic Plan for Women's Health Research.

- Findings from the Women's Health Initiative showed that hypertensive disorders of pregnancy and low birth weight were independently associated with atherosclerotic cardiovascular disease after adjustment for risk factors and other adverse pregnancy outcomes; this further supports previous findings that adverse pregnancy outcomes are sex-specific risk factors for atherosclerotic cardiovascular disease in women (Sondergaard et al., 2020).

  This clinical research relates to Objective 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health" of the Trans-NIH Strategic Plan for Women's Health Research.

- LIFE-Moms, funded by NHLBI and NIDDK, tested whether lifestyle interventions given to women during pregnancy could improve their health afterward. Compared with pregnant women who received standard prenatal care, those who received additional care and guidance—e.g., on healthy eating and physical activity—had less weight gain at 12 months postpartum (Phelan et al., 2020). This large study involved seven diverse U.S. regions, including Puerto Rico, and 1,150 women.

  This translational research relates to Objective 3.1 ("Design and test approaches to promote the adoption, adaptation, and integration of evidence-based interventions in public health, clinical practice, and community settings") of the Trans-NIH Strategic Plan for Women's Health Research.

The Women's Health Initiative (WHI) continues to support valuable research that focuses on strategies to improve the health of postmenopausal women.

- An analysis from the WHI found that older women (mean age 63) who slept 5 hours or less per night had higher odds of osteoporosis (Ochs-Balcom et al., 2020).

- WHI researchers reported an association between social and physical barriers to eating and poor performance on physical function tests that include grip strength, walking speed, and balance (Neuhouser et al., 2020).

- WHI investigators found that sedentary behavior increased the likelihood of hospitalization for heart failure. The association between sedentary hours and heart failure was present in postmenopausal women with a variety of health conditions and, strikingly, even among women who were active at guideline-recommended levels (LaMonte et al., 2020).

- A WHI study found that women older than 60 who engaged in even light physical activity each day had a lower risk of cardiovascular disease than those who were more sedentary (reduced stroke or heart failure by 22% and heart attack by about 42%). The link was clear across all racial groups (LaCroix et al., 2019).

This clinical research relates to Objective 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health" of the Trans-NIH Strategic Plan for Women's Health Research.

III. Promotion of Women's Health Research

In line with the institute's Strategic Vision, the NHLBI is advancing women's health research and clinical care for women with heart, lung, blood, and sleep disorders. NHLBI's Strategic Vision also expresses the institute's goal to understand the factors that lead to health disparities in underrepresented and underserved populations.

- NHLBI, with co-funding from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, is supporting the nuMoM2b Heart Health Study. The study has followed a diverse cohort of 4,508 women enrolled during their first pregnancy, with data and biospecimens prospectively collected thereafter. The study intends to define the relationship between adverse pregnancy outcomes and later cardiovascular disease to optimize disease prediction, prevention, and treatment strategies for women.

  This relates to Objective 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health" of the Trans-NIH Strategic Plan for Women's Health Research.

- NHLBI's new Maternal Health Community Implementation Project will support community-engaged research to ensure evidence-based maternal health interventions are appropriately implemented among underserved communities (Lipman, 2020).

  This relates to Objective 3.1 ("Design and test approaches to promote the adoption, adaptation, and integration of evidence-based interventions in public health, clinical practice, and community settings") of the Trans-NIH Strategic Plan for Women's Health Research.

- NHLBI is participating in a notice of special interest (NOSI) led by the National Institute of General Medical Sciences to support research on women's health in Institutional Development Award (IDeA) States.

  This relates to Objective 1.1 ("Discover basic biological differences between females and males") of the Trans-NIH Strategic Plan for Women's Health Research.

- The NHLBI-funded Risk Factors for CVD in Women study proposes to identify new risk factors for coronary heart disease at the metabolomics level, provide novel insight into mechanistic pathways, and advance the development of new preventive and therapeutic strategies (Manson, 2020).

  This relates to Objective 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes") of the Trans-NIH Strategic Plan for Women's Health Research.

- To improve pregnancy outcomes, the Prenatal Blood Pressure Patterns to Predict Pregnancy-Related Hypertension and Later Life Cardiovascular Risk study applies novel statistical methods to find clusters of blood pressure (BP) patterns for women during pregnancy that may signify serious pregnancy-related BP disorders and later-life cardiovascular disease outcomes allowing for additional monitoring and early interventions to improve outcomes and yield lifelong health benefits for women and their children (Gunderson, 2020).

This relates to Objective 2.1 ("Expand and develop advanced and innovative approaches for study design, data collection, and analysis to optimize data quality and the ability to detect the influences of sex and gender on health and disease") of the Trans-NIH Strategic Plan for Women's Health Research.

» For over a decade, *The Heart Truth*® has worked to increase awareness that heart disease is the leading cause of death among American women and to facilitate conversations between women and their health care providers. Recently, the program has amplified its efforts to raise awareness and reduce risk factors in populations that are most vulnerable to heart disease, including African American, Latina, and Native American women as well as those living in rural areas. The program creates culturally tailored messaging to promote evidence-based approaches to reduce heart disease risk that all women can use in their daily lives. Through *The Heart Truth*® Healthy Hearts Network, NHLBI works closely with long-standing partners, such as the American Heart Association, as well as newer organizations, such as GirlTrek, to reach women of all ages and backgrounds.

  This relates to Objective 3.2 ("Identify collaborative opportunities and leverage partnerships to disseminate research that improves the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

IV. Advancement of Women in Biomedical Careers

Ensuring the long-term stability of an inclusive workforce is a priority. NHLBI leadership and program staff make every effort to identify, grow, and retain women in the biomedical workforce; support them on a path to independence; and prepare them to train the next generation.

» For example, the Interdisciplinary Mentoring and Research in Women's Cardiovascular Health award provides mid-career health professionals who are focused on patient-oriented women's cardiovascular health research dedicated time to also mentor and support the next generation of patient-oriented research scientists.

  This relates to Objective 4.2 ("Develop the next generation of researchers to advance science on the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

» Additionally, to minimize departure from research because of critical life events, the NHLBI participated in NOT-OD-20-054, "Notice of Special Interest: Administrative Supplements to Promote Research Continuity and Retention of NIH Mentored Career Development (K) Award Recipients and Scholars." NHLBI funded six awards in fiscal year 2020, five of them from female academics.

  This relates to Objectives 4.3 ("Enhance and develop programs to recruit, support, retain, and advance women at all stages of their research careers, from early career to leadership positions") and 4.4 ("Promote and support policies, mentoring and networks, collaborations, and infrastructure to retain and advance women in their careers") of the Trans-NIH Strategic Plan for Women's Health Research.

» For women who have paused their career for family responsibilities, NHLBI funds administrative supplements to promote their re-entry.

  This relates to Objectives 4.3 ("Enhance and develop programs to recruit, support, retain, and advance women at all stages of their research careers, from early career to leadership positions") and 4.4 ("Promote and support policies, mentoring and networks, collaborations, and infrastructure to retain and advance women in their careers") of the Trans-NIH Strategic Plan for Women's Health Research.

V. Implementation of the NIH Policy on Sex as a Biological Variable (SABV)

A key part of understanding health and disease is to understand SABV. The NHLBI Strategic Vision expresses the institute's commitment to understanding sex differences to improve women's health and develop precision medicine approaches for women.

- To that end, NHLBI participates in trans-NIH funding opportunities such as RFA-OD-19-029, "The Intersection of Sex and Gender Influences on Health and Disease," and NOT-OD-20-049, "Notice of Special Interest: Administrative Supplements for Research on Sex/Gender Influences." Through this participation, for example, NHLBI funded a project to understand why the combined factors of obesity and female sex significantly escalate the risk of development of asthma and increase asthma severity in adult patients.
- NHLBI supports efforts to promote incorporation of SABV into scientific research, from basic science to clinical trials. To share this knowledge with others, NHLBI-funded researchers generated a special-edition textbook explaining sex-based differences in lung physiology (Silveyra & Tigno, 2021).
- An NHLBI-funded review showed the need for better reporting of SABV in heart failure trials. In trials from 2001 to 2016 about 30% overall did not report treatment effects by sex. However, that proportion dropped to less than 20% when looking at only NIH-funded trials (Vaduganathan et al., 2019).

VI. Inclusion of Women in Clinical Research

Inclusion of women in research, especially clinical trials, is necessary for understanding sex differences in disease progression and treatment and for promoting the health of all people.

In 2020, NHLBI enrollment of women in clinical research was 53.7% and enrollment of women in Phase III clinical trials was 46.6%.

- NHLBI continues to support the Women's Health Initiative (WHI), a long-term national health study that focuses on strategies for preventing heart disease, breast and colorectal cancers, and osteoporosis in postmenopausal women. Launched in 1991, the WHI recruited nearly 162,000 women ages 50–79 for a series of clinical trials that are among the most definitive, far-reaching trials to address women's health in the U.S. These trials addressed the use of hormone therapy after menopause and its effects on risk for breast cancer, heart disease, stroke, blood clots, and dementia and have helped profoundly reduce rates of cardiovascular disease and breast cancer among older women. Although the trials are complete, the WHI cohort continues to contribute to the science of women's health through extension and ancillary studies.
- Additionally, NHLBI is currently supporting the Multicenter Interventional LAM Early Disease (MILED) trial, which is a Phase III trial investigating whether early low-dose sirolimus, an immunosuppressive agent, could prevent disease progression in lymphangioleiomyomatosis (LAM) patients with preserved lung function. The study is being conducted using the infrastructure created for the Rare Lung Disease Clinic Network, which is currently following over 1,200 patients with LAM in the United States.

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Notice of Special Interest: Administrative Supplements to Promote Research Continuity and Retention of NIH Mentored Career Development (K) Award Recipients and Scholars. https://grants.nih.gov/grants/guide/notice-files/not-od-20-054.html

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National Institute on Aging

I. Executive Summary

Older women outnumber older men in the United States, and the proportion of the population that is female increases with age. In 2014, women accounted for 56% of the population age 65 or older and for 66% of the population age 85 or older (Federal Interagency Forum on Aging-Related Statistics, 2016). The National Institute on Aging (NIA) conducts and supports a diverse portfolio of research on older women's health, including studies on Alzheimer's disease and related dementias (AD/ADRD), ovarian aging, menopause and menopausal hormone therapy, and other diseases and conditions.

In FY 2019–2020, NIA-supported researchers reported important findings on a number of topics, including a possible influence of the X chromosome on longevity and mortality; causes of racial and ethnic differences in disability among older women; reasons behind sex differences in the emerging COVID-19 pandemic; and a surprising link between pregnancy history and cognition. Research programs such as the institute's flagship Study of Women's Health Across the Nation (SWAN) continued, along with the groundbreaking Interventions Testing Program and large-scale studies of menopause, hormones, and dementia. NIA now supports six sites in the Specialized Centers of Research Excellence (SCORE) on Sex Differences program and took a principal role in the second Inclusion Across the Lifespan national workshop, which had as a significant focus on the inclusion of pregnant women and lactating women in clinical research. Finally, NIA continues to support the recruitment of women, including those from underrepresented groups, to scientific research careers.

II. Scientific Advances

Sex and Gender Differences in COVID-19 Outcomes Among Older Individuals. Data from a number of countries show that mortality rates associated with COVID-19 are significantly higher among individuals ages 65 or older than among other age groups and that men have a higher risk of death from COVID-19 than women (Yanez, 2020). NIA-supported investigators have generated several hypotheses to explain the sex differences in COVID-19 presentation and outcome. For example, SARS-CoV-2, the virus that causes COVID-19, depends upon activity of the angiotensin-converting enzyme 2 (ACE2) receptor and the transmembrane protease serine 2 (TMPRSS2) to enter human cells. Sex-based differences in the expression of the ACE2 receptor and TMPRSS2 have been noted and may explain the disparities in COVID-19 severity and mortality rates. Sex-based differences in immunological responses may also be associated with differences in COVID-19 severity and outcomes. Gender differences in behaviors—e.g., smoking and reluctance to seek medical care—may also play a role (Mukherjee, 2021). Elsewhere, NIA-supported investigators note that low testosterone (T) is associated with development of the acute respiratory distress syndrome, which can occur as part of COVID-19's clinical course. They suggest that low T levels may exacerbate disease severity in older men (Papadopoulos 2020).

Research is ongoing to further elucidate the mechanisms underlying sex and gender differences in SARS-CoV-2 infection and COVID-19 outcomes (Papadopoulos & Samplaski, 2021). This is clinical research that addresses sex as a biological variable and relates to Objective 1.2 of the Trans-NIH Strategic Plan for Women's Health Research ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes").

Childbearing History May Influence Health and Cognition in Postmenopausal Women.

Pregnancy is accompanied by profound hormonal changes and places demands on numerous physiological systems. These "costs of reproduction" may accumulate with subsequent pregnancies and may accelerate biological and cognitive aging. NIA-supported investigators attempted to correlate several measures of biological aging with parity, or number of live births, among 4,418 participants in the National Health and Nutrition Survey. Controlling for chronological age, lifestyle, and health-related and demographic factors, the investigators found that parity exhibited a U-shaped relationship with accelerated biological aging in postmenopausal, but not premenopausal, women, with biological age acceleration being lowest among

postmenopausal women reporting between three and four live births. These findings suggest a link between reproductive function and physiological dysregulation but also suggest possible compensatory mechanisms that buffer those effects (Shirazi, 2020).

NIA-supported investigators are also determining the mechanisms through which the vascular system mediates long-term pregnancy-related changes in cognition. In particular, women with a history of preeclampsia appear to be at particular risk of postmenopausal cognitive decline. In one study, investigators identified a correlation between elevated aortic hemodynamics (patterns of blood flow and associated force in the aorta) and decreased function in some cognitive domains among women with a history of preeclampsia (Miller, 2020). The same investigators report that a history of preeclampsia is associated with occipital lobe atrophy in women with current hypertension and that blood velocity (the movement of blood through the circulatory system) was altered

among women with a history of preeclampsia (Miller, 2019). Mechanisms by which preeclampsia affects cerebrovascular structure and function, as well as through which pregnancy affects overall health in older age, require additional study.

https://pubmed.ncbi.nlm.nih.gov/33239686

https://pubmed.ncbi.nlm.nih.gov/31741134

https://pubmed.ncbi.nlm.nih.gov/32421781

This is basic research that relates to SABV, in that the studies focus on pregnancy and related outcomes, making the findings specific to women, and Objective 1.5 of the Trans-NIH Strategic Plan for Women's Health Research ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health").

APOE4 Genotype Combined with Poor Metabolic Profile: Reduced Cognitive Performance in Healthy Postmenopausal Women. Metabolic and vascular factors are associated with cognitive decline and dementia in both women and men, and the ApoE4 genotype is a well-established genetic risk factor for cognitive impairment, including Alzheimer's disease and related forms of dementia (AD/ADRD). However, less is known about how these risk factors interact. Investigators with the NIA-supported Early vs. Late Intervention Trial with Estradiol (ELITE), a study of the effects of hormone therapy on cardiovascular health and cognition in healthy postmenopausal women, used a suite of biomarkers to stratify study participants into three groups. Women in one group had healthy blood pressure and a healthy metabolic profile. In the second group, women had elevated blood pressure but were otherwise healthy. And in the third group, participants had a less healthy metabolic profile as defined by measurements of insulin resistance, glucose, cholesterol, triglycerides, and other biomarkers. Importantly, even the women in the "poor metabolic" group had borderline normal lab values.

The investigators further assessed measures of global cognition, executive functions, and verbal memory, and used linear models to determine whether an association of metabolic cluster with cognition differed by ApoE4 genotype. They found that verbal memory was lower in the poor metabolic cluster. Among women who carried at least one ApoE4 allele, performance in all cognitive domains was lowest in the poor metabolic cluster. Differences in executive functions among metabolic clusters were detected only in ApoE4+ women. These findings provide evidence that ApoE4 genotype and metabolic function may synergistically influence specific domains of cognition.

This is clinical research that addresses SABV, in that it studies only women, and relates to Objective 1.5 of the Trans-NIH Strategic Plan for Women's Health Research ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health").

https://pubmed.ncbi.nlm.nih.gov/29975287

SWAN: Racial and Ethnic Differences in Physical Performance are Mediated by Sociodemographic, Health, Behavioral, and Psychosocial Factors. Racial and ethnic differences exist in activity limitations among older women, with African Americans and Hispanics experiencing more disability than Caucasians or Asians. Investigators with the Study of Women's Health Across the Nation (SWAN) evaluated physical performance as demonstrated by several measures (grip strength, timed 4-meter walk, and timed repeat chair stand) among African American, Caucasian, Chinese, Hispanic, and Japanese participants (mean age = 61.8). They also identified a range of potential factors that could mediate results, including education, financial strain, comorbidities, pain, body mass index (BMI), physical activity, and perceived stress. They used statistical models to estimate the differences in physical performance among each group, as well as differences caused by direct effects of race and ethnicity and indirect effects through mediators.

They found that Japanese women as a group scored highest in these measures of physical performance, followed by Caucasian women and then African American women, Hispanic women, and Chinese women, respectively. They found that differences between Caucasian women and Chinese women and Japanese women were direct effects of race and ethnicity, whereas in African American women and Hispanic women, 75% or more of that disparity was through mediators, particularly education, financial strain, BMI, physical activity, and pain. These findings suggest that addressing issues of poverty, pain, and obesity could reduce some racial and ethnic disparity in functional limitations as women age (Sternfeld, 2020).

This is clinical research that addresses SABV, in that it studies only women, and relates to Objective 1.5 of the Trans-NIH Strategic Plan for Women's Health Research ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health").

https://pubmed.ncbi.nlm.nih.gov/31412129

Sex Chromosomes Influence Lifespan and Longevity in Mice. Women around the world live longer than men, and female longevity is also seen across the animal kingdom. However, the causes for this sex difference remain unknown. In addition, both sex chromosomes (XX/XY) and gonads cause sex differences in a number of physiologic systems in mammals, but how these differences impact lifespan has not been established.

NIA-supported investigators used a unique mouse model that decouples the Y chromosome from the development of male gonads to assess the contribution of the XX and XY genotypes on longevity. They generated four strains of mouse: XX with ovaries, XX with testes, XY with ovaries, and XY with testes, and observed each group of mice as it moved through middle age and beyond. They found that middle-aged XX mice with either ovaries or testes lived longer than XY mice, suggesting that sex chromosomes directly influence lifespan. Researchers also found that for XX mice, having ovaries further extends lifespan as XX mice with ovaries lived longer than XX females without ovaries. More study is needed to determine the role of ovarian aging and mechanisms underlying the association between sex chromosomal complement and lifespan and to determine whether the presence of a second X chromosome or the lack of a Y is implicated (Davis, 2019).

This basic research directly researches the effects of biological sex on longevity in a mouse model and relates to Objective 1.1 of the Trans-NIH Strategic Plan for Women's Health Research ("Discover the basic biological differences between males and females").

https://pubmed.ncbi.nlm.nih.gov/30560587

III. Promotion of Women's Health Research

The Study of Women's Health Across the Nation (SWAN): Characterizing and Understanding the Menopausal Transition. The goals of SWAN are to define the menopausal transition (MT) and to characterize its biological and psychosocial antecedents and sequelae in an ethnically and racially diverse sample of midlife women (Black, Chinese, Hispanic, Japanese, and White). Initially funded in 1994, SWAN is a cooperative agreement consisting of seven clinical field sites, a central reproductive hormone laboratory, a coordinating center, an advisory panel, and a repository of blood, urine, and DNA specimens. The study is supported by NIA, the National Institute of Nursing Research, and the NIH Office of Research on Women's Health.

Since its establishment, SWAN has characterized changes in reproductive axis and menstrual cycle patterns over the MT. This information informed the development of the widely used reproductive aging staging system STRAW+10. SWAN has also provided a wealth of information about MT-related symptoms and mental health (vasomotor symptoms, sleep, psychological symptoms, cognitive performance, and urogenital and sexual health), as well as MT-related changes in physiological systems and functions (cardiovascular and cardiometabolic health, bone health, and physical function). Importantly, SWAN investigators have identified relationships among these changes, as well as significant racial and ethnic differences in the rate and magnitude of change in a number of health indicators in midlife women.

SWAN participants, who were ages 42–52 at recruitment, have now reached early old age (67–77 years old). The study is now examining the relation between prospectively characterized MT and midlife health measures and later-life health and functional outcomes. Overall, SWAN's findings to date suggest that midlife is a critical stage for adopting healthy behavior and preventive strategies, and research findings linking the MT, midlife, and older age may suggest interventions that will preserve health and function as women age (El Khoudary, 2019).

This study relates to Objective 1.5 of the Trans-NIH Strategic Plan for Women's Health Research ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health").

https://pubmed.ncbi.nlm.nih.gov/31568098

Menopausal Hormone Therapy and Cognition. NIA-supported investigators continue to study the mechanisms through which estrogen and related hormones work on the brain, as well as the effects of different forms of menopausal hormone therapy (MHT) on cognition. Initiatives exploring the effects of age-related hormone changes and MHT on the brain include:

- **The Women's Health Initiative Memory (WHIMS) Suite of Studies.** NIA intramural researchers conduct and manage the WHIMS suite of studies, which assess the effects of MHT on memory, cognition, and mood in participants ages 65 or older without dementia who had been randomized to hormone therapy or placebo within the original WHI trial.
- **Perimenopause in Brain Aging and Alzheimer's Disease.** The goal of this large, long-running Program Project, which was renewed in FY 2016, is to determine how the brain changes during the perimenopausal transition and how these changes can lead to development of early risk factors for developing Alzheimer's disease.
- **Estrogen and the Aging Brain at Midlife.** An August 2019 workshop convened experts to consider the current knowledge base on the cognitive benefits and costs of hormone therapy and identify gaps that impede the development of clear recommendations about the timing, duration, and mechanisms by which perimenopausal hormone therapy may alter the trajectory of cognitive functioning in aging.
- **Endocrine Disruption and Risk of Alzheimer's Disease.** An NIA-supported site in the Specialized Centers of Research Excellence on Sex Differences (SCORE) program uses both humans and mice to establish the long-term cognitive effects of surgical removal of the ovaries and fallopian tubes, which often takes place during a hysterectomy in order to decrease the risk of pathology and the need for future procedures and which may be done to prevent breast and ovarian cancers in women at strong genetic risk. NIA anticipates that this research will suggest approaches to identify and mitigate adverse outcomes of this common surgery.

This relates to Objective 1.3 of the Trans-NIH Strategic Plan for Women's Health Research ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes").

Sex, Gender, and Alzheimer's Disease: Evolving Research. The prevalence of Alzheimer's disease is significantly higher among women than among men. Recent estimates suggest that nearly two-thirds of individuals diagnosed with the disease are women (Hebert et al., 2013), possibly because women, on average, live longer than men. At the same time, most studies conducted in the United States have not observed sex differences in the incidence of Alzheimer's disease—that is, in the rate of developing the disease. NIA has recently issued several solicitations for research on the roles of sex and gender in Alzheimer's disease and related dementias (AD/ADRD).

- One solicitation promotes multidisciplinary research to clarify sex and gender differences in the risk, development, progression, diagnosis, and clinical presentation of AD/ADRD, as well as studies that examine sex and gender differences in outcomes (e.g., clinical, functional, well-being) among people living with AD/ADRD. https://grants.nih.gov/grants/guide/notice-files/NOT-AG-20-038.html
- A second announcement solicits research to gain a comprehensive mechanistic understanding of the impact of sex differences on the trajectories of brain aging, phenotypes, and risk of AD/ADRD, and on precision medicine for treatment and prevention of AD/ADRD, including the responsiveness to pharmacologic and non-pharmacologic interventions. This solicitation was reissued in FY 2021.

  https://grants.nih.gov/grants/guide/pa-files/PAR-20-269.html

  SABV in AD: https://grants.nih.gov/grants/guide/rfa-files/RFA-AG-21-029.html

This relates to Objective 1.2 of the Trans-NIH Strategic Plan for Women's Health Research ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes").

Biology of Aging in Reproductive Tissues. In both men and women, aging of the reproductive system plays a pivotal role in both lifespan and health span, contributing to the development of comorbidities unrelated to reproduction, including cardiovascular, renal, bone, muscular, and neurological decline. Furthermore, male and female reproductive tissues display degenerative changes with aging before their

functional decline. In 2019, NIA released a funding opportunity announcement soliciting research addressing cellular and molecular mechanisms that regulate aging of the reproductive tissues. Six grants were awarded, including a study of the mechanisms underlying age- and pregnancy-related changes in breast tissue; a project to determine the role of cellular senescence and epigenetic changes in age-related loss of ovarian function; and genetic changes in the ovary that influence age at menopause.

https://grants.nih.gov/grants/guide/rfa-files/RFA-AG-20-036.html

This relates to Objective 1.1 of the Trans-NIH Strategic Plan for Women's Health Research ("Discover the basic biological differences between males and females").

IV. Advancement of Women in Biomedical Careers

NIA actively encourages participation of women in its training and career development initiatives. For example, the NIA Deputy Director co-chairs the NIH Women of Color (WOC) Committee of the NIH Working Group on Women in Biomedical Careers. The WOC subcommittee sponsors the Women of Color Research Network LinkedIn site, which provides women of color and supporters of their advancement in the biomedical sciences information about the NIH grants process, advice on career development, and a forum for networking and sharing information.

This relates to Objective 4.4 of the Trans-NIH Strategic Plan for Women's Health Research ("Promote and support policies, mentoring and networks, collaborations, and infrastructure to retain and advance women in their careers").

Another relevant activity is the Katies for Aging Research and Equity (KARE) program at St. Catherine University (St. Paul, MN), which is building the infrastructure to train the next generation of underrepresented minority women for successful aging research careers. (5R25AG060892)

This relates to Objective 4.4 of the Trans-NIH Strategic Plan for Women's Health Research ("Promote and support policies, mentoring and networks, collaborations, and infrastructure to retain and advance women in their careers").

V. Implementation of the NIH Policy on Sex as a Biological Variable (SABV)

Sex is evaluated as a biological variable in NIA-supported research consistent with NIH policy. Ongoing NIA-supported research specifically designed to identify and elucidate sex and gender differences in aging and age-related disease and dysfunction includes:

- Six sites in the Specialized Centers of Research Excellence on Sex Differences (SCORE) program, including centers that explore sex differences in the context of Alzheimer's disease, influenza, cardiovascular disease, chronic inflammation, and HIV infection.
- Studies of sex-specific genetic drivers of risk of and resilience to Alzheimer's disease.
- The Interventions Testing Program, which supports the testing of compounds with the potential to extend the lifespan and delay disease and

dysfunction in a genetically heterogeneous mouse model of aging. All interventions are tested in both male and female animals, and sex differences in responses to several compounds have been identified.

This relates to Objectives 1.1 ("Discover basic biological differences between females and males" and 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes") of the Trans-NIH Strategic Plan for Women's Health Research.

VI. Inclusion of Women in Clinical Research

NIA was instrumental in the development of the new NIH Inclusion Across the Lifespan (IAL) policy, which mandates that all applications for NIH-funded clinical studies received after January 25, 2019, include research participants across the lifespan, including children and older adults (unless there is a scientific justification to exclude them). The new policy also requires investigators to provide data on participant age at enrollment in progress reports. An NIA analysis that was foundational to the development of this policy was published in 2018 (Lockett et al., 2019).

In 2020, NIH, with NIA leadership, convened the virtual Inclusion Across the Lifespan-II Workshop: Implementation and Future Direction, which examined the science of inclusion of underrepresented populations, providing researchers evidence-based approaches to meeting the new IAL policy. Presentations focused on pediatric and geriatric populations, and discussions included considerations for a range of special populations, including pregnant women and lactating women as well as racial and ethnic minorities, rural populations, and others.

This relates to Objective 2.4 of the Trans-NIH Strategic Plan for Women's Health Research ("Expand and refine methodologies to improve the recruitment and retention of women underrepresented in clinical research").

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National Institute on Alcohol Abuse and Alcoholism

I. Executive Summary

The mission of the National Institute on Alcohol Abuse and Alcoholism (NIAAA) is to generate and disseminate fundamental knowledge about the effects of alcohol on health and well-being and apply that knowledge to improve the diagnosis, prevention, and treatment of alcohol-related problems, including alcohol use disorder (AUD), across the lifespan. Alcohol misuse refers to drinking in a manner, situation, amount, or frequency that could cause harm to an individual or those around them and could lead to AUD, a serious condition that affects nearly 16 million people in the U.S.

As a result of increased alcohol use, including binge drinking, by women over the past few decades, the once large differences in alcohol use and related harms between males and females are disappearing. Among adolescents, although alcohol use declined overall, the decreases were bigger for males than females. Adult alcohol use is increasing for women but not for men. These narrowing gender gaps in consumption are occurring amid growing evidence that women are more susceptible than men to physiological effects of alcohol, achieve higher blood alcohol concentrations, have a higher risk for the development of alcohol-related diseases, and show a higher vulnerability to AUD.

NIAAA-funded preclinical studies in animal models have begun to reveal the mechanisms underlying sex/gender differences in drinking behaviors and co-occurring conditions. NIAAA also maintains a strong research program examining sex differences in how environmental and social factors and the presence of other medical conditions can lead to different patterns of alcohol use and health vulnerabilities. Research is revealing how drinking behavior is influenced by changes in biology, psychology, and exposure to social and environmental inputs over a person's lifetime. This program will help identify life stage–appropriate strategies to inform the development of individualized prevention and treatment programs for girls and women and reduce health disparities in this critical population.

II. Scientific Advances

Emotion processing, gender, and AUD. Men and women may use alcohol to regulate emotions differently, with corresponding differences in neural responses. This functional magnetic resonance imaging (fMRI) study explored how viewing different types of emotionally salient stimuli impacts brain activity and is the *first* to explore the possible relationships between emotion processing, gender, and AUD. Four groups of adult volunteers included abstinent men and women with AUD and control groups of men and women without AUD. The two abstinent groups with AUD did not consume alcohol for at least 21 days, and the average length of abstinence was 7 years. Abstinent men with AUD showed muted brain responses to the emotionally charged images compared with their female counterparts. Abstinent men with AUD also showed smaller brain responses to the emotionally charged images than male controls. By contrast, abstinent women with AUD showed *larger* brain responses to the emotionally charged images than female controls. Overall, this study reported that functional abnormalities in cortical, subcortical, and cerebellar regions involved in emotional processing may explain why abstinent men and women with AUD differ in the way they process emotions (Sawyer et al., 2019).

This relates to Objective 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes") of the Trans-NIH Strategic Plan for Women's Health Research.

Sex differences in risk for self-medicating physical pain. Over 100 million Americans live with chronic pain, and adults with chronic pain may be more likely to experience alcohol-related problems or AUD. In this study, delayed onset muscle soreness induction, caused by an elbow straightening/biceps lengthening exercise regimen, produced clinically relevant but time-limited musculoskeletal pain, which was used to characterize physical pain as an antecedent for alcohol use in adult men and women. Participants (N = 53;

57% women) were randomly assigned to a delayed onset muscle soreness or sham condition, and alcohol demand was measured using the Alcohol Purchase Task. The delayed-onset muscle soreness procedure significantly increased pain ratings at the elbow flexors in both sexes. Increased alcohol demand in men in the delayed-onset muscle soreness group was consistent with epidemiological data suggesting men are at higher risk for self-medicating pain with alcohol than women. However, *decreased* alcohol demand in women was an unexpected finding and a factor for further consideration in alcohol research and treatment of female drinkers (Stennett et al., 2020).

This relates to Objective 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes") of the Trans-NIH Strategic Plan for Women's Health Research.

Combined prenatal smoking and drinking greatly increases sudden infant death syndrome (SIDS) risk. The NIH-funded Safe Passage Study provides a look at how SIDS risk is influenced by the timing and amount of prenatal exposure to tobacco and alcohol. From 2007 until 2015, PASS Network researchers followed the outcomes of nearly 12,000 pregnancies among women from two residential areas in Cape Town, South Africa; and five sites in the U.S., including two American Indian Reservations in South Dakota and North Dakota. The study sites were selected for their high rates of prenatal alcohol use and SIDS, and to include populations where the ethnic and socioeconomic disparities in SIDS remain understudied. A recent publication suggested that children born to mothers who both drank and smoked beyond the first trimester of pregnancy have a 12-fold increased risk for SIDS compared with those unexposed or only exposed in the first trimester of pregnancy. The study was funded by NIAAA, the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development and the National Institute on Deafness and Other Communication Disorders (Elliott et al., 2020).

This relates to Objectives 1.3 ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes") and 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health") of the Trans-NIH Strategic Plan for Women's Health Research.

Using death certificates to explore changes in alcohol-related mortality in the United States, 1999 to 2017. U.S. mortality data from the National Center for Health Statistics were analyzed to estimate the annual number and rate of alcohol-related deaths by age, sex, race, and ethnicity between 1999 and 2017 among people 16 or older. The number of alcohol-related deaths per year among people doubled from 35,914 to 72,558, and the rate increased 50.9% from 16.9 to 25.5 per 100,000. Nearly 1 million alcohol-related deaths were recorded between 1999 and 2017. Nearly half of alcohol-related deaths resulted from liver disease or overdoses on alcohol alone or with other drugs. Rates of alcohol-related deaths were highest among males, people in age groups spanning 45 to 74 years, and non-Hispanic American Indians or Alaska Natives. Rates increased for all age groups except 16–20 and 75+ and for all racial and ethnic groups except for initial decreases among Hispanic males and non-Hispanic Blacks followed by increases. The largest annual increase occurred among non-Hispanic White females. Rates of acute alcohol-related deaths increased more for people ages 55 to 64, but rates of chronic alcohol-related deaths, which accounted for most alcohol-related deaths, increased more for younger adults ages 25 to 34. This study notes that alcohol consumption, alcohol-related emergency department visits, and hospitalizations have all increased in the past two decades, particularly among women and people middle-aged or older. Findings confirm an increasing burden of alcohol on public health and support the need for improving surveillance of alcohol-involved mortality (White et al., 2020).

This relates to Objective 2.3 ("Leverage secondary data sources for research on the health of women through a big data enterprise that includes data sharing and analytic strategies") of the Trans-NIH Strategic Plan for Women's Health Research.

Associations among childhood household dysfunction, sexual orientation, and DSM-5 alcohol, tobacco, and other substance use disorders in adulthood: Evidence from a national U.S. survey. This study examined the associations between childhood household dysfunction and past-year DSM-5 alcohol, tobacco, and other substance use disorders across sexual orientation subgroups (e.g., lesbian/gay, bisexual, and heterosexual) in adulthood. Prevalence estimates were based on National Epidemiologic Survey on Alcohol and Related Conditions data collected from structured diagnostic

face-to-face interviews in a nationally representative sample of 36,309 U.S. adults. Sexual minorities, particularly sexual minority women, reported higher rates of childhood household dysfunction (e.g., parental/household history of substance-related problems) and adulthood DSM-5 alcohol, tobacco, and substance use disorders. Childhood histories of parental/household substance-related problems were associated with greater odds of past-year substance use disorders among sexual minorities than heterosexuals, and such histories may moderate differences among sexual orientation subgroups. The risk of substance use disorders among sexual minority women in relation to exclusively heterosexual women (i.e., heterosexual-identified women without same-sex attraction or behavior) remained high, even when accounting for household dysfunction. In contrast, there were no such differences between sexual minority men and exclusively heterosexual men after adjusting for parental/household history of substance-related problems and other household dysfunction. Overall, this study indicates that sexual minorities are more likely to have childhood household dysfunction, which in turn is associated with a higher risk of developing DSM-5 alcohol, tobacco, and substance use disorders in adulthood, especially among sexual minority women (McCabe et al., 2020).

This relates to Objectives 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes") and 2.3 ("Leverage secondary data sources for research on the health of women through a big data enterprise that includes data sharing and analytic strategies") of the Trans-NIH Strategic Plan for Women's Health Research.

III. Promotion of Women's Health Research

Conferences, Meetings, and Interagency Collaborations

The Interagency Work Group on Drinking and Drug Use in Women and Girls (IWG) comprises representatives from multiple Federal agency partners, academia, and health care provider organizations committed to improving access to high-quality alcohol prevention, treatment, and recovery services for women and girls. The vision and mission of the IWG were recently expanded to include access to mental health services and to services for all substance use disorders (SUDs), not only alcohol use disorder. Specifically, the IWG envisions that in the near future, all girls and women will have access to routine screening for mental health problems and disorders, alcohol misuse, and other substance misuse and SUDs and to comprehensive and effective prevention, treatment, and recovery services for all mental health disorders and SUDs.

Members of the IWG work collaboratively to develop and implement joint initiatives to improve the quantity, range, and quality of prevention, treatment, and recovery services for mental health and SUDs among women and girls across the lifespan. Because many of the issues relevant to these disorders have been understudied or entirely neglected in females, IWG members are committed to working toward expanding the research agenda so that it will provide critical information about women and girls. Recent activities of the IWG include:

1. **Virtual Issue of Alcohol Clinical and Experimental Research (ACER)** – A product of the National Conference publications committee, this online issue of ACER is based on a review of the current literature encompassing all aspects of substance use among women and girls. The full issue, published in April 2019, includes the cover article, "Alcohol and Women: A Brief Overview."
2. **Quarterly Webinars on Mental Health Problems and Substance Use Among Women and Girls** – Recent webinars have focused on substance use among adolescent girls and a collaborative care model for successful re-entry from incarceration, among other topics.

This relates to Goals 1 ("Advance rigorous research that is relevant to the health of women") and 3 ("Enhance dissemination and implementation of evidence to improve the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

NIAAA has supported the annual **International Conferences on Fetal Alcohol Spectrum Disorders (FASD)**, held in Vancouver, British Columbia, for the past 2 years with an R13 scientific conference grant (R13 AA028176) that provides travel awards to allow young

alcohol investigators to attend the conference. First held in 1987, the International Conference on FASD is widely known as the premier conference for the FASD field, providing a unique opportunity for professionals from around the world to interact and share research findings and ideas. Attendees come from a wide range of professional disciplines, including scientists, clinicians, educators, addiction specialists, policymakers, and social workers, as well as family members and individuals with FASD. Among the topics discussed at the 2019 meeting were emerging approaches to FASD prevention, international programs serving women at highest risk for substance use, and strategies to advise pregnant women about the dangers of drinking alcohol during pregnancy.

This relates to Goals 1 ("Advance rigorous research that is relevant to the health of women") and 3 ("Enhance dissemination and implementation of evidence to improve the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

The 2020 public meeting of the Interagency Coordinating Committee on Fetal Alcohol Spectrum Disorders (ICCFASD) convened on March 9, 2020. The meeting was organized and sponsored by the NIAAA. This year's Special Panel was focused on translating research to practice and included updates on the Collaborative Initiative on Fetal Alcohol Spectrum Disorders (CIFASD) and presentations on prevention and child health outcomes of prenatal substance exposure, with a special focus on concurrent prenatal exposure to alcohol and other substances. This in-person meeting was videocast and is archived at https://videocast.nih.gov. ICCFASD is sponsored and chaired by NIAAA and includes representatives from the member agencies, including ACF, ACL, ASPE, CDC, CMS, HRSA, IHS, SAMHSA, and NIH (NIAAA, NICHD, NIDA, and NIMH). ICCFASD fosters improved communication, cooperation, and collaboration among disciplines and Federal agencies that address issues related to prenatal alcohol exposure.

This relates to Goal 3 ("Enhance dissemination and implementation of evidence to improve the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

FUNDING INITIATIVES

Notice of Special Interest: Alcohol and Aging (NOT-AA-20-019). The purpose of this notice of special interest (NOSI) is to promote research to improve our understanding of the effects of alcohol consumption on aging across different levels of biological organization including the molecular, cellular, tissue, organ, organism, and societal levels. The following broad research areas are encouraged: (1) basic and clinical research defining the effects of alcohol consumption on lifespan, health span, and age-related diseases, depending on level of alcohol consumption, drinking pattern, and duration of drinking; (2) research to inform evidence-based guidance for identifying risk for alcohol use disorder (AUD) among older adults, as well as prevention, diagnosis, and treatment of AUD in this population; and (3) research to extend the health span of older adults who drink and decrease the health care burden of age-related diseases associated with alcohol use. People over 65 years constitute the fastest-growing segment of the U.S. population with increasing alcohol consumption, particularly among women. Diagnosing AUD in this population is more difficult, as symptoms may be masked by aging-related conditions. This silent epidemic represents a significant public health problem, as aging is one of the biggest risk factors of chronic, non-communicable diseases that are exacerbated by alcohol.

This relates to Goal 1 ("Advance rigorous research that is relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

The NIAAA Fetal Alcohol Spectrum Disorders (FASD) Working Group has released two initiatives (PAR-21-097 and PAR-21-098) to support research that advances interventions for fetal alcohol spectrum disorders and prevention approaches to reduce prenatal alcohol exposure and the incidence of FASD:

- PAR-21-097: Prevention and intervention approaches for fetal alcohol spectrum disorders (R34 Clinical trial optional)
- PAR-21-098: Prevention and intervention approaches for fetal alcohol spectrum disorders (R61/R33 Clinical trial optional)

This relates to Goal 1 ("Advance rigorous research that is relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

IV. Advancement of Women in Biomedical Careers

Building Interdisciplinary Research Careers in Women's Health (BIRCWH) K12 Scholars Program at MUSC and UIC:

- Building Interdisciplinary Research Careers in Women's Health at Medical University of South Carolina (MUSC). The overall objective of MUSC's BIRCWH program is to attract translational scientists in the neuroscience arena to broaden interdisciplinary research related to women's health in South Carolina and throughout the U.S. This program reaches across professional and scientific boundaries to transform women's health outcomes by developing a cadre of highly trained early-career scientists committed to interdisciplinary research to benefit the health of women, advance research on sex/gender influences on health, encourage interdisciplinary research methodology, and advance knowledge in the treatment of women's health issues related to brain and behavior across the lifespan (McGinty, K12 HD055885).

- University of Illinois at Chicago (UIC) Building Interdisciplinary Research Careers in Women's Health Program. The overall goal of the UIC's BIRCWH program is to align with the 2019–2023 Trans-NIH Strategic Plan for Women's Health Research to "promote training and careers to develop a well-trained, diverse, and robust workforce to advance science for the health of women." Its long-term objective is to promote training and career development of a new generation of researchers equipped with the knowledge and career skills necessary to advance science for the health of women in the next decade and beyond (Maki, K12 HD101373).

This relates to Objectives 4.2 ("Develop the next generation of researchers to advance science on the health of women") and 4.3 ("Enhance and develop programs to recruit, support, retain, and advance women at all stages of their research careers, from early career to leadership positions") of the Trans-NIH Strategic Plan for Women's Health Research.

NIAAA Summer Research Internship Program. This program provides research internships for high school and undergraduate students, with a goal of recruiting underrepresented racial/ ethnic students into research. This 8-week paid program exposes students to alcohol research and encourages them to pursue careers in biomedical and behavioral research. Students' activities include, but are not limited to, laboratory experiments, data collection activities, data analysis, patient recruitment, manuscript preparation, literature reviews, and library research. In 2019, NIAAA awarded 18 internships, of which 8 were to women (44%). In 2020, the Summer Research Internship Program was canceled because of the COVID-19 pandemic.

V. Implementation of the NIH Policy on Sex as a Biological Variable (SABV)

NIAAA has enforced and promoted the SABV policy at various stages of the biomedical research enterprise. The following are examples of NIAAA's SABV policy implementation:

- The National Advisory Council on Alcohol Abuse and Alcoholism advises and makes recommendations to the HHS Secretary, the NIH Director, and the NIAAA Director on research program and policy matters in the field of alcohol abuse and alcoholism. Dr. Jill Becker, a leader in research of sex differences in the brain and the effects on alcohol and substance use, serves on the Advisory Council and provides guidance on and awareness to the SABV policy. The NIAAA Director has highlighted numerous research findings addressing SABV in the Director's Report on institute activities at meetings of the National Advisory Council on Alcohol Abuse and Alcoholism in FYs 2019 and 2020.

- NIAAA has published *Alcohol Research: Current Reviews Issue on Women and Alcohol* (Volume 40, Number 2, 2020), https://www.arcr.niaaa.nih.gov/arcr402/toc.htm.

This issue, comprising 13 articles, highlights critical, ongoing sex-specific knowledge gaps in our understanding of the epidemiology of alcohol use, the interplay of physiology and alcohol, and best approaches to prevention and treatment. This research supports the importance of the NIH mandate not only to include female subjects in research but also to include them in sufficient numbers to permit sex-specific analyses of findings.

VI. Inclusion of Women in Clinical Research

Yale-Specialized Center of Research Excellence (SCORE) on sex differences in alcohol use disorder (AUD). Yale-Specialized Center of Research Excellence (SCORE) on sex differences in AUD brings together a team of leading basic and clinical science experts to pursue an interdisciplinary, translational, cross-species program of research aimed at identifying novel therapeutics to address the recent surge in rates of AUD among women. Using a negative reinforcement model, this grant targets key brain structures, neurochemical systems, hypothalamic–pituitary–adrenal axis activity, neuroimmune function, alcohol metabolism, and sex steroid hormones, which are hypothesized to differentially motivate alcohol consumption in women. This research contributes to the public health effort to improve AUD treatment by providing a neurobiologically informed approach to the development of sex-appropriate therapeutics for AUD, mentoring the next generation of interdisciplinary and translational researchers focused on alcohol use and women's health, and providing an institutional, regional, and national center of research excellence on sex differences in alcohol use spanning T1 to T4 translation. (T1 research tests findings from basic research for clinical effect and/or applicability. T1 research yields knowledge about human physiology and the potential for intervention. T2 research tests new interventions in controlled environments to form the basis for clinical application and evidence-based guidelines. T2 research yields knowledge about the efficacy of the interventions in optimal settings. T3 research explores ways of applying recommendations or guidelines in general practice. T3 research yields knowledge about how interventions work in real-world settings. T4 research studies factors and interventions that influence the health of populations. T4 research ultimately results in improved global health.) (McKee, U54 AA027989)

This relates to Objective 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health") of the Trans-NIH Strategic Plan for Women's Health Research.

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National Institute of Allergy and Infectious Diseases

I. Executive Summary

The National Institute of Allergy and Infectious Diseases (NIAID) conducts and supports basic and applied research to understand, diagnose, prevent, treat, and, ultimately, cure infectious and immune-mediated diseases, including diseases that affect the health of women and girls. NIAID research activities satisfy requirements in the 21st Century Cures Act to include women and minority populations in clinical studies on treatment and prevention of human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS), autoimmune diseases, and other diseases. NIAID intramural and extramural researchers continue to analyze data for sex-based differences in basic, translational, and clinical studies and conduct research within NIAID's mission areas that aims to improve women's health and reduce health disparities.

This biennial report provides an overview of selected NIAID-supported research findings relevant to women's health. Sex-based differences in immune responses to infectious disease—including COVID-19, influenza, and methicillin-resistant bacterial infections—have been investigated. Also highlighted are research findings that characterize immune mechanisms during pregnancy, including at the maternal–fetal interface. Women are getting infected with HIV at a higher rate than men, particularly in developing countries, making studies of HIV treatment critical to resolving this public health concern. One such study found that an investigational antiretroviral therapy (ART) in pregnant women with HIV is more effective in suppressing HIV and safer for the infant than a different, commonly used regimen.

In addition to highlighting research that increases our understanding of women's health, this report also features NIAID's activities to support the advancement of women in biomedical careers. Through these efforts and others, NIAID continues its commitment to the inclusion of women in its scientific mission.

II. Scientific Advances

Bacteria Are Selectively Killed by Maternal Immune Cells to Protect the Placenta from Infection

During pregnancy, the mother's immune system dampens in order to accept, or tolerate, the presence of the fetus rather than reject it as something "foreign" in the body. This dampened immune response can make it difficult for a pregnant woman's immune system to prevent an infection from spreading to the placenta and then to the developing fetus. One such infection is caused by the bacterium *Listeria monocytogenes*. Pregnant women are 10 times more likely than other people to get a *Listeria* infection, which can result in miscarriage, stillbirth, premature birth, or serious illness or even death in newborns.

A NIAID-funded study used animal models and cells grown in the laboratory to show that a protein called granulysin is transferred from decidual natural killer cells—a type of immune cell found at the maternal–fetal interface—through a tiny molecular nanotube to *Listeria*-infected placental cells. Once inside the cell, granulysin selectively kills the bacteria by making holes in the bacteria's protective outer membrane without harming the placental cell. This process defends against infection while maintaining tolerance to the developing fetus. These findings, which expand our understanding of reproductive and maternal health, may have broader implications and explain how maternal cells may protect the fetus from other disease-causing microbes (Crespo et al., 2020).

This basic research relates to Objective 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health") of the Trans-NIH Strategic Plan for Women's Health Research.

Immune Responses to COVID-19 Differ Between Males and Females

There is increasing evidence that men tend to have more severe symptoms of COVID-19 and a higher death rate than women with the disease. To investigate whether there are sex-based differences in the body's immune responses to infection with SARS-CoV-2, the virus that causes COVID-19, a NIAID-funded study enrolled male and female COVID-positive patients admitted to the hospital.

Blood, nasal swabs, and saliva, urine, and stool samples were collected at the time of enrollment and every 3 to 7 days after that. Investigators compared immune responses between patients who recovered and those who progressed to worse stages of disease. Males and females were matched by age, body mass index, and the number of days after their symptoms began.

Several key differences in immune responses were seen between male and female patients with COVID-19. Males had higher blood levels of several inflammatory proteins called cytokines, including two known as IL-8 and IL-18, and lower activation of immune cells called T cells than females, which can recognize and help eliminate invading viruses. The clinical course of COVID-19 in study participants showed that poor T-cell responses in males, but not in females, were associated with progression of disease. Also, T-cell responses declined with age in males only. By contrast, elevated cytokine levels were associated with worse disease outcomes in females but not in males. Together, the results suggest that therapeutic approaches to increasing the T-cell immune responses to SARS-CoV-2 might work best for males, whereas female patients might benefit from therapies that reduce the activation of inflammatory proteins early in disease.

This study investigated the influence of sex and gender on COVID-19 presentation and outcomes and identified a potential immunological basis for the difference in disease outcomes between males and females with the disease. The findings underscore the need to consider distinct treatment strategies for COVID-19 in male and female patients (Takahashi et al., 2020).

This clinical research relates to Objective 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes") of the Trans-NIH Strategic Plan for Women's Health Research.

Replenishing Beneficial Bacteria Prevents Recurring Bacterial Vaginosis

Bacterial vaginosis (BV) is inflammation caused by an overgrowth of microorganisms that normally populate a woman's vagina. BV may be uncomfortable or painful, can increase the risk of contracting HIV or other sexually transmitted infections, and is associated with higher rates of premature birth and low birth weight babies in pregnant women. While BV can be cured with antibiotics, achieving a durable cure is difficult, as infection often recurs after antibiotic treatments are completed. A NIAID-supported trial conducted by investigators from the Sexually Transmitted Infections Clinical Trials Group tested whether the administration of LACTIN-V following antibiotic treatment in women with BV could lower the incidence of recurrence. LACTIN-V, an intravaginal live biotherapeutic product, is designed to repopulate the vaginal microbiome with the beneficial bacteria typically found in the vaginas of healthy women.

The trial enrolled 228 women who were diagnosed with BV. Participants first received a 5-day vaginal course of metronidazole antibiotic gel to treat BV and then were randomly assigned to receive either LACTIN-V or a placebo. Researchers took vaginal swabs to track bacteria in the volunteers' vaginal microbiomes at follow-up visits 4, 8, 12, and 24 weeks later. After 12 weeks, volunteers who had received LACTIN-V had significantly fewer recurrences of BV than volunteers who had received placebo. After 24 weeks, 39% of volunteers who had received LACTIN-V experienced recurring BV, while 54% of participants in the placebo group had experienced a recurrence. These findings suggest that LACTIN-V treatment can prevent harmful bacteria from causing BV recurrence, and they expand our knowledge about female-specific conditions and gynecologic health. A larger clinical trial to confirm the results and further investigation into whether LACTIN-V can reduce the risk of sexually transmitted infections and premature birth are warranted (Cohen et al., 2020).

This clinical research relates to Objective 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and

gynecologic health") of the Trans-NIH Strategic Plan for Women's Health Research.

Tuberculosis Preventive Therapy Poses Greater Risk in Pregnancy than Postpartum in Women with HIV

Tuberculosis (TB) is a leading cause of death worldwide and the leading cause of death for people with HIV. When active TB disease develops during pregnancy or in the weeks after birth, it is associated with poor health outcomes for both the mother and baby. Isoniazid therapy to prevent active TB in people with HIV is generally considered beneficial. However, because pregnant women have previously been excluded from clinical trials of isoniazid preventive therapy, information is lacking about the safety, efficacy, and appropriate timing of this approach in pregnant women with HIV.

A clinical trial expanding research on female-specific conditions and maternal health was conducted by the IMPAACT (International Maternal Pediatric Adolescent AIDS Clinical Trials) Network, which is co-funded by NIAID. The study enrolled 956 pregnant women with HIV and assigned them to take isoniazid either during pregnancy or 12 weeks after delivery. Both groups of women—those who took isoniazid during pregnancy and those who began taking it 12 weeks after delivery—experienced some poor health outcomes for fetuses and newborns (stillbirth, spontaneous abortion, low birth weight, preterm delivery, and congenital abnormalities). However, the percentage of pregnancies with poor fetal and newborn health outcomes was reduced in the group who began isoniazid after delivery (17%) versus during pregnancy (24%). Thus, for women living with HIV, treatment during pregnancy with isoniazid posed significantly greater risk of poor health outcomes and death for the fetuses and newborns than treatment during the postpartum period. Study investigators noted that this finding is concerning and merits research into alternative approaches to TB preventive therapy in pregnant women (Gupta et al., 2019).

This clinical research relates to Objective 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health") of the Trans-NIH Strategic Plan for Women's Health Research.

Interruption of HIV Treatment Is Well Tolerated in Women Following Childbirth

Antiretroviral therapy (ART) is used to treat HIV infection by suppressing levels of virus in the body, which can prevent transmission. Interruption of ART can permit HIV transmission or progression of disease. A clinical study examined the safety of interrupting HIV treatment in women following childbirth and compared the results with findings in men to investigate the influence of sex on disease management/outcome and expand research into maternal health.

As part of the NIAID-funded Promoting Maternal and Infant Survival Everywhere (PROMISE) trial, researchers studied the safety of discontinuing ART following childbirth. They also measured the amount of time required for HIV to return to detectable levels in the blood, known as viral rebound. The trial enrolled women with HIV from Africa, Asia, North America, the Caribbean, and South America who were virally suppressed and did not have symptoms of HIV/AIDS. The women were randomly assigned either to continue or to discontinue ART in the period after childbirth. Treatment interruption was well tolerated by study participants, with very few serious adverse health events resulting from viral rebound.

Researchers compared the time to viral rebound of women in this clinical trial with results from another set of studies that enrolled predominantly U.S. male participants, called the AIDS Clinical Trials Group (ACTG). This comparison showed that the virus remained suppressed longer among women participating in the PROMISE study than in men participating in the ACTG study. The results of the PROMISE study suggest that brief interruptions in ART may be well tolerated in women with HIV. In addition, they underscore the importance of considering sex differences in future HIV cure studies. Identifying relevant factors related to cure research that differ by sex will be important for developing effective therapies for all people with HIV (Le et al., 2019).

This clinical research relates to Objectives 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes") and 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and

maternal and gynecologic health") of the Trans-NIH Strategic Plan for Women's Health Research.

III. Promotion of Women's Health Research

» ***Sex Differences in Antibody Responses to Various Influenza Strains***
The NIAID Centers of Excellence for Influenza Research and Surveillance (CEIRS) is funding a study of sex differences in immune responses to different strains of influenza, which will help discover basic biological differences between females and males and investigate the influence of sex on disease presentation and outcomes. Using human clinical samples collected in Taiwan and the United States from participants admitted to the hospital with confirmed influenza and at 28 days post-admission, CEIRS investigators will characterize antibody responses that are associated with differing influenza strains and disease severity. Leveraging both the human samples and a mouse model, researchers will test the hypothesis that sex affects intrinsic properties of antibody-producing immune cells, called B cells, to result in differential antibody responses and protection against influenza in females compared with males. This study, funded in 2019, expands on previously funded work that demonstrated that influenza vaccine efficacy is higher in females than males.

This relates to Objectives 1.1 ("Discover basic biological differences between females and males") and 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes") of the Trans-NIH Strategic Plan for Women's Health Research.

» ***Sex-Based Differences in Murine Methicillin-resistant Staphylococcus aureus (MRSA) Bacteremia*** (3 U01 AI124319-03)
Methicillin-resistant *Staphylococcus aureus* (MRSA) bacteria can cause life-threatening infections. About one-third of MRSA infections are resistant to established MRSA treatment, resulting in the persistent presence of bacteria in the bloodstream, or bacteremia. In an ongoing NIAID-supported study, initiated in 2018, a model of MRSA infection in male and female mice is being used to study new approaches to preventing and treating persistent bacteremia. The data show significantly greater levels of infection in target organs of male mice and less susceptibility to antibiotics in male kidneys and spleens compared with female mice. Importantly, the finding that males are at risk for worsened disease and less antibiotic efficacy appears

to reflect clinical trends seen in human MRSA infection. Further studies are underway utilizing this innovative study design to evaluate the influence of sex on the ability to resolve bacterial infections.

This relates to Objectives 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes") and 2.1 ("Expand and develop advanced and innovative approaches for study design, data collection, and analysis to optimize data quality and the ability to detect the influences of sex and gender on health and disease") of the Trans-NIH Strategic Plan for Women's Health Research.

» ***Ongoing Research to Provide Tools for HIV Prevention and Treatment in Women and Adolescent Girls and During Pregnancy***

NIAID continues to support the development of HIV prevention tools, including the dapivirine ring, a vaginal ring that continuously releases the anti-HIV drug dapivirine over the course of 1 month. In July 2020, the European Medicines Agency approved the dapivirine ring for use by cisgender women in developing countries to reduce their risk of HIV infection. This announcement disseminated important information about the increased number of pharmacologic HIV prevention options available to women in sub-Saharan Africa, who are among those most affected by the HIV epidemic. Pre-exposure prophylaxis (PrEP), a single antiretroviral therapy (ART) pill taken daily, is another powerful HIV prevention strategy that could potentially protect pregnant and postpartum adolescent girls and young women from acquiring HIV. A NIAID-supported clinical study, IMPAACT 2009, is assessing whether pregnant and postpartum adolescent girls and young women are willing and able to consistently take daily PrEP and whether it is safe for them and their infants. Early results showed that among participants who took PrEP daily under direct observation, levels of the PrEP drug tenofovir were more than 30% lower in those who were pregnant than in those who had recently given birth, underscoring the critical importance of daily adherence to PrEP for this population. Like prevention of HIV, treatment of pre-existing HIV infection during pregnancy is also complicated because of metabolic changes in the mother and the possibility that therapy will be harmful to the fetus. A large international trial recently demonstrated that ART regimens containing dolutegravir were more effective in suppressing HIV and safer for the infant than a different, commonly used regimen.

This relates to Objectives 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes"), 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health"), 3.1 ("Design and test approaches to promote the adoption, adaptation, and integration of evidence-based interventions in public health, clinical practice, and community settings"), and 3.2 ("Identify collaborative opportunities and leverage partnerships to disseminate research that improves the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

» ***Clinical Development Plan to Test Malaria Vaccine in Pregnant Women***

Malaria in pregnancy is a major cause of maternal and infant mortality in areas where malaria is endemic. No malaria vaccine candidate has ever been tested in pregnant women. In 2019, NIAID investigators and collaborators in Mali developed a clinical testing site for vaccine studies in pregnant women. As a first step, a study to assess the safety and efficacy of a malaria vaccine candidate, called PfSPZ, in women of child-bearing potential is currently enrolling participants. In this randomized, placebo-controlled clinical trial, researchers will administer the vaccine at 1, 8, and 29 days at two different doses to assess its safety and tolerability in nonpregnant Malian women (ClinicalTrials.gov Identifier: NCT03989102). Women who become pregnant during the study and their infants will be followed to assess maternal clinical outcomes. The next steps in the vaccine clinical development plan are studies of the safety and efficacy of PfSPZ vaccine in all trimesters of pregnancy. This research investigates the influence of sex and gender on malaria prevention, expands research on malaria vaccination during pregnancy, and expands and refines methodologies to improve the recruitment and retention of pregnant women in clinical research.

This relates to Objectives 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes"), 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health"), and 2.4 ("Expand and refine methodologies to improve the recruitment and retention of women underrepresented in clinical research") of the Trans-NIH Strategic Plan for Women's Health Research.

» ***Immune Mechanisms at the Maternal–Fetal Interface (RFA-AI-18-02)***

Eleven projects were awarded in 2019 under the NIAID funding opportunity titled "Immune Mechanisms at the Maternal-Fetal Interface (R01 Clinical Trial Optional)" (RFA-AI-18-023), which aims to support innovative research that uses advanced study designs to determine the roles and interactions of immune cells at the maternal–fetal interface throughout pregnancy. This work includes the study of mechanisms underlying maternal responses to vaccination and infection that protect or impact the fetus and how they might influence fetal immune system development. The funded projects explore a diverse array of key immunological parameters. Several projects focus on developing a better understanding of the immune cells that fight infection, such as uterine natural killer cells, which play a key role in the maternal immune response during pregnancy. Another project will define placental immune responses that are critical for resolution of bacterial infections, while others will investigate factors that alter maternal–fetal sensitivity to viral infections such as hepatitis B virus, Zika virus, rubella virus, and herpesvirus-2. The biological phenomenon of how the fetus and placenta avoid rejection by the maternal immune system will also be explored.

This relates to Objectives 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health") and 2.1 ("Expand and develop advanced and innovative approaches for study design, data collection, and analysis to optimize data quality and the ability to detect the influences of sex and gender on health and disease") of the Trans-NIH Strategic Plan for Women's Health Research.

IV. Advancement of Women in Biomedical Careers

Women in Immunology: 2020 and Beyond

In February 2020, four female NIH intramural scientists, including two from NIAID, published a perspective article, Women in immunology: 2020 and beyond. Despite the progress that women have made in the field of immunology, challenges to retention and career advancement remain. The authors outlined a three-pronged approach to creating exemplary work environments that allow every female scientist to achieve her fullest potential: (1) equalizing resource allocation, (2) optimizing mentorship and providing advocacy, and (3) challenging stereotypes and beliefs emerging from a patriarchal culture. Their approach aligns with Objective 4.5 of the Trans-NIH Strategic Plan for Women's Health Research ("Promote and support policies, mentoring and networks, collaborations, and infrastructure to retain and advance women in their careers").

The article highlights the critical need to equalize both quantitative and qualitative resources and to have women in leadership positions, as those positions are often responsible for allocating discretionary funds. For effective mentorship and advocacy, women must be models for the younger generation and provide career advancement advice. In addition, both men and women in positions of power must actively promote and advocate for women within their departments. Finally, a change is needed in the criteria by which promotion and advancement are evaluated, as many of these metrics tend to favor males. The authors believe that some of the straightforward changes identified in their article can translate into significant advances for women in science (Pierce et al., 2020).

Bilateral and Multilateral International Programs Support Women in Biomedical Science Careers

NIAID participates in collaborative research funding opportunities and conferences through the East Asia Science and Innovation Area Joint Research Program (e-ASIA-JRP) and the U.S.-Japan Cooperative Medical Sciences Program (USJCMSP). Both programs promote

and foster the inclusion and leadership of diverse women scientists in collaborative biomedical research, which aligns with Objective 4.3 of the Trans-NIH Strategic Plan for Women's Health Research ("Enhance and develop programs to recruit, support, retain, and advance women at all stages of their research careers, from early career to leadership positions").

The e-ASIA JRP supports collaborative research projects that promote and include scientific exchange and capacity building activities. Research project review criteria indicate that each project should conduct activities to engage female researchers where strengthening capacity is needed.

The purpose of the USJCMSP, established in 1965, was to undertake an expanded, cooperative research effort in the medical sciences, concentrating on health problems in Southeast Asia. In their 2016 Declaration of Bethesda, the USJCMSP Joint Committee declared that it would "make a special effort to involve female scientists and other underrepresented groups in USJCMSP activities." Since then, one objective of the USJCMSP Collaborative Awards Program is to encourage the mentoring and training of early-stage and female investigators through collaborations with mid-career and senior investigators in the areas of infectious diseases and immunology. Each collaborative research team must include at least one early-stage or female investigator and requires that either the Japanese sub-team or the U.S. sub-team include an early-stage or female investigator as a primary investigator. Recipients of the USJCMSP Collaborative Awards participate and present their research at the program's annual international conference on emerging infectious diseases.

V. Implementation of the NIH Policy on Sex as a Biological Variable (SABV)

NIAID continues to support research and practices in alignment with the SABV policy:

- In the **NIAID Scientific Review Program**, peer reviewers evaluate the SABV policy's elements in grant applications as one element of the Rigor and Reproducibility policy's four areas of focus (scientific premise, scientific rigor, biological variables, and authentication). For awarded grants, NIAID program officers evaluate compliance with the SABV policy when reviewing yearly progress reports.
- In 2019, NIAID staff participated in the ORWH ***GWAS, Sex, and Chromosomes Think Tank***, helping to identify gaps and opportunities related to genetic association analyses of the sex chromosomes and the consideration of SABV in genome-wide association studies (GWAS).
- NIAID also participates regularly in the **Trans-NIH SABV Working Group**, which is mandated to inform SABV policy development. In 2020, NIAID staff presented to the SABV Working Group on sex and gender influences in coronavirus disease.
- The **Trans-NIAID Women's Health Research Working Group** focuses on women's health and gender-based research activities that advance the mission and research priorities of NIAID and provides recommendations for future women's health research opportunities. The working group meets quarterly to disseminate information regarding NIH's SABV policy updates and trans-NIAID and trans-NIH collaborations on women's health research activities and to heighten awareness of the importance and substance of women's health research.
- NIAID encourages evaluation of sex-based differences in all research on HIV/AIDS, non-HIV infectious diseases, and immunology and immune-mediated diseases. For example, in FY 2020, NIAID prepared a **notice of special interest (NOSI)** on pan-coronavirus vaccine development program projects to highlight the critical need to develop vaccine candidates capable of providing broad and durable protective immunity against multiple coronavirus strains, especially SARS-CoV-2 and others with pandemic potential. The NOSI, to be published in FY 2021, expresses NIAID's interest in funding highly collaborative, multidisciplinary studies that will investigate vaccine-induced responses across the lifespan, including investigation of age- or sex-related effects on vaccine efficacy.

VI. Inclusion of Women in Clinical Research

Women face a greater risk of acquiring HIV than men, in part because of substantial exposure to semen at mucosal membrane sites, prevalence of nonconsensual sex, and sex without condom use. The **Office of HIV/AIDS Network Coordination Women's HIV Research Collaborative (WHRC)** has successfully promoted the inclusion of cisgender and transgender women in HIV prevention and cure research, with trainings, a statement advocating for the inclusion of women in HIV and COVID-19 research that was signed by 58 individuals and organizations, and an infographic for National Women and Girls HIV/AIDS Awareness Day.

The NIAID **HIV Prevention Trials Network (HPTN) and HIV Vaccine Trials Network (HVTN)** are international clinical trial networks that analyze data for gender differences regarding safety, tolerability, and immune responses to interventions. HPTN develops and tests non-vaccine HIV prevention strategies such as pre-exposure prophylaxis (PrEP). HPTN efforts to develop long-acting forms of HIV prevention include an ongoing study, HPTN 084, comparing the efficacy and safety of injectable cabotegravir with daily oral PrEP (a dose of two antiretrovirals in a single pill) in cisgender women. HVTN is working toward the development of an effective and safe HIV vaccine. HVTN 703/HPTN 081 is assessing the safety and efficacy of a broadly neutralizing monoclonal antibody called VRC01 in reducing acquisition of HIV in cisgender women in sub-Saharan Africa. HVTN 705 (Imbokodo study) is evaluating a vaccine regimen among women and has fully enrolled 2,600 women in southern Africa. HVTN 706 (Mosaico study) is a large international study to test whether an investigational vaccine regimen can safely and effectively prevent HIV among 3,800 cisgender men and transgender individuals, which has enrolled just over 500 participants.

NIAID also promotes the inclusion of women in clinical trials beyond the HIV/AIDS clinical trials networks. The **Vaccine Research Center** Clinical Trials Program strives to enroll a diverse group of participants, including women and underrepresented minorities, in all clinical studies. In a recent study of SARS-CoV-2, the virus that causes COVID-19 (NIAID Protocol #20-I-0083), NIAID investigators engaged an innovative system that recognizes potential needs for increased participation while enrollment is underway to ensure inclusion of women from diverse populations. A SARS-CoV-2 clinical trial funded by NIAID (5U01AI144673-02) is leveraging existing mother–infant cohorts originally established to study influenza to investigate how COVID-19 impacts women's health.

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National Institute of Arthritis and Musculoskeletal and Skin Diseases

I. Executive Summary

The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) supports a broad range of research, research training and career development activities, and health information programs for numerous debilitating diseases affecting Americans. Many of these—including fibromyalgia, osteoarthritis (OA), osteoporosis, rheumatoid arthritis (RA), scleroderma/systemic sclerosis, systemic lupus erythematosus (SLE, or lupus), and juvenile idiopathic arthritis (JIA)—disproportionately affect women.

With support from the Office of Research on Women's Health and other NIH components, NIAMS provides an information dissemination and outreach program to distribute health information to patients, health care providers, and other members of the public. For example, NIAMS oversees the NIH Osteoporosis and Related Bone Diseases ~ National Resource Center (ORBD~NRC), which is co-funded by the National Institute on Aging, the National Institute of Diabetes and Digestive and Kidney Diseases, and the Office of Research on Women's Health.

In accordance with the 21st Century Cures Act (Public Law 114–255), the NIAMS Director consults with the Director of the Office of Research on Women's Health regarding NIAMS objectives to ensure its future activities take into account the health needs of women and are focused on reducing health disparities. NIAMS works closely with the Office of Research on Women's Health, and NIAMS staff are active participants in standing and ad hoc committees related to NIH priorities for women's health and health disparities. These relationships enable the institute to align its work in these areas with broader NIH efforts and to leverage and synergize with related activities across NIH. The importance of such research to NIAMS is reflected in the NIAMS Strategic Plan for Fiscal Years 2020–2024 section titled "Health and Disease in Diverse Populations."

II. Scientific Advances

Identification of Sex-Dependent Pain Differences Following Trauma

Motor vehicle collisions and sexual assault are common sources of traumatic stress. Research suggests that for every 10 individuals experiencing such an event, 2 will develop persistent post-traumatic widespread pain (PTWP) and 3 to 7 will develop post-traumatic stress symptoms (PTSS). PPWP and PTSS frequently occur together, suggesting shared mechanisms. They also are more common in women than in men.

In this study, researchers demonstrated that a specific microRNA (miR-19b) in the blood serum is influenced by estrogen and exposure to a motor vehicle collision or sexual assault. The observed expression levels of this microRNA indicate a sex-dependent difference in vulnerability to PTWP and PTSS. Furthermore, miR-19b regulation appears to affect the circadian rhythm and implicates circadian rhythm genes in the development of PTWP and PTSS.

Though much more work remains to be done, pain research and the response to traumatic situations is a growing field, and understanding the mechanisms by which a person responds to trauma and pain will help identify appropriate physical or biopsychosocial therapies (Linnstaedt et al., 2020).

This clinical research relates to Objective 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes") of the Trans-NIH Strategic Plan for Women's Health Research.

Pregnancy and Lactation Lead to Bone Changes in Rats That Protect Against Bone Loss Due to Hormonal Changes

Osteoporosis, which is most common in postmenopausal women and the elderly, is primarily

characterized by significant bone loss and changes in bone structure that lead to increased bone fragility and fracture risk. During their reproductive years, women who become pregnant and lactate undergo significant bone loss that is recovered post-weaning. Data suggest that the recovered bone has a different structure than the bone that was there previously, and epidemiological studies suggest that a history of pregnancy and lactation may protect against postmenopausal osteoporosis.

Using a rat model, researchers sought to determine why there is no increased osteoporosis development or fracture following estrogen loss associated with pregnancy- and lactation-induced bone structure changes. Recovered bone in the tibias of rats that had been pregnant and nursed their pups differed from bone in rats with no reproductive history; trabecular (inner) bone was thicker, and cortical (outer) bone was larger. The rats with and without a history of pregnancy and lactation then underwent surgery to induce a loss of ovarian function (ovariectomy, OVX) to mimic estrogen deficiency associated with menopause. Following OVX, rats with a reproductive history had a slower rate of trabecular bone loss and no cortical bone effects, leading to less structural changes than those with no birth history. Rats that had given birth also had no change associated with bone strength as measured by whole bone stiffness after OVX. The researchers concluded the slower rate of bone loss caused by these differences in bone structure following pregnancy and lactation may protect against estrogen-deficient bone loss.

Despite their success, public concern about current osteoporosis therapies has led to a decline in their usage and a change in osteoporosis prevalence. Understanding how bone rebuilding following pregnancy- and lactation-induced bone loss may protect against osteoporosis risk during postmenopause could provide targets for novel therapies (de Bakker et al., 2018).

This translational research relates to Objective 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health") of the Trans-NIH Strategic Plan for Women's Health Research.

Novel Link Identified Among Gut Bacteria, Pregnancy, and Worsened Lupus

Systemic lupus erythematosus, or lupus, is a chronic, inflammatory autoimmune disease. It is far more common in females than in males, with peak incidence between the ages of 15 and 45. Increasing evidence indicates that imbalances within a person's microbiome may contribute to metabolic and immune abnormalities that spark the development of autoimmune diseases such as lupus. Recent studies suggest major changes in the microbiota occur during pregnancy, which could explain why pregnant women with lupus have a higher risk of worsening symptoms after delivery.

Previous findings showed that lupus-prone mice treated with vancomycin, an antibiotic that combats bacteria in the gut, displayed diminished disease symptoms. However, in the current study, the investigators demonstrate that, surprisingly, in lupus-prone mice that had experienced pregnancy and lactation (named "postpartum" or "PP" mice), vancomycin treatment worsened lupus symptoms. The investigators next examined vancomycin-induced changes to the gut microbiota and found that both PP and nonpregnant lupus-prone control mice had less bacteria overall but an increase in levels of a bacterial species called *L animalis*. Control and PP mice treated with *L. animalis* instead of vancomycin exhibited similar features as when treated with vancomycin; the PP group exhibited exacerbated lupus, indicating that *L. animalis* recapitulated the effects of vancomycin. Furthermore, the investigators went on to show that *L. animalis* acted by inhibiting an enzyme called indoleamine 2,3-dioxygenase, an immune regulator associated with suppression of autoimmunity. This inhibition occurred only in the PP mice, which may explain the differential effects of vancomycin in control versus PP mice.

Though further studies in humans are warranted, these findings suggest that beneficial and pathogenic gut bacterial might be targeted therapeutically to change the gut microbiota for beneficial effect. For lupus patients, diet and probiotics would be relatively easy and tolerable approaches for modulating gut microbiota and potentially improving disease management (Mu et al., 2019).

This translational research relates to Objective 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health") of the Trans-NIH Strategic Plan for Women's Health Research.

Characterization of Molecular Events Leading to Rheumatoid Arthritis Flares

Rheumatoid arthritis (RA) is a complex disease involving chronic inflammation of the joints that results in the progressive loss of joint tissue and mobility. RA symptoms occur as episodes of unpredictable worsening called flares, followed by improvement. Like many autoimmune diseases, it disproportionately affects women.

Investigators who examined changes of gene expression in blood samples collected weekly from RA patients over 4 years found that a type of immune cells called B cells become activated about 2 weeks before a flare, whereas the number of unexpected type of cells called PRIME cells, which are normally present in low levels in the blood, greatly increase in the days just prior to a flare and disappear during the flare itself. Importantly, the PRIME cells share gene expression features with the RA joint tissue cells called fibroblasts, which are known to increase in numbers, become invasive, and are critical to persistent inflammation in RA. Taken together, these results suggest a model in which circulating precursors of inflamed joint fibroblasts become activated in the weeks prior to RA flares and move from blood to the joint.

Studying the mechanism of RA flares and trying to predict them is important, as RA flares occur even in patients with good disease control and most permanent joint damage is thought to accumulate during repeated flares. The insights gained pursuing this line of research may hold a key to understanding the root causes of RA and, potentially, to improve management of disease (Orange et al., 2020).

This clinical research relates to Objective 2.3 ("Leverage secondary data sources for research on the health of women through a big data enterprise that includes data sharing and analytic strategies") of the Trans-NIH Strategic Plan for Women's Health Research.

Sex Differences in Neutrophil Biology

There are striking differences between men and women in their ability to respond to certain infections, predisposition to and prognosis in certain cancers, and risk for developing an autoimmune disease. However, the underlying mechanisms that drive the differences between the male and female immune systems remain insufficiently characterized, especially for innate immune system cells such as neutrophils. Recent work showed that female neutrophils have striking upregulation of type I interferon-stimulated genes (ISGs), suggesting an enhanced response to this group of antiviral cytokines. In addition, the sex differences in type I interferon (IFN) response observed were specific to neutrophils and not seen in other immune cell types. Therefore, the sex differences are likely related to the enhanced maturation and activation status of female cells when compared with male neutrophils.

In addition to the upregulated ISGs in female neutrophils, the researchers also identified differences in the cellular metabolism of female and male neutrophils. This difference appeared to be driven by sex hormones such as estradiol. The differences in neutrophil phenotype and function between adult males and females were not observed in prepubertal boys and girls, further supporting a role of sex hormones rather than the X chromosome. Also, neutrophils from subjects with Klinefelter's syndrome (men who have an XXY karyotype) did not differ in their type I IFN response when compared with males without Klinefelter's (Gupta et al., 2020).

This basic research relates to Objectives 1.1 ("Discover basic biological difference between females and males") and 2.1 ("Expand and develop advanced and innovative approaches for study design, data collection, and analysis to optimize data quality and the ability to detect the influences of sex and gender on health and disease") of the Trans-NIH Strategic Plan for Women's Health Research.

III. Promotion of Women's Health Research

Accelerating Medicines Partnership (AMP)—Rheumatoid Arthritis (RA) and Systemic Lupus Erythematosus (SLE)

The Accelerating Medicines Partnership (AMP) is a collaboration among NIH, the Foundation for the NIH (FNIH), the Food and Drug Administration (FDA), biopharmaceutical companies, and nonprofit organizations to increase the number of diagnostics and therapies and reduce the time and cost of developing them. NIAMS, in partnership with the National Institute of Allergy and Infectious Diseases, contributes to the AMP in two disease areas: RA and SLE. The AMP RA/SLE research network focuses on immune and tissue cells from organs affected by the diseases, including cells from the joints of individuals with RA and from the kidneys and skin of people with SLE. The network is adapting new technologies to allow those cells to be analyzed individually using high-throughput approaches. The program is making its data available to the broader research community to foster additional research on autoimmune diseases and enhance the return on investment in the program.

During the first phase of AMP RA/SLE, investigators compared cells taken from the tissues of RA or SLE patients with cells from unaffected individuals, with the goal of identifying changes in cells and biological pathways that occur in disease but not in health. Results from Phase I studies of RA revealed that certain subpopulations of immune cells and fibroblasts are increased in individuals with RA compared with controls (Zhang et al., 2019). One finding from Phase I studies of SLE was the discovery of subsets of white blood cells that are active in the disease and identified specific proteins that could be explored as therapeutic targets (Arazi et al., 2019).

In Phase II, the network explored differences at the molecular level among patients with the same disease to determine why disease course and response to therapy vary. Early indications from the SLE studies suggest that differences in so-called "interferon signatures" between individuals with lupus can help predict whether a particular patient is likely to respond to therapy (Der et al., 2019). Additional Phase II studies are expected to provide further insights into differences that could be used to personalize therapy for RA and SLE patients.

This has been ongoing since FY 2014 and relates to Goal 1 of the Trans-NIH Strategic Plan for Women's Health Research ("Advance rigorous research that is relevant to the health of women").

NIH Pathways to Prevention Workshop: Appropriate Use of Drug Therapies for Osteoporotic Fracture Prevention

More than 10 million people in the United States have osteoporosis (Wright et al., 2014). Lifestyle changes, including exercise and a healthy diet, may help reduce a person's risk of fracture. However, medications are often needed to prevent fractures if a person has osteoporosis and are essential if a person has experienced a previous fragility fracture. Effective FDA-approved medications can prevent debilitating and sometimes life-threatening fragility fractures. Reducing osteoporosis prevalence and hip fracture incidence are among the major objectives of Healthy People 2020 and 2030, the U.S. Department of Health and Human Services' national health promotion and disease prevention initiatives.

Rigorous clinical studies have demonstrated that 3 to 5 years of osteoporosis medication therapy prevents fractures. Clinical guidelines recommend bisphosphonates as a first line of treatment for most people who have osteoporosis, but treatment rates are low and medication adherence is poor. Reports of rare but serious adverse events and greater public concern about them have coincided with a marked decrease in the use of osteoporosis drugs and a leveling off in what had been a promising decline in the incidence of osteoporotic fractures (Lewiecki et al., 2018; Wysowski & Greene, 2013). Furthermore, as osteoporosis is considered a lifelong condition, the use of medications continues to be the cornerstone of therapy for osteoporosis. However, the benefits and risks of long-term osteoporosis drug therapies are not fully known.

In early fiscal year 2019, NIAMS, the National Institute on Aging, and the NIH Office of Disease Prevention hosted the "Pathways to Prevention Workshop on the Appropriate Use of Drug Therapies for Osteoporotic

Fracture Prevention" to identify research gaps and suggest focus areas that could move the field forward. As part of the workshop process, based on an Agency for Healthcare Research and Quality (AHRQ) systematic review of the scientific evidence (Fink et al., 2019), speaker presentations, audience input, and public comments, an independent panel issued a report that lays the foundation for future research activities (Siu et al., 2019). Strategies for disseminating and implementing these findings, including the notice of special interest described below, are being developed by Federal agencies.

This relates to Goal 1 of the Trans-NIH Strategic Plan for Women's Health Research ("Advance rigorous research that is relevant to the health of women").

Notice of Special Interest: Promoting Research on Mechanisms of Pathogenesis and Pathophysiology of Atypical Femoral Fracture (AFF) and Osteonecrosis of the Jaw (ONJ) (NOT-AR-21-006)

In a follow-up to the fiscal year 2019 NIH "Pathways to Prevention Workshop on Appropriate Use of Drug Therapies for Osteoporotic Fracture Prevention," NIAMS, the National Institute on Aging, the National Institute of Dental and Craniofacial Research, and the Office of Research on Women's Health issued a notice of special interest (NOSI) to enhance research on improving understanding of the mechanisms of pathophysiology and pathogenesis leading to the rare conditions of atypical femoral fracture (AFF) and osteonecrosis of the jaw (ONJ) associated with bone antiresorptive medications. This NOSI invites research applications that focus on improving the understanding of mechanisms of AFF and ONJ. Applications that propose to utilize existing resources including cohorts, registries, existing databases, and other resources such as the NIH Common Fund's Health Care Systems (HCS) Research Collaboratory program for their studies are encouraged.

This relates to Goal 1 of the Trans-NIH Strategic Plan for Women's Health Research ("Advance rigorous research that is relevant to the health of women").

Accelerating Basic and Translational Research in Hidradenitis Suppurativa (PA-18-718 and PA-18-719; R21 and R01 Clinical Trial Not Allowed)

Hidradenitis suppurativa (HS) is a complex, chronic, inflammatory skin disease characterized by recurrent, painful, red nodules and abscesses in different areas of the body. Nodules and abscesses can develop quickly, and it is unpredictable when and where they might burst. As a result, HS is associated with a significant negative impact in patients' quality of life. There are no biological or pathological tests to diagnose HS, which is defined only by its clinical features. The condition is more common in women than men and in Blacks than Whites.

In fiscal years 2019 and 2020, NIAMS funded three grants under two program announcements to accelerate basic and translational research in HS. Two address HS genetics, while another focuses on rebalancing the immune system in HS.

This relates to Goal 1 of the Trans-NIH Strategic Plan for Women's Health Research ("Advance rigorous research that is relevant to the health of women").

25th Anniversary Celebration of Lupus Clinical Research

In May 2019, the NIAMS lupus clinical research team gathered with more than 175 guests for the 25th anniversary of the natural history of systemic lupus erythematosus (SLE, or lupus) protocol. The purpose of the celebration, which took place as part of the fourth annual D.C. Lupus Consortium (DCLC) meeting, was to recognize the patients, providers, researchers, and advocates who have supported lupus research at the NIH Clinical Center over the past 25 years. The meeting highlighted the progress in lupus clinical research made by institutes across NIH, specifically noting the success of the lupus natural history protocol over a quarter-century. The event featured testimonials from research participants, updates on current lupus studies at NIAMS, and discussions on future topics to explore.

This relates to Objective 3.2 ("Identify collaborative opportunities and leverage partnerships to disseminate research that improves the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

IV. Advancement of Women in Biomedical Careers

NIAMS Culture Committee

Based on an evaluation of the NIAMS-specific results from the 2019 NIH Workplace and Harassment Survey, as well as the results from the 2019 Federal Employee Viewpoint Survey, NIAMS leadership decided to establish a committee broadly representative of NIAMS staff to advise leadership on issues impacting the institute's organizational climate. While the committee places emphasis on addressing the issues of sexual and gender harassment in the workplace, it is envisioned that it will also play a key role in dealing with all factors that impact organizational climate in NIAMS, such as diversity and inclusion, civility in the workplace, or any other matter that might become a priority for NIAMS in the future. The committee's vision is to further integrate a culture of civility, diversity, and inclusion and all other factors that impact organizational climate into the NIAMS mission; to continually assess organizational climate within NIAMS, make recommendations for training or initiatives to address issues that negatively impact the NIAMS climate, and actively participate in implementing solutions to identified challenges; and to work closely with NIAMS leadership to ensure tight alignment with NIAMS Core Values and to help institutionalize human capital practices that support and accelerate diversity and inclusion.

This relates to Objective 4.4 ("Promote and support policies, mentoring and networks, collaborations, and infrastructure to retain and advance women in their careers") of the Trans-NIH Strategic Plan for Women's Health Research.

NIAMS Forum for Clinical Mentored K Awardees

In fiscal years 2019 and 2020, NIAMS continued to host annual forums for recipients of K08 and K23 Mentored Research Career Development Awards. The NIAMS K Forums bring together clinician scientists who are in the third year of their NIAMS clinical career development award and established clinician scientist mentors, including some who have had an NIH K award in the past, along with representatives of professional and voluntary organizations. The purpose of the meeting is to foster a shared, open discourse on the challenges K investigators face in pursuing research independence. The forum also provides an opportunity for the K awardees to network with one another and to interact with NIAMS leadership and staff. The long-term goal of the meeting is to enhance the institute's support of early-stage clinician scientists by encouraging and enabling them to continue performing basic, translational, and/or patient-oriented research in their chosen fields. As part of the fiscal year 2020 meeting while the investigators with K awards were speaking with extramural staff, the other participants met with the NIAMS Acting Director, Dr. Robert Carter, to discuss challenges facing NIH and the research community; topics included issues that affect the participation of women and underrepresented minority groups in research careers.

This has been ongoing since FY 2013 and relates to Objective 4.4 ("Promote and support policies, mentoring and networks, collaborations, and infrastructure to retain and advance women in their careers") of the Trans-NIH Strategic Plan for Women's Health Research.

V. Implementation of the NIH Policy on Sex as a Biological Variable (SABV)

NIAMS supports the NIH policy requiring that sex as a biological variable (SABV) be a scorable component of grant applications and reported in the progress report. First, the institute relies on the peer review process to ensure that SABV is adequately reflected in an application; if it is not, the reviewers will report and its absence and alter the score appropriately.

Then NIAMS program directors monitor progress related to all aspects of the proposed research if investigators propose to determine SABV. When such information is missing from the progress report, applicants are contacted, and non-competing awards are not made until the missing information is provided.

Few NIAMS-funded clinical trials are sufficiently powered to see significant differences between men and women. However, NIAMS ensures that women are

enrolled in sufficient numbers in its clinical studies as mentioned below.

VI. Inclusion of Women in Clinical Research

NIAMS supports a broad range of research, research training and career development activities, and health information programs for many debilitating diseases affecting Americans. NIAMS funds clinical studies on a number of diseases that disproportionately affect women, including fibromyalgia, osteoarthritis (OA), osteoporosis, rheumatoid arthritis (RA), scleroderma/systemic sclerosis, systemic lupus erythematosus (SLE, or lupus), and juvenile idiopathic arthritis (JIA). Therefore, women are well represented in the NIAMS clinical research portfolio.

Intramurally, the NIAMS Lupus Clinical Trials Unit conducts innovative translational and clinical research into the causes, treatment, and prevention of SLE. It maintains a comprehensive clinical database of SLE patients that includes patient demographics, SLE disease activity and damage indices, patient-reported outcome tools, and other data for phenotyping the cohort. The SLE Natural History and Pathogenesis protocol serves as a pivotal resource for understanding and characterizing the heterogeneity of this disease, providing biological specimens and outstanding clinical phenotyping to various intramural and extramural labs involved in lupus research. This collaborative research model has led to several biomarker discoveries and scientific hypothesis generation. These discoveries have been translated into clinical trials by the Lupus Clinical Trials Unit.

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National Institute of Biomedical Imaging and Bioengineering

I. Executive Summary

The National Institute of Biomedical Imaging and Bioengineering (NIBIB) fosters, conducts, supports, and administers research and research training programs in biomedical imaging and bioengineering by means of grants, contracts, and cooperative agreements; provides coordination, integration, and review of progress and planning of biomedical imaging and bioengineering research; formulates research goals and long-range plans with the guidance of the National Advisory Council for Biomedical Imaging and Bioengineering; and sponsors scientific meetings and symposia, collaborates with industry and academia, and fosters international cooperation regarding biomedical imaging and bioengineering.

NIBIB supports a research portfolio that pursues cutting-edge technology development, and a number of projects, directly and indirectly, focus on women's health research. During FY 2019 and FY 2020, NIBIB funded grants that focused on technologies aimed at improving health care for women, including projects ranging from advanced imaging methodologies to bioengineering activities, specifically for women's diseases, such as breast cancer, and diseases with profound consequences for women, such as sexually transmitted diseases.

II. Scientific Advances

Highlighted NIBIB projects focus on technology development in several biomedical areas, including breast cancer (detection, imaging, and therapy), endometriosis, and engineering biomaterials for ovarian endocrine function.

3D Super-resolution ultrasound imaging for cancer detection and treatment monitoring (R01 EB025841): Neoadjuvant chemotherapy is the standard of care for treatment of locally advanced breast cancer, which is a major clinical issue. Access to inexpensive and noninvasive methods to determine early treatment response is essential to determine whether a chosen anticancer therapeutic regimen is efficacious. Tumor angiogenesis is a key biomarker of breast cancer growth and metastasis. This tumor microvascularity is known to exhibit distinct perfusion characteristics and morphologic features during the early stages of breast tumor development, which fundamentally change during a positive response to neoadjuvant treatment. The overarching goal of this research project is to develop an innovative three-dimensional (3D) super-resolution ultrasound (SR-US) imaging system and new image processing solutions to improve the ability to perform imaging for detection of early tumor response to neoadjuvant treatment (Brown, et al. 2020; Ghosh, et al. 2019; Hall, et al. 2019; Hsieh, et al. 2019; Jahanandish, et al, 2019; Khairalseed, et al. 2019; Oezdemir, et al. 2019; Oezdemir, et al. 2020; Raut, et al. 2019; Tai, et al. 2020).

This relates to Objective 1.5 of the Trans-NIH Strategic Plan for Women's Health Research ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health").

A Multimodal Imaging System and Targeted Nanoprobes for Image-Guided Treatment of Breast Cancer (R01 EB020601): This project is developing a novel dual photoacoustic and fluorescence endoscope and tumor targeted optical probes for detection of breast cancer and removal of primary tumor and local metastases. The device would allow for three-dimensional detection of small tumors (approximately 30µm) at a depth of approximately 3cm, which was previously unachievable. The optical probes are near-infrared (NIR) dye-labeled nanoparticles targeted to different cellular receptors that are highly expressed in triple-negative breast cancer (TNBC) cells, which are especially aggressive and drug-resistant, to allow for multiplexed specific and sensitive molecular imaging of heterogeneous TNBC cells. Beyond application to image-guided surgery of breast cancer, the particles could also be used to enhance therapeutic response to chemotherapy or radiation therapy if additional molecules are conjugated to the particles.

This relates to Objective 1.5 of the Trans-NIH Strategic Plan for Women's Health Research ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health").

Probiotic guided CAR-T therapy (ProCARs) for breast cancer (R01 EB030352): Though adoptive cell therapy such as CAR-T has shown promise in cancer treatment, a major barrier exists in using this strategy for solid tumors such as triple-negative breast cancer, a form of breast cancer that does not respond to traditional chemotherapeutic strategies. This project aims to develop a novel form of CAR-T cell therapy for solid tumors by co-engineering bacteria and CAR-T cells together to form a probiotic-guided CAR-T cell. This platform, dubbed ProCAR, will allow CAR-T cells to use the engineered bacteria to home to solid tumors, taking advantage of the immune stimulation the bacteria provide and engineering the CAR-T cells to respond. This work will establish the clinical utility of engineered communities of living medicines as therapeutics for solid tumor types.

This relates to Objective 1.5 of the Trans-NIH Strategic Plan for Women's Health Research ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health").

Microvascular Permeability, Inflammation, and Lesion Physiology in Endometriosis: A Microphysiological Systems Approach (U01 EB029132): Endometriosis is a debilitating disease affecting an estimated 200 million women and girls worldwide, causing pain and infertility. Unfortunately, endometriosis often takes years to diagnose and has very limited treatment options, partially because of the lack of accurate *in vitro* or *in vivo* models to aid in critical drug screening and basic science research. This project aims to create microphysiological models of early-stage endometriosis lesions by building on existing models to accurately recapitulate metabolically active tissue, including microvasculature and inflammation. This platform will then be used to learn more about endometriosis lesion behavior using donor tissues, as well as to evaluate efficacy of several established and experimental therapies for this disease.

This relates to Objective 1.5 of the Trans-NIH Strategic Plan for Women's Health Research ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health").

Engineering an immuno-isolating hydrogel for restoring ovarian endocrine function (R01 EB022033): Premature ovarian insufficiency or failure (POF) can occur in women and girls who have received chemotherapy or radiation to treat certain cancers. This not only hinders development in younger girls who undergo cancer treatment before puberty but also causes a host of long-term effects, including accelerated cardiovascular disease and muscle wasting. This project aimed to address this critical issue through development of novel hydrogel-based capsules to hold ovarian allografts for implantation. These implants are designed to support follicle survival, growth, and function, preventing the debilitating long-term effects of POF. In a recent paper, it was found that this technology restored hormonal balance in ovariectomized mice over a period of 60 days with no evidence of immune degradation, a very promising result for future clinical translation (Day, et al. 2019; Tomaszewski, et al. 2019).

This relates to Objective 1.5 of the Trans-NIH Strategic Plan for Women's Health Research ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health").

III. Promotion of Women's Health Research

FUNDING INITIATIVES

Alzheimer's Disease and its Related Dementias (AD/ADRD)-Focused Administrative Supplements for NIH Grants That Are Not Focused on Alzheimer's Disease (NOT-AG-20-008 & NOT-AG-20-034): NIBIB participates in this National Institute on Aging supplement program. Nearly two-thirds of Alzheimer's patients are women. This initiative allows current NIH awardees to apply for administrative supplements to expand existing awards that are not currently focused on Alzheimer's disease (AD) and its related dementias (ADRD) to allow them to develop a focus on AD/ADRD. Topics supported in the past 2 years range from the assessment of cognitive impairment and progressive brain degeneration using AI methods to new and upgraded brain, vascular, and lymphatic imaging techniques, including the

identification of new biomarkers. These areas of investigation will lead to improvements in disease monitoring and the development of new therapies for the treatment of AD and improvements in women's health.

IV. Advancement of Women in Biomedical Careers

NIBIB Science, Technology, Engineering, and Mathematics (STEM) Training Efforts

NIBIB supports training programs at undergraduate, doctoral, postdoctoral, and early faculty stages and strives to maintain gender balance in its training grants. All institutional programs are required to indicate the sex/gender of the supported trainees and asked to justify any imbalances and describe plans for overcoming them. NIBIB participates in a number of trans-NIH initiatives aimed at enhancing diversity—including women, who are underrepresented in biomedical research careers. NIBIB participates in "Research Supplements to Promote Re-Entry into Biomedical and Behavioral Research Careers (Admin Supp)" (PA-18-592), "Notice of Special Interest: Administrative Supplements to Promote Research Continuity and Retention of NIH Mentored Career Development (K) Award Recipients and Scholars" (NOT-OD-20-054), "BRAIN Initiative Advanced Postdoctoral Career Transition Award to Promote Diversity (K99/R00)" (RFA-NS-19-043), "NIH Blueprint Program for Enhancing Neuroscience Diversity through Undergraduate Research Education Experiences (BP-ENDURE)" (RFA-NS-20-015), and "Maximizing Opportunities for Scientific and Academic Independent Careers (MOSAIC) Postdoctoral Career Transition Award to Promote Diversity (K99/R00)" (PAR-19-343).

Enhancing Science, Technology, EnginEering, and Math Educational Diversity (ESTEEMED): NIBIB is committed to increasing the participation and success of undergraduates in STEM. NIBIB's Enhancing Science, Technology, EnginEering, and Math Educational Diversity (ESTEEMED) initiative relies on firsthand research experiences and mentoring activities to recruit and support underrepresented undergraduates in STEM fields through their critical freshman and sophomore years. The program prepares the participants to pursue a Ph.D. or M.D./Ph.D. and ultimately a biomedical research career in academia or industry. NIBIB funded two new programs each of 2019 and 2020, reaching a total of six active programs around the country. The majority of trainees supported by the ESTEEMED program are women.

Bioengineering Experience for Science Teachers (BEST): NIBIB supports the Bioengineering Experience for Science Teachers (BEST) program at the University of Illinois at Chicago. High school science teachers participate in research in the laboratories of bioengineering faculty over the summer. The majority of high school teachers participating in this program are women. Female science teachers, who can engage their students in STEM topics, are especially important as role models inspiring female students to go into STEM fields. Concurrently, College of Education faculty provide guidance to the science teachers in translating their research experiences into classroom material. This summer research experience enhances the skills of science teachers and enables them to more effectively understand and communicate current trends in bioengineering research to their students, enhancing overall science literacy. Moreover, by sharing the developed curricula on the internet, the BEST program extends its impact not only to participating science teachers and their students but to those around the country and even the world.

Finally, NIBIB runs a challenge program for undergraduate biomedical engineering students.

Design by Biomedical Undergraduate Teams (DEBUT) Challenge: As part of its STEM training efforts, NIBIB continues to hold an undergraduate prize competition for biomedical design projects. This annual competition, Design by Biomedical Undergraduate Teams (DEBUT) Challenge, receives numerous entries from across the country. Three winning submissions were directly related to women's health in the reporting period. In 2020, the "Healthcare Technologies for Low-Resource Settings Prize" was awarded to a team that designed a low-cost, 3D-printed universal obturator for brachytherapy, which could help expand treatment of late-stage cervical cancer in areas where medical providers have limited training or experience with brachytherapy. Using a phantom, the team demonstrated that its device allowed even untrained undergraduate students to position needles

as accurately as physicians. Notably, this team was composed of all female biomedical engineering students.

In 2019, an Honorable Mention was awarded to "The Hera Bra and Hera Mobile Application" for the detection of subclinical mastitis in breastfeeding mothers via an instrumented bra that monitors breast temperature fluctuations and alerts mothers of anomalous trends. Mastitis is inflammation of the breast tissue caused by milk stasis or bacterial infection and is reported in up to 33% of lactating mothers. However, often it goes undiagnosed until symptoms become severe. As a result, many mothers experience both severe physical pain as well as the emotional distress that arises from the inability to breastfeed. Here, too, the project was achieved by a team composed of all female biomedical engineering students.

Also, in 2019, NIBIB's DEBUT partner VentureWell awarded its Venture Prize to Cath Path—a vaginal insert to improve the success rate of inserting a catheter needed to treat neurogenic bladder. Neurogenic bladder is a condition in which bladder control is compromised and affects more than 250,000 women in the United States. The solution to this is to use a catheter four to six times a day to void the bladder. However, patients often have difficulty locating the urethra and inserting the catheter correctly, which can result in social embarrassment and urinary tract infections. The vaginal insert designed by this team from Stanford University aligns a catheter guide with the urethra to help women with the insertion of the catheter. Half of the members of this team are female biomedical engineering students.

V. Implementation of the NIH Policy on Sex as a Biological Variable (SABV)

The NIBIB Inclusion and SABV Policy Officer works closely with Program Directors and Investigators to ensure compliance with inclusion policies and to promote opportunities related to women's health research. The NIBIB Inclusion and SABV Policy Officer, along with the NIBIB staff, works with grantees to ensure compliance with the policy on SABV and on how developing technologies may be applied to support women's health.

VI. Inclusion of Women in Clinical Research

NIBIB staff members work with grantees to ensure compliance with the policy on SABV and on how developing technologies may be applied to support women's health. Women are included in clinical research as appropriate for the biomedical technology development projects supported by NIBIB.

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Eunice Kennedy Shriver National Institute of Child Health and Human Development

I. Executive Summary

The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) leads research and training to understand human development, improve reproductive health, enhance the lives of children and adolescents, and optimize abilities for all. NICHD's Strategic Plan 2020 encompasses women's health in all of its themes, emphasizing promoting gynecologic and reproductive health, setting the foundation for healthy pregnancies and lifelong wellness, and advancing safe and effective therapeutics and devices for pregnant women, lactating women, children, and people with disabilities. In FY 2019, NICHD supported approximately 10% of women's health research and 51% of maternal health research at NIH.

As COVID-19 swept across the globe, NICHD utilized already established research networks to ensure that vulnerable populations were not left behind. NICHD's Maternal-Fetal Medicine Units Network is analyzing how COVID-19 affects pregnancy outcomes through the Gestational Research Assessments for COVID (GRAVID) study, using medical records from up to 24,500 women. NICHD's Global Network for Women's and Children's Health Research is tracking the prevalence and impact of SARS-CoV-2 infection among 16,000 pregnant women in low- and middle-income countries. NICHD's new Maternal and Pediatric Precision in Therapeutics (MPRINT) Hub program will enable therapeutics-focused research in obstetrics, lactation, and pediatrics while enhancing inclusion of people with disabilities.

Women's reproductive health conditions—such as uterine fibroids, pelvic floor disorders, endometriosis, vulvodynia, and polycystic ovarian syndrome—lead to pain, abnormal menstrual bleeding, infertility, and other medical complications for millions of American women. NICHD supports research in maternal morbidity and mortality, pregnancy, gynecologic conditions, fertility and infertility, and contraception, with basic, translational, and clinical research studies at both the individual and the population levels. NICHD aims to establish Centers to Advance Research in Endometriosis (CARE) and collaborates with the Centers for Disease Control and Prevention (CDC) to support the National Survey of Family Growth (NSFG), the major source of nationally representative data on family life, marriage, divorce, pregnancy, infertility, contraception use, and reproductive health.

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https://www.cdc.gov/nchs/data/nvsr/nvsr68/nvsr68_13-508.pdf

https://www.nichd.nih.gov/research/supported/COVID

https://www.nih.gov/news-events/news-releases/nih-funded-study-investigate-pregnancy-outcomes-resulting-covid-19-pandemic

https://www.nichd.nih.gov/newsroom/news/051920-MFMU-COVID-19

https://www.nichd.nih.gov/newsroom/news/090120-COVID19-pregnancy

https://www.nichd.nih.gov/about/org/der/branches/opptb/mprint

https://grants.nih.gov/grants/guide/rfa-files/RFA-HD-21-025.html

https://grants.nih.gov/grants/guide/rfa-files/RFA-HD-21-002.html

https://www.cdc.gov/nchs/nsfg/about_nsfg.htm

II. Scientific Advances

Placenta lacks major molecules used by SARS-CoV-2 to cause infection

To assess the risk of pregnant women transferring severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) to their fetus, scientists studied whether the placenta contains molecules that may serve as potential routes for infection. They found that the placental membranes that encompass the fetus and amniotic fluid lack the messenger RNA (mRNA) molecule required to manufacture the ACE2 receptor, the main cell surface

receptor used by this virus to cause infection. These placental tissues also lack mRNA needed to make an enzyme, called TMPRSS2, that SARS-CoV-2 uses to enter a cell. Both the receptor and enzyme are present in only minuscule amounts in the placenta, suggesting a possible explanation for why SARS-CoV-2 has only rarely been found in fetuses or newborns of women infected with the virus. The researchers found that the placenta contains molecules that previous studies have suggested as potential routes for SARS-CoV-2 infection, and they also detected in placental and membrane tissue a type of macrophage (immune cell) that has the ACE2 receptor. However, the scientists noted that there is little evidence showing that infected macrophages could spread SARS-CoV-2 to the placenta, membranes, and fetus in normal pregnancy. Finally, the researchers found that the placenta contains large amounts of receptors used for infection by Zika virus and cytomegalovirus, which are both known to carry serious health risks when passed from a woman to her fetus during pregnancy (Pique-Regi et al., 2020).

This translational research relates to Objective 1.5 of the Trans-NIH Strategic Plan for Women's Health Research ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health").

Placental DNA in maternal blood could predict later pregnancy complications

Pregnancy complications such as gestational diabetes and preeclampsia are often diagnosed later in pregnancy, during the second or third trimester. However, earlier detection of the risk of these disorders could help health care providers better monitor the health of their patients and possibly prevent complications from occurring. Researchers adapted methods to identify traces of genetic material, called cell-free DNA, shed from the placenta and other organs into the pregnant woman's bloodstream. Next, the study team detected patterns in these genetic traces associated with the development of gestational diabetes and preeclampsia. These patterns were apparent as early as the first trimester, well before these conditions can be diagnosed with existing tests. The team also linked patterns in genetic material shed from the mother's pancreas to later gestational diabetes. Overall, the findings show that such genetic signatures can be detected early and may serve as biomarkers to identify women at risk for complications (Del Vecchio et al., 2020).

This translational research relates to Objectives 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health") and 2.2 ("Develop and adapt reliable and valid measures relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

Nonsurgical accurate diagnosis of endometriosis using serum microRNAs

Endometriosis is an inflammatory disorder in which the endometrial cells that normally line the uterus spread outside of it, causing pain and infertility in affected women. Endometriosis often has a negative impact on many aspects of daily life, from work to relationships. Almost 10% of reproductive-age women are affected by endometriosis; that said, on average, a reliable diagnosis is made 5 to 10 years after their first nonspecific symptoms. The only current option for a definitive diagnosis is a surgical procedure called laparoscopy. Reluctance to undergo an invasive procedure, however, can delay endometriosis diagnosis while the disease progresses. In searching for a diagnostic alternative to surgery, researchers recently tested whether microscopic bits of genetic matter in blood serum, known as microRNAs (miRNAs), could reliably diagnose endometriosis. Researchers analyzed serum samples of 100 women with symptoms suggestive of endometriosis who were undergoing laparoscopy. The scientists looked at a number of suspect miRNAs, singly and in combination. They found significantly higher levels of four miRNAs and lower levels of two of the miRNAs in women in whom endometriosis had been confirmed by laparoscopic surgery compared with women with other gynecologic disorders. In addition, these miRNAs had high specificity and high sensitivity to diagnose endometriosis—regardless of timing within the menstrual cycle and even in women who were taking hormonal medication, such as hormonal oral contraceptives. The current analysis of miRNA expression levels indicated that the quantity of miRNA genetic fragments in the serum could not distinguish between the first stages (I/II) and later stages (III/IV) of endometriosis. The ability to use miRNAs to diagnose endometriosis noninvasively could shorten time to diagnosis, as well as risks and costs related

to diagnosis, sparing years of patient discomfort and disease progression and yielding health care savings and other benefits (Moustafa et al., 2020).

This translational research relates to Objectives 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health") and 3.1 ("Design and test approaches to promote the adoption, adaptation, and integration of evidence-based interventions in public health, clinical practice, and community settings") of the Trans-NIH Strategic Plan for Women's Health Research.

Homicide is a leading cause of pregnancy-associated death in Louisiana

Although maternal deaths are higher in the United States compared with many other countries, few researchers have looked at non-obstetric causes of death during pregnancy and the year after birth. Scientists analyzed maternal death and homicide data from the Louisiana Department of Health and the Centers for Disease Control and Prevention. For every 100,000 women who were pregnant or postpartum in Louisiana, there were an estimated 12.9 homicide deaths, which outnumbered deaths from any single obstetric cause, including hypertensive disorders (3.2) and amniotic fluid entering the bloodstream (4.8). The risk of homicide death was twice as high for women and girls during pregnancy and the postpartum period than it was for women and girls who were not pregnant. Pregnancy and postpartum deaths were highest for women and girls ages 10 to 29. The researchers stated that women's increased contact with the health care system during pregnancy provides clinicians with an opportunity to offer violence prevention services and interventions (Wallace et al., 2020).

This clinical (population study) research relates to Objective 1.5 of the Trans-NIH Strategic Plan for Women's Health Research ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health").

Variation in hysterectomy rates by race and ethnicity

Hysterectomy, or removal of the uterus, is a frequent surgical procedure with major consequences for women's health and well-being. To look for evidence of health disparities by racial and ethnic identity in hysterectomy rates, researchers analyzed data on all inpatient and outpatient hysterectomy procedures performed in North Carolina from 2011 to 2014. Estimates that accounted for the portion of the population who had previously undergone the procedure showed that non-Hispanic Black women and non-Hispanic American Indian women had higher hysterectomy rates than non-Hispanic White women. Hysterectomy rates for Hispanic and non-Hispanic Asian/Pacific Islander women were lower than the rates for non-Hispanic White women. Notably, uterine fibroids and associated bleeding are one of the most frequent reasons women have hysterectomies. The incidence of fibroids is much higher in Black women than in women from other races and ethnicities. Further research is necessary to understand the underlying causes of these differences to ensure that women of all races and ethnicities are provided with appropriate care (Gartner et al., 2020).

This clinical research relates to Objectives 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health") and 2.3 ("Leverage secondary data sources for research on the health of women through a big data enterprise that includes data sharing and analytic strategies") of the Trans-NIH Strategic Plan for Women's Health Research.

III. Promotion of Women's Health Research

NICHD supports extramural and intramural research in maternal health, gynecologic conditions, fertility and infertility, and contraception.

Establishing Best Practices in Maternal Health Research

NICHD's research infrastructure supports clinical studies in maternal and newborn health, emphasizing recruitment of minority groups to better understand health disparities. Examples include:

- The **Human Placenta Project (HPP)** develops tools to study in real time how the placenta develops and functions throughout pregnancy. One promising technology uses noninvasive imaging to more accurately monitor contractions for signs of preterm labor.

- NICHD's **Maternal and Fetal Medicine Units (MFMU) Network** conducts rigorous clinical trials to inform practice guidelines for obstetric practice. MFMU is currently conducting the Gestational Research Assessments for coVID (GRAVID) study, evaluating medical records of 24,500 pregnant women to discern possible impacts of health care changes implemented because of the pandemic.
- Within NICHD's **Intramural** program, scientists are studying how to prevent preeclampsia, a blood pressure disorder in pregnant women that can have serious effects for both mother and fetus. Other researchers are analyzing population studies to identify factors that determine long-term risks. For example, decades after giving birth, women with a history of gestational diabetes who had breastfed their infants were less likely to have developed type 2 diabetes and more likely to have positive biomarkers of metabolic health (Ley et al., 2020).
- NICHD's **Global Network for Women's and Children's Health Research** launched a study to track the prevalence and impact of SARS-CoV-2 infection among approximately 16,000 pregnant women in low- and middle-income countries, to compare maternal, fetal, and newborn outcomes of those who have been infected with the outcomes of those who have not been infected. In addition, a clinical trial funded by NICHD and the Bill & Melinda Gates Foundation will assess whether a single oral dose of the antibiotic azithromycin during labor reduces the risk of maternal and infant bacterial infection and death in these countries.

This relates to Goals 1 ("Advance rigorous research that is relevant to the health of women"), 2 ("Develop methods and leveraging data sources to consider sex and gender influences that enhance research for the health of women"), and 3 ("Enhance dissemination and implementation of evidence to improve the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

https://www.nichd.nih.gov/newsroom/news/090120-COVID19-pregnancy

https://www.nichd.nih.gov/newsroom/news/060320-labor-azithromycin

Accelerating Endometriosis Research

Endometriosis is a leading cause of chronic pelvic pain and infertility in reproductive-aged women, where some endometrial tissue grows abnormally outside of the uterus, causing inflammation, painful menstruation, and infertility. Endometriosis affects about 10% of reproductive-aged women, yet many cases go undetected for years, as its genetic, molecular, or environmental causes are not well understood. Current treatments include pain medications, surgery, or hormone treatment, but these remedies are complex, can have long-term side effects, and have limited effectiveness for many women. Understanding the mechanisms, diagnosis, and treatment of endometriosis is a key research priority for NICHD. For example, NICHD-funded research led to the first pill approved by the Food and Drug Administration specifically to treat pain associated with endometriosis. Elagolix (also Orilissa) is used as part of hormonal therapy, stopping the body's production of certain hormones to prevent ovulation, menstruation, and the growth of endometriosis. Researchers determined that levels of specific microRNAs (miRNAs) in the blood could collectively be a biomarker to diagnose endometriosis (Moustafa et al., 2020). If developed further, this approach could lead to less invasive and more rapid diagnosis, sparing years of patient discomfort, disease progression, and health care costs. NICHD supports the National Centers for Translational Research in Reproduction and Infertility (NCTRI), which addresses the impact of endometriosis on infertility. NICHD aims to accelerate endometriosis research through investing in new Centers to Advance Research in Endometriosis (CARE). These multidisciplinary programs will incorporate basic, translational, and/or clinical studies in a collaborative entity to accelerate research advances to prevent and treat endometriosis.

This relates to Goal 1 ("Advance rigorous research that is relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

https://www.nichd.nih.gov/about/org/od/directors_corner/prev_updates/endometriosis-research

https://www.fda.gov/drugs/drug-approvals-and-databases/drug-trials-snapshots-orilissa

https://www.nichd.nih.gov/research/supported/NCTRI

https://obgyn.ucsf.edu/center-reproductive-sciences-0

https://grants.nih.gov/grants/guide/rfa-files/RFA-HD-21-002.html

Understanding Diagnosis, Treatments, and Health Disparities in Uterine Fibroids

Uterine fibroids, pelvic floor disorders, endometriosis, vulvodynia, and polycystic ovary syndrome (PCOS) lead to pain and infertility for millions of American women. Recent estimates indicate that fibroids affect nearly 70% of women by age 50, with prevalence increasing to more than 80% for African American women. Uterine fibroids are the most common cause for hysterectomies in the United States. Scientists are developing a technique to shrink fibroids as a less invasive alternative to surgical removal (Borahay et al., 2021). This method, tested successfully in mice, delivers nanoparticles with a tumor-killing drug directly to the fibroid. Minority women are disproportionately affected by many gynecologic conditions. African American women are up to three times more likely to suffer from fibroids than White women, which could be linked to racial and ethnic variations in the rates of hysterectomies. As research advances, it is vital to include underrepresented minorities in research to ensure development of accurate diagnostic methods and effective treatments for all populations. NICHD also published a funding opportunity announcement supporting development, advancement, and validation of new devices and methods for noninvasive diagnosis and/or screening of endometriosis, adenomyosis, and/or uterine fibroids. NICHD-supported research led to Food and Drug Administration approval of a drug (Oriahnn) for heavy menstrual bleeding caused by fibroids.

This relates to Goal 1 ("Advance rigorous research that is relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

https://grants.nih.gov/grants/guide/rfa-files/RFA-HD-21-020.html

https://www.nichd.nih.gov/newsroom/news/071320-fibroids

https://www.fda.gov/news-events/press-announcements/fda-approves-new-option-treat-heavy-menstrual-bleeding-associated-fibroids-women

Comparing Effective Interventions through the Pelvic Floor Disorders Network (PFDN)

Pelvic floor disorders, which occur when the muscles or connective tissues of the pelvic area weaken or are injured, affect from 25% to 60% of adult women and can cause urinary incontinence, fecal incontinence, and pelvic organ prolapse. About 11% of women will have surgery to treat urinary incontinence or pelvic organ prolapse during their lifetime, and 30% of those having surgery will require at least two surgical procedures. NICHD established the Pelvic Floor Disorders Network (PFDN) to encourage collaborative research on pelvic floor disorders (PFDs) and to improve patient care. PFDN research aims to advance diagnosis, care, and treatment of women with PFDs while improving the quality of life for women with PFDs and their families. General areas of research include observational and clinical studies examining the effectiveness of surgical and nonsurgical interventions for PFDs, including pharmacological agents, short- and long-term anatomical or functional outcomes of interventions (e.g., quality of life, sexual function, urinary function, and gastrointestinal function), and preventive strategies. PFDN also compares the effectiveness of current standard-of-care options in order to establish clinical care guidelines and best practices. Pelvic floor disorders are most commonly treated surgically. NICHD has supported the challenging research to help determine which surgical approaches lead to better outcomes. For example, researchers compared the 2-year surgical outcomes of two different surgical approaches in women with advanced pelvic organ prolapse and stress urinary incontinence. The study results showed equal overall surgical success (58%) at 2 years for women undergoing each type of procedure (Meyer et al., 2020).

This relates to Goals 1 ("Advance rigorous research that is relevant to the health of women") and 2 ("Develop methods and leveraging data sources to consider sex and gender influences that enhance research for the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

https://www.nichd.nih.gov/research/supported/pelvicfloor

Developing Contraceptive Methods

Contraceptive research and development is critical for providing safer, more effective methods of preventing unintended pregnancies. By supporting research on a variety of contraceptive methods and evaluating their safety and efficacy, NICHD is helping to ensure that the health needs of individuals across the Nation and globe are being met. NICHD's Contraceptive Clinical Trials Network (CCTN) supports clinical field centers that are selected for their capacity to conduct Phase I, II, and III trials of oral, vaginal, intrauterine, injectable, implantable, or topical contraceptive drugs and devices. NICHD-supported researchers are exploring better contraceptive methods for women, particularly nonhormonal options that woman can use on demand. Researchers are also developing contraceptives that offer protection against sexually transmitted infections (STIs), giving women better control over their reproductive health and well-being. One group is researching a vaginal film that serves as a contraceptive via antibodies that recognize sperm, trap them, and clump them together (Anderson et al., 2020). This NICHD-supported team is also testing whether this method could offer another level of protection against common STIs, including HIV and herpes simplex virus.

This relates to Goal 1 ("Advance rigorous research that is relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

https://www.nichd.nih.gov/research/supported/cctn

Bringing Together Stakeholders to Advance Women's Health Research

In FY 2019 and FY 2020, NICHD hosted several workshops to advance rigorous research that is relevant to the health of women. In April 2019, NICHD hosted a workshop with the National Cancer Institute on gynecological and women's health, focusing on the relationship between cancer and benign gynecological conditions, including endometriosis, uterine fibroids (leiomyoma), and adenomyosis (Samimi et al., 2020). NICHD also hosted a workshop on Menstruation and Society, which has informed NICHD gynecological health and disease priorities (Tingen et al., 2020; Critchley et al., 2020). NICHD-led research promotes the use of menstruation as a "vital sign," meaning it can serve as a health metric, like blood pressure, to assess a woman's well-being. Scientists and small businesses funded by NICHD are developing innovative technologies, including a "smart" tampon that can potentially diagnose gynecologic conditions in a noninvasive manner, using menstrual effluent that is otherwise thrown away.

Over 6 million women are pregnant in the United States each year. In identifying priorities for addressing the relatively high rates of maternal mortality, NICHD engaged researchers and community-based experts on data measurement, social determinants, health disparities, and community engagement (Chinn et al., 2020). In 2020, NICHD co-sponsored a workshop with the Office of Research on Women's Health, the Office of Disease Prevention, and the National Heart, Lung, and Blood Institute to develop a research agenda targeted at the clinical causes of maternal morbidity and mortality and also partnered with the National Institute of Nursing Research, the Office of Research on Women's Health, the National Institute on Minority Health and Health Disparities, and the Tribal Health Research Office for a virtual workshop on innovative models of care for reducing inequities in maternal health. In September 2020, NICHD sponsored the "COVID-19 in Pregnancy: Clinical, Research, and Therapeutics Updates Virtual Workshop," which attracted over 1,300 registrants and brought together experts in the field to discuss the progress and challenges in obstetric therapeutic research and patient care, share experiences in clinical management of pregnant women and newborns with COVID-19, and explore effective approaches to obstetric therapeutics during the COVID-19 pandemic.

This relates to Goals 1 ("Advance rigorous research that is relevant to the health of women"), 2 ("Develop methods and leveraging data sources to consider sex and gender influences that enhance research for the health of women"), and 3 ("Enhance dissemination and implementation of evidence to improve the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

https://www.cdc.gov/nchs/data/nvsr/nvsr68/nvsr68_13-508.pdf

https://pubmed.ncbi.nlm.nih.gov/32709301/

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https://www.nichd.nih.gov/newsroom/news/072220-menstruation-research

https://www.nichd.nih.gov/about/meetings/2020/051920

https://www.ninr.nih.gov/newsandinformation/events/maternalhealth2020

https://www.nichd.nih.gov/about/meetings/2020/091520

IV. Advancement of Women in Biomedical Careers

Women's Reproductive Health Research (WRHR) Career Development Program

NICHD and ORWH support this national program of mentored institutional career development programs for junior faculty who have recently completed postgraduate training in obstetrics and gynecology and who are committed to independent research careers in women's reproductive health. The supervised research training assists junior faculty in their transition into productive physician-scientists. During FY 2019–2020, 71% of K12 scholars participating in this program for any amount of time were women.

https://www.nichd.nih.gov/research/supported/wrhr

Reproductive Scientist Development Program (RSDP)

The program's goal is ongoing development of a cadre of reproductive physician-scientists based in academic departments who can employ cutting-edge cell and molecular technologies to address important problems in the field of obstetrics and gynecology. The mentored research experiences this program offers seek to assist junior faculty members in their transition to productive, independent physician-scientists who are highly competitive for research funding. The program accepts approximately four scholars each year for a 5-to-6-year training period. During FY 2019–2020, 78% of K12

scholars participating in this program for any amount of time were women.

https://www.nichd.nih.gov/research/supported/rsdp

V. Implementation of the NIH Policy on Sex as a Biological Variable (SABV)

NICHD Program Directors and Investigators promote inclusion policies and opportunities related to women's health research. NICHD staff members work with grantees to ensure compliance with the SABV policy, which resulted in highlights of biological differences in research findings funded by NICHD. For example, NICHD-supported researchers analyzed data from a longitudinal study that followed adolescents for approximately 12 years into adulthood, finding that earlier puberty put both girls and boys at an increased risk of poor psychosocial, behavioral, and physical health during adolescence, whereas later puberty often had protective effects. As young adults, the health effects of pubertal timing were more persistent for young women than they were for young men.

VI. Inclusion of Women in Clinical Research

Up to 59% of the United States population consists of people who typically are not included in research studies, including pregnant women, lactating women, children, older individuals, and individuals with intellectual and physical disabilities (Spong & Bianchi, 2018). As a result, pregnant women and lactating women, as well as all parents of children, face difficult choices—either going without treatment or undergoing a treatment that has not been tested for their use. NIH has long-standing policies to ensure inclusion of women, minority groups, and children in research studies. Recent revisions to these inclusion policies have been aimed at increasing the enrollment of those historically underrepresented in research and improving the reporting of those participating in clinical research, including older populations, children, pregnant women, lactating women, and individuals with intellectual and physical disabilities.

Federal Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC)

Historically, there have been highly publicized cases of prescription drug use by pregnant women that ended with tragic results. As a result, although about 9 in 10 women take at least one medication during pregnancy, pregnant women are often excluded from clinical research and there is very little scientific evidence available to guide treatment decisions during pregnancy and lactation. Established by the 21st Century Cures Act, through the Federal Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC), NICHD brought together clinical, research, advocacy, public health, regulatory, and pharmaceutical industry leaders to address the significant gap in research on safety, efficacy, and dosing of medications currently used by pregnant women and lactating women.
The task force generated 15 recommendations and multiple concrete steps to guide public- and private-sector efforts to implement them. Major areas for action include developing a systematic plan to collect data on therapeutics' safety, pharmacokinetics, pharmacodynamics, and pharmacogenomics during pregnancy and lactation and establishing a prioritization process for studies in pregnancy and lactation.
Other implementation steps focus on task force recommendations to address ethical considerations and industry concerns about liability and to encourage participation in obstetric therapeutics research. NICHD's Maternal and Fetal Medicine Units (MFMU) Network conducts rigorous clinical research in maternal, fetal, and obstetric medicine across the country. For example, MFMU is currently conducting a clinical trial evaluating whether tranexamic acid, a drug used to prevent hemorrhage in trauma and high-risk surgery patients, can prevent obstetric hemorrhage after cesarean delivery.

https://www.cdc.gov/pregnancy/meds/treatingfortwo/research.html

https://www.congress.gov/bill/114th-congress/house-bill/34

https://www.nichd.nih.gov/about/advisory/PRGLAC/recommendations

Program in Obstetric Pharmacology

NICHD leads NIH's efforts to develop and disseminate research in maternal and pediatric pharmacology and therapeutics. There is a lack of effective and safe therapies for conditions that arise during pregnancy or for existing comorbidities that contribute to high rates of maternal morbidity and mortality. A key requirement for the advancement of therapeutics that can restore the foundation for healthy pregnancies is understanding how drug action is altered during normal pregnancy, the postpartum period, and lactation. Developmental pharmacology research and approaches are exploring the intersections of physiological changes in women and during fetal development with drug action (e.g., pharmacokinetics, pharmacodynamics, and pharmacogenomics) and with molecular pathways that may serve as novel therapeutic targets for disease-modifying therapies specific to these populations. Critical areas include pain management in pregnant women and lactating women, treatment of gestational diabetes and preeclampsia, and prevention of preterm delivery. Significant challenges exist in the design and execution of pediatric and obstetric clinical trials, including recruitment, retention, and ethical concerns, among others. Innovative approaches and algorithms are being developed to determine drug dosing, safety, and effectiveness in children and in women during pregnancy and lactation. These include artificial intelligence–driven modeling and simulation methods, novel approaches to utilizing existing data and archived biosamples/biospecimens, and pragmatic trials. A new addition to NICHD's infrastructure, NICHD's Maternal and Pediatric Precision in Therapeutics (MPRINT) Hub program, will provide pharmacology expertise and technology platforms to scientists conducting pharmacology research in pregnant women, lactating women, and children.

https://www.nichd.nih.gov/about/org/der/branches/opptb

https://grants.nih.gov/grants/guide/rfa-files/RFA-HD-21-025.html

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National Institute on Drug Abuse

I. Executive Summary

The mission of the National Institute on Drug Abuse (NIDA) is to advance science on the causes and consequences of drug use and addiction and to apply that knowledge to improve individual and public health. Integral to this mission is the elucidation of sex/gender differences in the risk factors associated with substance use disorder (SUD), in its consequences, and in treatment response. This theme cuts across NIDA divisions of basic research, services, medication development, and clinical trials. Additionally, NIDA supports active programs for recruitment and career development of a diverse workforce, particularly women and underrepresented minorities. This FY 2019–2020 biennial report highlights NIDA's accomplishments related to women's health research.

Recent NIDA-supported science highlights the power of computational analysis of large datasets to determine how sex and gender interact with biological, socioeconomic, and environmental factors to shape brain development and cognitive and behavioral consequences. These large longitudinal studies have predictive power that will guide prevention strategies. Other research is identifying the neurobiological basis for sex differences in characteristics of SUD, from molecules to cells to circuits. This research discovered sex differences in gene expression regulation by stressors that can account for sex differences in characteristics of substance use. NIDA-supported research is also uncovering fundamental biological principles of the sexual differentiation of the brain that underlie sex-distinct behaviors.

NIDA-supported women's health research related to maternal health is advancing our knowledge of the optimal treatment of SUD in pregnant women and the impact of COVID-19 on pregnant women, lactating women, and their children. Other studies, comparing characteristics of women who overdose in the postpartum period, are informing on ways to predict and prevent overdose in the future. NIDA's commitment to women's health and sex differences research is visible in its support of the NIDA Women & Sex/Gender Differences Research Group, which conceptualizes and organizes initiatives on women's health and sex/gender differences in biology, ensures that this is an integral part of the NIDA strategic plan, and disseminates information to the scientific community and the public.

II. Scientific Advances

1. Deep Learning Predicts Sex Based on Pre-adolescent Brain Structure Differences from the ABCD Study®{Adeli, 2020 #260}{Adeli, 2020 #260}. Many studies that have found sex-specific differences in the development of brain structures are complicated by confounding factors, such as head size, wide age distributions, and small sample sizes. In this study, the authors use a deep learning framework to predict the sex of participants from the MRIs of over 8,000 pre-adolescents from the Adolescent Brain Cognitive Development (ABCD) Study. The prediction score was 89.6% accurate for the sex of the participants based on the MRI. The prediction accuracy held up against numerous controls—including age, socioeconomic status, and pubertal development—and outperformed other machine learning models. This novel discovery demonstrated that sex could be accurately predicted in individual pre-adolescents through a pattern of 10 brain regions. Sex prediction scores were positively correlated with scores on cognitive tests, which is consistent with other studies in adolescent populations and suggests that sex-specific structural differences may be related to differences in cognitive performance. The predictive power of this score provides evidence for sex differences in pre-adolescent neurodevelopment and may further our understanding of sex-specific vulnerability or resilience to mental health disorders. This clinical study relates to multiple goals of the Trans-NIH Strategic Plan for Women's Health Research. It exemplifies the power of applying computational approaches to analyze large datasets to predict sex biases in vulnerability to neurobehavioral disorders. The rigorous design that compared males and females in a large population was in line with the NIH Policy on Sex as a Biological Variable (SABV) (Adeli et al., 2020).

This relates to Objectives 1.1 ("Discover basic biological differences between females and males"), 1.3 ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes"), 2.1 ("Expand and develop advanced and innovative approaches for study design, data collection, and analysis to optimize data quality and the ability to detect the influences of sex and gender on health and disease"), 2.2 ("Develop and adapt reliable and valid measures relevant to the health of women"), and 2.3 ("Leverage secondary data sources for research on the health of women through a big data enterprise that includes data sharing and analytic strategies") of the Trans-NIH Strategic Plan for Women's Health Research.

2. Maternal and infant characteristics are associated with maternal opioid overdose in the year following delivery. Maternal mortality and severe maternal morbidity have increased dramatically in the U.S. and are a major medical challenge. One-third of pregnancy-related deaths occur 1 week to 1 year postpartum. Women are at risk for mental disorders (including depression), suicide, and drug use during this period. To better understand and potentially predict those who would be vulnerable to overdose, this retrospective cohort study of 164,765 women in Massachusetts examined the association between maternal and infant factors with maternal overdose in the first year postpartum. Postpartum overdose occurred at the rate of 11 per 10,000 deliveries. This rate is similar to that of postpartum psychosis. Notably, less than 50% of these had documented opioid use disorder (OUD) prior to delivery. Factors associated with overdose for both women with and without previous OUD were infant diagnosis of neonatal abstinence syndrome and high unscheduled health care utilization. Engagement in methadone or buprenorphine treatment in the month prior to delivery was insufficient to reduce the odds of postpartum overdose, suggesting that continuous access to health care and postpartum care providers may be necessary to increase adherence. Sustained postpartum support is critical to reducing pregnancy-associated morbidity. These clinical findings exemplify rigorous research relevant to the health of women and leverage data sources that enhance research for the health of women (Nielsen et al., 2020).

   This relates to Objectives 1.3 ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes"), 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health"), and 2.3 ("Leverage secondary data sources for research on the health of women through a big data enterprise that includes data sharing and analytic strategies") of the Trans-NIH Strategic Plan for Women's Health Research.

3. Neurobiological mechanisms underlying sex differences in tobacco smoking. Sex differences exist in the behavioral characteristics of tobacco smoking. Males are more likely to smoke for the reinforcing effects of nicotine, whereas females report mood regulation or stress reduction as an incentive to smoke. Females are also more likely to relapse. This neuroimaging study provided a potential neurobiological basis for this sex difference by examining the dopamine reward system in the dorsolateral prefrontal cortex (dlPFC) of male and female smokers and nonsmokers before and after a challenge of amphetamine, which releases dopamine. They found that dopamine 2 receptors (D2R) were lower in the smokers than in nonsmokers, and this difference was driven by males. Importantly, the ability of amphetamine to release dopamine was blunted in female smokers compared with all other groups. This discovery that smoking disrupts the dopamine system so that it is less responsive in females could account for greater resistance to becoming abstinent and a worse treatment response to nicotine replacement therapy. This may be a basis for developing sex-specific therapies for nicotine use cessation. This study is an example of rigorous research relevant to the health of women. As a rigorous and sufficiently powered comparison of males and females, it fulfilled the NIH SABV policy (Zakiniaeiz et al., 2019).

   This relates to Objectives 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes") and 1.3 ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes") of the Trans-NIH Strategic Plan for Women's Health.

4. Gene networks that are differentially regulated by stress in females compared with males could explain sex biases in stress-related psychiatric disorders. The prevalence of stress-related disorders is nearly twice as high in females as it is in males. In this basic research study, behavior and genes that were regulated by chronic stress in the mesocorticolimbic circuit were compared between the sexes. To determine whether differences were caused by genetic sex or gonadal sex, the investigators used the four core genotype (FCG) model, where the Sry gene, which determines the testes, is manipulated to yield males with ovaries or females with testes. Stress-related behaviors were more pronounced in females than in males, and this was related both to genetic and gonadal sex. There was little overlap in the pattern of gene regulation by stress between males and females, and in some cases, stress altered gene networks in opposite directions. Stress altered transcriptional coherence between regions with distinct patterns in males and females. These differences highlight how stress can have very different effects on brain circuitry underlying affect and motivated behavior. The identification of these differences may guide the development of sex-specific circuit-based therapies. This basic research study done in mice is research relevant to the mental health of both males and females, highlighting sex differences that may be based on either genetic or gonadal sex. This research informs the authors' previous work using human post-mortem brain tissue that identified sex differences in gene expression patterns in brain circuits relevant to mood disorders. Their ability to compare results from animal and human studies makes the work highly translational. The rigorous design, analysis, and reporting is consistent with the NIH SABV policy (Paden et al., 2020).

   This relates to Objectives 1.1 ("Discover basic biological differences between females and males"), 1.2 ("Discover basic biological differences between females and males"), and 1.4 ("Promote research that explores the influence of sex and gender on the connection between the mind and body, and its impact on health and disease") of the Trans-NIH Strategic Plan for Women's Health Research.

5. Biological basis for sex differences in play behavior: Cells that eat other newborn cells early in development sculpt the circuits that direct sex-specific behavior. Uncovering the fundamental biology that is the basis for sex differences in behavior is essential to understanding sex differences that drive normal behavior, as well as prevention and treatment of neurobehavioral disorders in both sexes. A well-known sex difference in behavior that is conserved across mammals is juvenile physical play that is more prominent in males. Through an elegant and rigorous series of experiments, these researchers identified the basis for sex differences in the expression of that social behavior. This behavior is mediated by the medial amygdala. This study showed that testosterone during development elevates the brain's endogenous cannabinoid system, and this drives microglia, which are phagocytotic cells in the brain, to engulf and destroy newborn astrocytes. The elimination of these astrocyte precursors alters neuronal excitability in neurons in a circuit that regulates play behavior. The administration of testosterone to females during early development can mimic the increase in endocannabinoids, increase in phagocytotic cells, decrease in newborn astrocytes, and increase in play behavior. Conversely, blocking testosterone at an early development stage in males can prevent these effects. Thus, testosterone at an early stage of development sculpts sexually distinct behavior by engaging endocannabinoids, leading to an increase in phagocytosis of newborn astrocytes in the medial amygdala and increased excitability of circuits that regulate play behavior. In addition to elucidating the basic biology of sex differences in behavior, the results of this study have implications for cannabis exposure during pregnancy, given the role of the endocannabinoid system in sculpting these effects (VanRyzin et al., 2019).

   This relates to Objectives 1.1 ("Discover basic biological differences between females and males") and 1.4 ("Promote research that explores the influence of sex and gender on the connection between the mind and body, and its impact on health and disease") of the Trans-NIH Strategic Plan for Women's Health Research.

III. Promotion of Women's Health Research

1. NIDA leads two large trans-NIH longitudinal studies that are designed to determine how sex, genetic, biological, and socioeconomic factors interact to affect brain development, cognitive function, and behavior in the long term.

   This relates to Goal 1 ("Advance rigorous research that is relevant to the health of women") and Objectives 2.1 ("Expand and develop advanced and innovative approaches for study design, data collection, and analysis to optimize data quality and the ability to detect the influences of sex and gender on health and disease"), 2.2 (Develop and adapt reliable and valid measures relevant to the health of women"), and 2.3 ("Leverage secondary data sources for research on the health of women through a big data enterprise that includes data sharing and analytic strategies") of the Trans-NIH Strategic Plan for Women's Health Research.

   a. HEAL Initiative: HEALthy Brain and Child Development Study (HEALthy BCD), RFA-DA-19-029, RFA-DA-19-036. The HEALthy Brain and Child Development (HBCD) Study will establish a large cohort of pregnant women from regions of the country significantly affected by the opioid crisis and follow them and their children for at least 10 years. Findings from this cohort will help researchers understand normative childhood brain development, as well as the long-term impact of prenatal and postnatal opioid and other drug and environmental exposures. The study will collect data on pregnancy and fetal development; infant and early childhood structural and functional brain imaging; anthropometrics; medical history; family history; biospecimens; and social, emotional, and cognitive development. Knowledge gained from this research will be critical to helping predict and prevent some of the known effects of prenatal and postnatal exposure to certain drugs or environmental exposures, including risk for future substance use, mental disorders, and other behavioral and developmental problems.

   b. Adolescent Brain Cognitive Development (ABCD) Study, RFA-DA-15-015 and DA-20-003. The ABCD Study is a landmark longitudinal study of brain development and child health of more than10,000 children, conducted at 21 sites across the country and reflecting the diversity of the U.S. in terms of sex, race and ethnicity, socioeconomic status, and urbanicity. This study is designed to increase our understanding of environmental, social, genetic, and other biological factors that affect brain and cognitive development and that can impact a young person's life trajectory. The study was launched in 2015 and renewed in 2020.

2. NIDA also administers or participates in the following funding opportunity announcements (FOAs) related to women's health or the role of sex/gender in health and disease:

   a. Women and Sex/Gender Differences in Drug and Alcohol Abuse/Dependence, PA-18-603; PA-18-602; PA-18-601. NIDA is advancing research on male–female differences in drug and alcohol abuse and addiction and on factors specific to women. This relates to Goals 1 ("Advance rigorous research that is relevant to the health of women") and 2 ("Develop methods and leveraging data sources to consider sex and gender influences that enhance research for the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

   b. Substance Use/SUD Dissertation Research Award, PA-20-208. The goal of this FOA is to enhance the diversity of the drug use research workforce by providing dissertation awards on topics related to the study of basic and clinical neuroscience, development, epidemiology, prevention, treatment, services, or women and sex/gender differences. This relates to Goals 1 ("Advance rigorous research that is relevant to the health of women") and 2 ("Develop methods and leveraging data sources to consider sex and gender influences that enhance research for the health of women") and Objective 4.2 ("Develop the next generation of researchers to advance science on the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

c. Notice of Special Interest: Administrative Supplements for NIH grants to Add or Expand Research Focused on Maternal Mortality, NOT-OD-20-104. NIDA grantees received administrative supplements under the Implementing a Maternal health and PRegnancy Outcomes Vision for Everyone (IMPROVE) initiative to reduce causes of maternal deaths and improve health for women before, during, and after delivery. This relates to Objectives 1.3 ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes"), 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health"), and 3.1 ("Design and test approaches to promote the adoption, adaptation, and integration of evidence-based interventions in public health, clinical practice, and community settings") of the Trans-NIH Strategic Plan for Women's Health Research.

d. The intersection of sex and gender influences on health and disease, RFA-OD-029. NIDA funded an application from a female early stage investigator to determine the role of DNA methylation in patterns of substance use in sexual and gender minorities. This relates to Goals 1 ("Advance rigorous research that is relevant to the health of women") and 2 ("Develop methods and leveraging data sources to consider sex and gender influences that enhance research for the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

e. ORWH Specialized Centers of Research Excellence (SCORE) on Sex Differences, RFA-OD-19-013. NIDA supports the center at the Medical University of South Carolina, which studies sex/gender differences in addictive disorders and the relationship between stress and relapse. This relates to Goals 1 ("Advance rigorous research that is relevant to the health of women"), 2 ("Develop methods and leveraging data sources to consider sex and gender influences that enhance research for the health of women"), 3 ("Enhance dissemination and implementation of evidence to improve the health of women"), and 4 ("Promote training and careers to develop a well-trained, diverse, and robust workforce to advance science for the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

f. ORWH Administrative supplements for research on sex/gender differences, NOT-OD-20-049. A recent example is the supplement awarded to (3R01DA045108-03) that focuses on sex differences in the impact of pandemic-related stress on substance use by adolescents. This relates to Goals 1 ("Advance rigorous research that is relevant to the health of women") and 2 ("Develop methods and leveraging data sources to consider sex and gender influences that enhance research for the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

g. ORWH Research on the Health of Women of Understudied, Underrepresented and Underreported (U3) Populations, NOT-OD-20-048. This relates to Objectives 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes"), 1.3 ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes"), 1.4 ("Promote research that explores the influence of sex and gender on the connection between the mind and body, and its impact on health and disease"), 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health"), 2.1 ("Expand and develop advanced and innovative approaches for study design, data collection, and analysis to optimize data quality and the ability to detect the influences of sex and gender on health and disease"), 2.2 ("Develop and adapt reliable and valid measures relevant to the health of women"), 2.3 ("Leverage secondary data sources for research on the health of women through a big data enterprise that includes data sharing and analytic strategies"), and 2.4 ("Expand and refine methodologies to improve the recruitment and retention of women underrepresented in clinical research") of the Trans-NIH Strategic Plan for Women's Health Research.

3. NIDA has an organized Women & Sex/Gender Differences Research Group (WGRG). NIDA's WGRG is dedicated to the promotion of the conduct, translation, and dissemination of research on (1) sex/gender differences in the pharmacological, neurobiological, behavioral, and socioeconomic determinants of SUD and responses to drugs of abuse and (2) interactions of SUD risk factors, SUD, and drugs of abuse with changes in female physiology and behavior across the lifespan. A primary part of the mission is to promote the careers of women scientists. The group hosts monthly discussions on research and policy updates, recently published papers, workshops, and training opportunities. WGRG members also serve on the trans-NIH Coordinating Committee on Research on Women's Health (CCRWH) to advance research on sex and gender differences and women's health. See 4b below for the Maternal Brain series sponsored by this workgroup.

   This relates to Objectives 1.4 ("Promote research that explores the influence of sex and gender on the connection between the mind and body, and its impact on health and disease"), 4.1 ("Enhance knowledge of sex and gender influences on health and disease among all scientists, clinicians, and other health professionals to accelerate the translation of that knowledge into practice"), 4.2 ("Develop the next generation of researchers to advance science on the health of women"), and 4.4 ("Promote and support policies, mentoring and networks, collaborations, and infrastructure to retain and advance women in their careers") and Goal 5 ("Improve evaluation of research that is relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

4. Conferences or workshops focused on emerging issues in women's health.

   a. Dr. Rita Valentino, Director of the Division of Neuroscience and Behavior at NIDA, was instrumental in the organization of a National Academy of Sciences meeting titled "Sex Differences in Brain Disorders: Emerging Transcriptomic Evidence and Implications for Therapeutic Development–A virtual Workshop," held on September 23, 2020. This highly attended (more than 500 attendees) workshop focused on transcriptomic and genome-sequence variations that may be part of the biological underpinnings of sex differences in clinical features and treatment responses of neuropsychiatric disorders. The public workshop brought together experts and stakeholders from academia, government, industry, and nonprofit organizations to explore emerging evidence regarding differences in transcriptomic abnormalities that occur in the brains of males versus females with a variety of brain disorders, including depression, post-traumatic stress disorder, drug addiction, and neurodegenerative conditions. This relates to Objectives 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes"), 1.3 ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes"), 1.4 ("Promote research that explores the influence of sex and gender on the connection between the mind and body, and its impact on health and disease"), and 3.2 ("Identify collaborative opportunities and leverage partnerships to disseminate research that improves the health of women") and Goal 5 ("Improve evaluation of research that is relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

   b. The NIDA WGRG held a monthly seminar series throughout 2020 on the maternal brain in response to NIH efforts to address the dramatic rise in maternal morbidity and mortality in the U.S. Mental health disorders during pregnancy can contribute to poor outcomes and postpartum suicidal tendencies. It is recognized that the maternal brain is undergoing changes to prepare for the organization of parental behavior and that it is particularly vulnerable to perturbations such as exposure to stress or drugs at this time. However, research in this area, particularly human research, is scant. The WGRG monthly webinar featured talks from nationally and internationally recognized speakers that centered on how pregnancy changes the brain to prime maternal behaviors and mother–infant bonding. Several talks focused on how drug exposure, environmental exposures, or

adverse events occurring during pregnancy can disrupt normal processes and have long-term neurobehavioral consequences or influence the risk of developing neurobehavioral disorders for mother and child. This relates to Objectives 1.4 ("Promote research that explores the influence of sex and gender on the connection between the mind and body, and its impact on health and disease"), 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health"), 4.1 ("Enhance knowledge of sex and gender influences on health and disease among all scientists, clinicians, and other health professionals to accelerate the translation of that knowledge into practice"), and 5.2 ("Identify priority areas for additional study to advance the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

5. Intra- or inter-agency collaborations to promote clinical care practices that reduce health disparities in women and underrepresented populations.

    a. SAFE4BOTH is a mobile health (mHealth) platform that engages postpartum mothers suffering from OUD with their case managers to provide better coordination of services and support for mother and baby (R43DA048673-01A1) (Phase I, FY 2019). Mothers recovering from OUD are at a greater risk of not having the support of extended families or social networks in their parenting and may lack coping skills. SAFE4BOTH, supported by a NIDA Small Business Innovation Research (SBIR) grant, will build on Plans of Safe Care (POSC), in response to the Family First Prevention Services Act (2018). Long-term, SAFE4BOTH will reduce fragmentation of postnatal and infant care and promote interactions with child services and other services. This relates to Goal 3 ("Enhance dissemination and implementation of evidence to improve the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

    b. Parent HBCD: The Cumulative Risk of Substance Exposure and Early Life Adversity on Child Health Development and Outcomes (3R34DA050288-01S2). The objective of these administrative supplements is to test the feasibility of using a remote sensing device to (1) quantify sleep indices in pregnant and postpartum women, including American Indian (AI) women; (2) assess percentage of good data obtained and sleep stage scoring; and (3) assess agreement of objective and subjective sleep parameters. The study will take place in Sioux Falls and Rapid City, SD. The results of this study may lead to the development of a cost-effective tool to assess a modifiable risk factor (sleep) for maternal morbidity and mortality. This relates to Goals 2 ("Develop methods and leveraging data sources to consider sex and gender influences that enhance research for the health of women") and 3 ("Enhance dissemination and implementation of evidence to improve the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

    c. Women's Justice Community Opioid Innovation Network (W-JCOIN)–Public outreach programs to educate at-risk communities of women (1UG1DA050069-01). As part of the Justice Community Opioid Innovation Network (JCOIN), W-JCOIN organizes outreach and research focused on the unique challenges of OUD for women. The study will connect incarcerated women with community OUD services during the jail-to-community transition and will determine whether this intervention is successful in reducing opioid relapse and overdose among high-risk justice-involved women. This relates to Objective 2.4 ("Expand and refine methodologies to improve the recruitment and retention of women underrepresented in clinical research") and Goal 3 ("Enhance dissemination and implementation of evidence to improve the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

IV. Advancement of Women in Biomedical Careers

1. Women Scientists Advisors (WSA), NIDA Intramural Research Program (IRP). The mission of NIDA's IRP's WSA is to foster achievement and support career

development among women scientists. Annual events include:

a. Honoring women scientists from NIDA and National Institute on Aging (NIA) Intramural Research Programs by inviting them to talk about their research. This event is followed by a social;

b. Sponsoring the "Successful Women in Science" series, where informal discussions are held with incoming women seminar speakers. These speakers share information and advice on success at all stages of career development from a woman's prospective;

c. Hosting a Winter Tea to promote communication among women scientists from different laboratories and to discuss ways in which WSA can serve the scientific community;

d. Sponsoring Achievement Awards for Excellence in Scientific Research. These are competitive, highly distinguished awards that are given to a Senior Investigator, Staff Scientist, and Postdoctoral Fellow each year from the NIDA and NIA Intramural Research Programs.

This relates to Goals 4 ("Promote training and careers to develop a well-trained, diverse, and robust workforce to advance science for the health of women") and 5 ("Improve evaluation of research that is relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

V. Implementation of the NIH Policy on Sex as a Biological Variable (SABV)

1. Tracking and Analysis of SABV Implementation in NIDA's Preclinical Grant Portfolio. NIDA's long history of supporting research on sex differences in the biology of SUD has built a robust portfolio of studies in which sex as a biological variable (SABV) is "built in." NIDA tracks inclusion of both sexes in animal studies and the proportion of planned experiments in which sex differences are analyzed through its Extramural Project System—NEPS. Over the past 2 years, the percentage of animal research applications including the study of females or sex differences in the "Specific Aims" was 25%, an increase from a pre-SABV policy rate of about 14%. Notably, the success rates of grants that analyze sex differences has been higher (21%) than the average (16%).

   This relates to Goal 5 ("Improve evaluation of research that is relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

2. Developing Best Practices. The NIDA WGRG has formed an SABV Training and Implementation Workgroup. The first aim of the workgroup is to work with program officers to develop best practices for ensuring post-award SABV implementation. Another major aim is to stimulate and support SABV education at multiple levels of training along the career pipeline. As part of this effort, the WGRG is hosting discussions with other ICs on specific strategies and tools for tracking and incentivizing SABV implementation throughout the life of funded projects and holding listening sessions with program officers.

   This relates to Goals 1 ("Advance rigorous research that is relevant to the health of women") and 5 ("Improve evaluation of research that is relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

VI. Inclusion of Women in Clinical Research

1. Medication Treatment for OUD in Expectant Mothers (MOMs) study. The growing opioid-use epidemic in the U.S. has been associated with a significant increase in the prevalence of pregnant opioid-dependent women and neonatal abstinence syndrome, which is associated with adverse health effects for the infant and with costly hospitalizations. Maintenance with sublingual (SL) buprenorphine (BUP) is efficacious for OUD but has disadvantages that may be heightened in pregnant women, including the potential for poor adherence, treatment dropout, and negative maternal/fetal effects associated with daily BUP peak-trough

cycles. Extended-release (XR) formulations may address some of these disadvantages. The primary objective of CTN-0080 is to evaluate the impact of treating OUD in pregnant women with BUP-XR, compared with BUP-SL, on maternal–infant outcomes. Testing a conceptual model of the mechanisms by which BUP-XR may improve maternal–infant outcomes, in relation to BUP-SL, is a secondary trial objective. This study conducted by the NIDA Clinical Trials Network (CTN) evaluates the impact of treating OUD in pregnant women with extended release buprenorphine compared to sublingual buprenorphine (NCT03918850).

This relates to Objectives 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health"), 2.4 ("Expand and refine methodologies to improve the recruitment and retention of women underrepresented in clinical research"), and 3.1 ("Design and test approaches to promote the adoption, adaptation, and integration of evidence-based interventions in public health, clinical practice, and community settings") of the Trans-NIH Strategic Plan for Women's Health Research.

2. The NIDA Clinical Trial Network (CTN). The NIDA CTN is a national consortium of researchers and providers whose aim is to generate the evidence needed for the integrated management of patients with substance misuse/SUD at general medical settings and linked specialty care treatment settings. Study results from 41 multi-site clinical trials directed by the CTN are posted at https://datashare.nida.nih.gov. NIDA encourages researchers to leverage these datasets for addressing gender-based questions. As new trials are planned, NIDA invites scientists to work with the trial investigators to plan ancillary or platform studies that can provide needed information on issues that can affect women in drug use disorder treatment.

   The CTN established a Gender Special Interest Group (GSIG), whose mission is to promote and provide guidance on the inclusion and consideration of gender and sex in CTN studies. The GSIG plays a key role in the overall gender research across the CTN studies and in identifying SUD research areas that could benefit from additional attention to gender-related outcomes. The GSIG developed guidance for investigators to address sex as a biological variable and recommendations to better adhere to NIH requirements to include sex and gender in study design. In 2020, in response to issues of social justice and equity, the GSIG worked with colleagues in the racial and ethnic minorities special interest groups and submitted a letter to Drs. Nora Volkow and Betty Tai with recommendations for multiple initiatives across CTN and NIDA. The letter provides areas to consider, such as increasing diversity in the addiction research workforce, increasing diversity of participants in clinical trials, and consideration of relevant research questions.

   This relates to Goals 2 ("Develop methods and leveraging data sources to consider sex and gender influences that enhance research for the health of women") and 3 ("Enhance dissemination and implementation of evidence to improve the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

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National Institute on Deafness and Other Communication Disorders

I. Executive Summary

The National Institute on Deafness and Other Communication Disorders (NIDCD) supports and conducts biomedical research, behavioral research, and research training in the normal and disordered processes of hearing, balance, taste, smell, voice, speech, and language. These disorders affect approximately 46 million people in the United States, and NIDCD is committed to fostering and advancing research and research training to improve the health of people who have communication impairments or disorders.

Deafness and other communication disorders cross all gender, social, and ethnic groups. The NIDCD Strategic Plan prioritizes research to understand the basis of health disparities within its mission areas by determining how communication disorders may contribute to, or be worsened by, differences in health among populations. Recognizing that women, minorities, and underserved populations are underrepresented in NIDCD-sponsored research and research training activities, the NIDCD is working to increase participation of individuals and groups from diverse backgrounds. This report highlights several accomplishments, ongoing activities, and efforts made by NIDCD to promote women's health research, expand the understanding of sex differences on health, cultivate and retain women in biomedical careers, and ensure the inclusion of women in research.

II. Scientific Advances

Millions of Americans will experience a hearing disorder at some point in their lives. Loss of hearing impacts quality of life and imposes a significant social and economic burden upon individuals, their families, and the communities in which they live. Hearing loss at an early age can hinder speech, language, social, and cognitive development. In the United States, approximately 37.5 million adults have some degree of hearing loss, and 2–3 of every 1,000 children born have detectable hearing loss. Etiologies of hearing loss include congenital, infectious, noise-induced, age, and ototoxic causes. The NIDCD is committed to improving hearing health care across the lifespan and strives to raise awareness about this public health issue.

Several NIDCD-supported studies recently advanced the understanding with regard to the differences in outcomes, potential disparities, and treatment efficacy related to the hearing health for women.

» Dr. Maria Rubio authored a chapter highlighting NIDCD-supported research (R01DC013048) elucidating the importance of glutamatergic synapses for the mediation of fast synaptic transmission in the central nervous system. Recognizing that sex differences play a role in the vulnerability to hearing loss in humans, one of Dr. Rubio's basic research goals is to evaluate sex-specific differences in the subunit composition of mice auditory synapse receptors that may account for the sex differences in susceptibility to noise-induced hearing loss. Specifically, she is evaluating whether estrogen causes a change in the subunit composition of a neurotransmitter receptor that would make inner hair cell synapses more vulnerable to noise damage (Rubio, 2020).

  This relates to Objectives 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes") and 1.3 ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes") of the Trans-NIH Strategic Plan for Women's Health Research.

» Dr. Michael Hoa's NIDCD intramural Auditory Development and Restoration Program collaborates with other scientists to better understand the role of estrogen on sex differences in hearing physiology and susceptibility to noise-induced hearing loss (NIHL) seen in animal models and humans. Their prior basic research studies showed that estrogen may confer protection to NIHL in mice. Dr. Hoa's laboratory evaluates the effects of estrogen supplementation on the endocochlear potential

(EP) in ovariectomized mice in an effort to see whether estrogen contributed to the generation or augmentation of EP. Recent findings provide a framework to understand estrogen's protective effect (Shuster, 2020).

This relates to Objectives 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes") and 1.3 ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes") of the Trans-NIH Strategic Plan for Women's Health Research.

» Dr. Katharine Fernandez from NIDCD's intramural Laboratory of Hearing Biology and Therapeutics conducted translational research that examined the effect of the cholesterol-lowering drug lovastatin on cisplatin-induced hearing loss in mice. Lovastatin-mediated protection was significantly greater among female mice than among male mice, and the dose of lovastatin required for protection was different between the sexes. Her data indicate that statins may represent a therapeutic approach to protecting the hearing of patients undergoing cisplatin therapy and highlight the importance of potential differences between the sexes in this protective effect (Fernandez et al., 2020).

This relates to Objective 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes") of the Trans-NIH Strategic Plan for Women's Health Research.

III. Promotion of Women's Health Research

The NIDCD is dedicated to improving the health and quality of life for people living with communication disorders by supporting and managing a broad portfolio of both basic and clinical research in the areas of hearing, balance, taste, smell, voice, speech, and language. NIDCD-supported research advances the science in several diseases and disorders that are more common or detrimental for women. In addition, NIDCD recognizes that women have pivotal roles in our society; the research activities below highlight some of these roles and how they have the potential to profoundly impact the health of women and those under their care.

Maternal Involvement & Childhood Development

» NIDCD is supporting the first randomized controlled trial to determine whether sweet preferences can be downshifted in preschoolers by a 4-month exposure to daily snacks containing reduced levels of added sugars and sweetness (intervention group) compared with a similarly aged control group whose daily snacks will be more than twofold higher in total sugar and fivefold higher in added sugar. The knowledge gained will lead to targeted nutrition-related recommendations for reducing added sugar intake, with health implications for the prevention of obesity. Mother–preschooler dyads will be recruited for this study. In addition to examining sweet preferences of the preschoolers, investigators are examining whether sweet preferences will be affected in the mothers of the intervention group. They hypothesize that there will be a trickledown effect of the intervention, with mothers in the intervention group downshifting their own sweet preference. (R01DC016616)

This relates to Objective 1.3 ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes") of the Trans-NIH Strategic Plan for Women's Health Research.

» A randomized clinical trial is currently underway to evaluate the efficacy of a sequentially targeted naturalistic intervention to maximize language outcomes for preschoolers with developmental language disorder. The Enhanced Milieu Teaching-Sentence Focus (EMT-SF) intervention is implemented by caregivers and interventionists, in relation to a control condition. This clinical trial will enroll 108 30-month-old children and their caregivers, and it is anticipated that most of the parents involved in the study will be mothers or female caregivers (aunts, grandmothers), although a small number of fathers (less than 10%) participated in past studies. (U01 DC017135)

This relates to Objective 1.3 ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes") of the Trans-NIH Strategic Plan for Women's Health Research.

» A new technology-supported platform with three parent-mediated intervention components is being tested for babies with early communication delays. The research team is using mobile technology for virtual parent meetings and virtual parent coaching, for children beginning at 12 months of age. From prior experience in parent training research studies, it is expected that about 90% of the parents in the study will be female. This study is identifying an easily implemented means of increasing the likelihood of mothers receiving an efficacious early intervention for children who are at risk for communication delays. This research is addressing a pressing need to leverage resources and test new methods to support families as early as possible when their children begin to show small lags in communication development and to illustrate the critical role of mothers in reducing these lags. (R21 DC018128)

  This relates to Objective 1.3 ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes") of the Trans-NIH Strategic Plan for Women's Health Research.

» Focus is made on maternal communication skills to develop early intervention strategies for infants and toddlers with fragile X syndrome (FXS) and comorbid autism spectrum disorder (ASD), in order to facilitate better outcomes of early language development. The contribution of child and maternal gestures and responsive maternal language input properties to word learning opportunities and spoken vocabulary growth is being examined. Investigators are also evaluating the influence of child autism spectrum disorder symptoms on maternal mental health (anxiety and depression) and maternal gestures and language input. This study will inform future efforts to develop and evaluate early interventions to positively impact long-term outcomes for individuals with FXS. (R21 DC017800)

  This relates to Objectives 1.3 ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes") 1.4 ("Promote research that explores the influence of sex and gender on the connection between the mind and body, and its impact on health and disease") of the Trans-NIH Strategic Plan for Women's Health Research.

» Utilizing a mouse model, investigators are trying to determine the mechanisms underlying the natural functioning of the processing stream between a primary and higher-order auditory cortical field in the context of species-specific communication. This research examines the neural processing of pup vocalizations in mice and their specialized neural responses in dams (moms), virgin females that help care for pups (co-carers), estrogen-manipulated co-carers, and adult males. By elucidating the normal operation of this system, investigators hope the results will inform aspects of communication coding and plasticity that may fail in auditory processing disorders, social disorders with auditory dysfunctions, hearing loss, and temporal lobe strokes. (R01 DC008343)

  This relates to Objectives 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes") and 1.3 ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes") of the Trans-NIH Strategic Plan for Women's Health Research.

Voice and Occupation

» Women make up the majority of several high-voice-use occupations (e.g., public school teachers, call center workers) and, as a result, tend to have a higher incidence of reported voice problems than men. Research is being conducted to better understand the sex discrepancy in vocal health issues among one group of occupational voice users, elementary and secondary education teachers. Investigators are evaluating the underlying physiological differences and compensatory adjustments women use in different communication environments and how these adjustments contribute to their increased risk of voice issues. (R01 DC012315)

  This relates to Objectives 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes") and 1.3 ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes") of the Trans-NIH Strategic Plan for Women's Health Research.

» Muscle tension voice disorders, such as primary muscle tension dysphonia (pMTD), are more common in women. NIDCD investigators are working to determine the functional and clinical relevance of stress on the motor control for voice and speech production in the brain and will determine neural (functional MRI), psychobiological (cortisol, personality), and vocal function (surface EMG, acoustic) signatures of stress responders and nonresponders in early-career female teachers with vocal fatigue and female control participants. The results of this project will provide a better fundamental understanding of the role of stress in muscle tension voice disorders and help to identify "laryngoresponders" for preventive measures and optimize the long-term success of interventions for a broad range of behavioral voice and speech disorders under consideration for potential neurorehabilitative interventions. (R01DC 018026)

This relates to Objectives 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes") and 1.3 ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes") of the Trans-NIH Strategic Plan for Women's Health Research.

IV. Advancement of Women in Biomedical Careers

The NIDCD's training and career development programs are critical to our mission, as they cultivate and advance the next generation of diverse, well-prepared, and talented investigators with knowledge and expertise in all areas supported by the institute: hearing, balance, taste, smell, voice, speech, and language.

Female applicants to NIDCD have a higher average award rate for extramural fellowship and career grants. In FY 2019, 51.4% of NIDCD career development awards (K01, K08, K18, K23, K24, K25, and K99) were awarded to women, and 42.9% were awarded to men. Similarly, 51% of fellowship grants (F31, F32, and F33) were awarded to women, and 41.4% awarded to men.

NIDCD's FY 2019 success rate for female and male awardees for the R01s are higher than the overall NIH success rates. In FY 2019, the success rate for female early-stage investigators (ESIs) applying to the R01 ESI grant was better than the success rate for male ESI investigators, 47.4% versus 43.3%. However, the success rate for women was slightly less than for men in FY 2019, 45.5% versus 47% for R01s. NIDCD acknowledges that continued efforts are needed to move toward a more gender-balanced biomedical workforce; the institute's extramural training programs are impactful in moving toward this goal.

In alignment with Objective 4.2 ("Develop the next generation of researchers to advance science on the health of women") of the Trans-NIH Strategic Plan for Women's Health Research, efforts and success in the advancement of women in biomedical careers have also been seen in NIDCD's intramural program. For example, Dr. Matthew Kelley's NIDCD Laboratory of Cochlear Development consists of 66% women. Dr. Kelley's lab participates in NIH IRTA Program, which provides recent college graduates who are planning to apply to graduate or professional school an opportunity to spend 1–2 years performing full-time research at the NIH. In FY 2019–2020, three female postbaccalaureate IRTAs successfully completed this program. One entered medical school at the University of Maryland. One entered the Biomedical Graduate Program at Baylor University. And one entered the Medical Scientist Training Program (MD/PhD) at the University of Pennsylvania.

Related to Objective 4.3 ("Enhance and develop programs to recruit, support, retain, and advance women at all stages of their research careers, from early career to leadership positions") of the Trans-NIH Strategic Plan for Women's Health Research, NIDCD participates in several trans-NIH initiatives to promote diversity in the biomedical research workforce, such as K99/R00 Maximizing Opportunities for Scientific and Academic Independent Careers (MOSAIC) Postdoctoral Career Transition Award to promote diversity, the Faculty Institutional Recruitment for Sustainable Transformation (FIRST) program, and the Support of Competitive Research (SCORE) Research Advancement Award.

NIDCD funds scientific meetings directed toward research objectives within the field of communication sciences and disorders. These scientific meetings relate to Objective 4.4 ("Promote and support policies, mentoring and networks, collaborations, and

infrastructure to retain and advance women in their careers") of the Trans-NIH Strategic Plan for Women's Health Research by providing a forum to help mitigate barriers and advance women in biomedical careers. For example, the Symposia for Association for Research in Otolaryngology (R13 DC017684) has hosted a Women in Science Roundtable event for the past 2 years. It provided an opportunity for women at all stages of their careers a platform to come together and discuss challenges and solutions to women in science. This event is in high demand, with standing-room-only capacity both years.

V. Implementation of the NIH Policy on Sex as a Biological Variable (SABV)

To evaluate NIDCD's compliance with NIH's SABV policy, the NIDCD's Science Tracking & Reporting System (STaRS) is utilized to categorize, code, and track funded research that addresses health conditions that are specific to women, are more common or more serious in women, have distinct causes or manifestations in women, have different outcomes or treatments in women, and/or have high morbidity or mortality in women. In addition, NIDCD uses the Research, Condition, and Disease Categorization (RCDC) system Women's Health for IC Use Fingerprint to also help identify relevant projects. All relevant projects from STaRS and/or RCDC are entered into RCDC's Manual Categorization System at the end of the fiscal year for reporting in RCDC.

NIDCD funding opportunity announcements include review criteria evaluating the adequacy of the investigator's plans to address relevant biological variables, such as sex, for studies in vertebrate animals or human subjects. NIDCD's Scientific Review Officers meet with new reviewers to provide guidance on expectations and preparation for critiques. Prior to each meeting, all reviewers are provided the NIH Reviewer Guidance to Evaluate Sex as a Biological Variable.

NIDCD scientific staff members also make efforts to include the analysis of sex as a biological variable in NIDCD-funded clinical trials. Higher risk and more complex clinical trials are funded through the U01 cooperative agreement mechanisms where the NIDCD Medical Officers have substantial involvement and work in partnership with the study investigators in the design and implementation of clinical trials. When scientifically appropriate, NIDCD Medical Officers work with the study team to incorporate outcomes to provide insight on the impact of sex as a variable.

VI. Inclusion of Women in Clinical Research

In 2019, NIDCD (both extramural and intramural) had 48.7% females and 43.4% males enrolled in NIH-defined clinical research; in 2020, 47.1% females and 44.9% males were in NIDCD NIH-defined clinical research. (Note: 7.9% unknown in 2019 and 8.0% unknown in 2020; subjects did not report their sex/gender.)

NIDCD funding opportunity announcements (FOAs) promote the inclusion of women in research by specifying the inclusion of women, minorities, and individuals across a lifespan as an additional review criterion for projects involving human subjects and/or clinical research. The adequacy of project plans to include individuals on the basis of sex/gender, race, ethnicity, and age may have bearing overall application impact score.

NIDCD has additional processes in place to ensure the inclusion of women in scientifically relevant research projects. Program Officers carefully review inclusion data submitted by grantees and monitor the progress of research projects. If necessary, the NIDCD Inclusion Officer will communicate with investigators, guide them through the policy and eRA systems, and resolve complicated issues. Inclusion data are analyzed qualitatively and quantitatively to proactively detect anomalies, which will be explained or corrected. After all inclusion issues are resolved, Grants Management will issue award notices. With the direct involvement of the NIDCD Inclusion Officer, minor errors are corrected expeditiously, and all NIDCD data are reconciled by the end of each fiscal year. NIDCD's successful operation is based on teamwork and effective communication among Program Officers, the Inclusion Officer, and Grants Management.

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National Institute of Dental and Craniofacial Research

I. Executive Summary

The mission of the National Institute of Dental and Craniofacial Research (NIDCR) is to promote the general health of the American people by improving dental, oral, and craniofacial health through research and research training. NIDCR funds clinical and basic research to understand, prevent, and treat oral diseases and craniofacial conditions, including those that disproportionately or solely affect women. Among these diseases are orofacial pain conditions, including temporomandibular joint disorders (TMD) and autoimmune salivary gland diseases. NIDCR also supports research on the acquisition and persistence of oral human papillomavirus (HPV) and interventional research to improve the oral health of pregnant women, mothers, and their children. Recognizing the importance of gene–gene, gene–environment, and behavioral interactions, NIDCR has long emphasized basic, genetic, behavioral, social science, and epidemiologic research. This report highlights accomplishments and initiatives in key areas related to women's health and research focused on advancing the understanding of sex as a biological variable (SABV) and gender differences.

In fiscal years (FY) 2019 and 2020, NIDCR supported a variety of initiatives to advance women's health. These have included: administrative supplement programs and a career mentoring network to support, retain, and advance women in biomedical careers at the postdoctoral, early career, and investigator career stages; research on diseases and disorders that disproportionately affect women; and the creation of a working group to help NIDCR prioritize training and research strategies for TMD. Further, NIDCR has promoted the inclusion of women and girls in clinical research by supporting clinical trials in pregnant women to improve maternal and child oral health and has performed activities to implement NIH's policy to consider SABV in research design, analysis, and reporting.

II. Scientific Advances

Oral Health Disparities in Children Consortium

NIDCR funds a research consortium consisting of four clinical trials and a central data coordinating center to improve the oral health of children in underserved groups. Because caregivers have a strong influence in the oral health of their young children, all four studies are enrolling mothers in addition to their children. Research interventions of each study involve improving the oral health knowledge and behaviors of women caregivers. Studies include: (1) Using financial incentives and smart toothbrush technology to improve caregivers' brushing behaviors with their children: A pilot trial for the test intervention recruited 36 mother–child dyads and found that digital monitoring of toothbrushing and using lotter incentives was feasible (White et al., 2020). (2) Conducting oral health interventions in primary care settings: Baseline data from 1,024 caregivers and their children found that race, increased child age, having received dental care in the past 12 months, and lower caregiver oral health quality of life was associated with increased odds of children having caries at baseline (Selvaraj et al., 2020). (3) Using text message–based interventions to reduce caries in children: A pilot trial involving 55 caregivers to assess feasibility of the oral health text (OHT) messaging intervention found that 84% would recommend the program and reported high perceived impact of the OHT program on brushing their child's teeth (Borrelli et al., 2019). (4) Promoting preventive oral health behaviors via oral health education and support from community health workers: A pilot study involving 45 families found that observation and video-recording of brushing routines are feasible and acceptable to families (Martin et al., 2019).

This clinical research relates to Goal 1 ("Advance rigorous research that is relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

Temporomandibular Disorders and Chronic Overlapping Pain Conditions

Temporomandibular disorders (TMDs) are a diverse and poorly understood set of painful conditions that affect between 5% and 10% of the U.S. population, with an annual incidence rate that is greater in females than in males (about 2:1). TMDs share high levels of comorbidity with other chronic pain conditions (COPCs)—fibromyalgia (FM), low back pain (LBP), headache, and irritable bowel syndrome (IBS)—that are more common among women. NIDCR-supported investigators performed comprehensive evaluations of five COPCs to compare risk factors and clinical features specific to a COPC or shared across COPCs. Assessment of the degree of overlap between COPCs indicated that the magnitude of overlap varied by COPC, with the greatest overlap between FM, TMD, and LBP. Additionally, TMD clinical findings were frequently present with other COPCs, even when a formal TMD diagnosis was absent. Pain sensitivity varied according to number of pain conditions experienced, suggesting that the combination of pain conditions influences nociception. Measures of symptom burden showed the strongest associations with number of COPCs, while negative mood, perceived stress, and pain catastrophizing were increased among people with multiple COPCs. Within each index COPC, pain intensity, pain interference, and the proportion of participants with high-impact pain increased with each additional comorbid COPC. Taken together, these findings represent the most comprehensive biopsychosocial assessment of COPCs conducted to date, suggest possible common pathophysiologic mechanisms and risk factors for multiple COPCs, and highlight the need to adequately assess overall pain status while studying specific chronic pain conditions (Fillingim et al., 2020; Greenspan et al., 2020; Sanders et al., 2020; Sharma et al., 2020; Ohrback et al., 2020; Slade et al., 2020).

These clinical research findings are directly relevant to Goal 1 ("Advance rigorous research that is relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

Composition and Diversity of the Subgingival Microbiome in Older Women

Periodontal disease is a condition signified by loss of bone and supporting structures surrounding teeth and is the most common cause of tooth loss among adults. The Buffalo Osteoporosis and Periodontal Disease study is a prospective observational study that enrolled 1,342 postmenopausal women ages 50–79 to assess the relationship of periodontal disease with osteoporosis. Participants are community-dwelling women without selection on periodontal status at enrollment who have undergone comprehensive oral examinations assessing periodontal parameters (probing pocket depth, clinical attachment loss, gingival bleeding, alveolar crestal height), decay/caries, and tooth status. Additionally, systemic bone density (measured by DXA) and blood, saliva, and plaque biospecimens have been collected. To assess the extent to which the composition and diversity of the oral microbiome varies with age, correlations between microbiota abundance and age were evaluated. Of the 267 species identified overall, 12 species differed across age groups; 5 (42%) were higher in women ages 50–59, and 7 (48%) were higher in women 70 or older (LaMonte et al., 2019). The composition and diversity of the subgingival microflora in health and levels of periodontal disease were also investigated. Diversity of the microbiome differed significantly across the 3 periodontal disease categories. Of the 267 bacterial species identified, 56 (20.9%) differed significantly in abundance according to periodontal disease status. Among older women, taxonomic differences in subgingival microbiome composition and diversity were observed in relation to clinical periodontal disease measures (Genco et al., 2019). Taken together, these study findings indicate that diversity of the oral microbiome increases with disease severity and that several bacterial species within the subgingival microbiota correlate with age.

These translation research study findings align with Goal 1 ("Advance rigorous research that is relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

Sex Differences in HPV Immunity among Adults without Cancer

The incidence of human papillomavirus (HPV)–associated head and neck cancers is rising, particularly in men. It is unclear whether observed epidemiologic differences in sex are explained by differences in sexual exposure and/or by immune response. In this cross-sectional, multi-institutional study, seroprevalence of antibodies to the HPV L1 capsid antigen was compared by patient characteristics among 374 adult patients (median age 60) without cancer. A significantly higher seroprevalence was observed among women compared with men for HPV16 (OR, 2.96; 95% CI, 1.21–7.21) and HPV18 (OR, 2.84; 95% CI, 1.06–7.60) L1 antibodies. This difference persisted for HPV16 after controlling for lifetime and recent sexual behavior. After controlling for sex, HPV16 and HPV18 L1 seroprevalence was also significantly associated with higher number of lifetime (HPV16 OR, 1.05; 95% CI, 1.01–1.08; HPV18 OR, 1.04; 95% CI, 1.01–1.08) and recent (HPV16 OR, 1.54; 95% CI, 1.15–2.07; HPV18 OR, 1.40; 95% CI, 1.07–1.82) oral but not vaginal sexual partners. This study provides evidence that oral sexual exposure, but not vaginal exposure, is independently associated with HPV16 and HPV18 L1 seroprevalence. The study findings suggest a more robust immune response to HPV16/18 among women compared with men that may not be explained by differences in number of sexual partners and thereby presumably HPV exposure. The independent association of HPV16/18 L1 seroprevalence with a higher number of oral sexual partners suggests a possible role for the site of mucosal exposure in the HPV immune response (Windon et al., 2019).

These clinical research study findings align with Objective 1.1 ("Discover basic biological differences between females and males") of the Trans-NIH Strategic Plan for Women's Health Research.

Sex-mediated Elevation of Lipid Mediator Levels in Sjögren's Syndrome

Sjögren's syndrome (SS) is an autoimmune disorder where salivary and lacrimal gland function is progressively diminished. The disease affects 0.1%–0.6% of the population, with an average of onset greater than 50 years of age and a nine times greater prevalence in females. SS is characterized by immune cell infiltration into the salivary glands, leading to destruction of the normal tissue architecture and secretory dysfunction. A hallmark of the disease is chronic inflammation in the salivary glands, a process that is not completely understood. NIDCR-supported investigators used a combination of metabololipidomics and enzyme-linked immunosorbent assay (ELISA) and found that specialized pro-resolving mediator (SPM) levels were broadly elevated in plasma collected from SS-affected female mice after disease onset, whereas these changes did not occur in male mice. Changes were noted in salivary gland expression of SPM biosynthetic genes that are responsible for the production of Resolvin enzymes. Although the expression of the SPM biosynthetic genes was dysregulated, the abundances of their enzyme products remained unaltered in salivary gland cells. However, Resolvin plasma levels in SS female mice were found to be elevated after disease onset, suggesting that other cell populations (e.g., immune cells) besides salivary gland cells may be responsible for the overabundance of SPMs in female SS mice. Given that SS primarily affects females, these results suggest that immune cells from SS female mice may have a specific defect in SPM production. This study provides insights into mechanisms underlying the observed sexual dimorphism in SS inflammation, illustrating that SPM Resolvin is dysregulated in SS mice and that this alteration is sex-mediated (Parashar et al., 2020).

This basic research is aligned with Goal 1 ("Advance rigorous research that is relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

III. Promotion of Women's Health Research

Multi-Council Temporomandibular Joint Disorder (TMJD) Working Group

At least 10 million people in the United States are affected by temporomandibular joint disorders (TMJDs), a diverse, complex group of conditions that cause jaw joint and muscle dysfunction and pain, with women about two times as likely to be affected as men. Because TMJDs continue to confound medical and dental health care providers and researchers, NIDCR and the NIH Office of the Director commissioned the National Academies of Sciences, Engineering, and Medicine

(NASEM) to conduct a study assessing the state of TMJD research and care. The report, *Temporomandibular Disorders (TMD): Priorities for Research and Care*, identified significant gaps in our understanding of TMJD and included 11 recommendations, four of which pertain to research and building and sustaining a multidisciplinary TMJD research community. To address the research and training recommendations, in 2020, NIDCR announced the formation of a Multi-Council TMJD Working Group, whose members come from several different NIH Institute, Center, and Office (ICO) advisory councils with relevant expertise and interests. This working group is using the 2020 report as a guide to help develop a roadmap to prioritize NIH and NIDCR's TMJD training and research strategies.

This working group is aligned with Objective 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health") of the Trans-NIH Strategic Plan for Women's Health Research.

Mini Focus Groups with People Diagnosed with Temporomandibular Disorders (TMD)

In 2020, NIDCR gathered input from people with TMD to update its consumer brochure *Temporomandibular Disorders*. In the summer of 2020, NIDCR conducted seven virtual mini focus groups to test the understanding and resonance of the TMD brochure with its target audience. Because TMDs are significantly more common in females than in males, 17 of the 24 participants (71%) were female. Each focus group lasted 1 hour and was conducted by a trained facilitator. The project had participants of different races/ethnicities, education levels, and geographic areas. The participants provided feedback about the brochure's content and design. Some of the most salient findings included:

- Almost none of participants had heard the term "temporomandibular disorders." Most participants use "TMJ."
- Almost half of participants suggested adding more symptoms (ear-related issues, teeth grinding).
- Participants wanted to know how to participate in research studies.

NIDCR staff will use information from the focus groups and recommendations from the institute's experts to create and update TMD products for consumers.

This project directly relates to Goal 3 ("Enhance dissemination and implementation of evidence to improve the health of women") of the Trans-NIH Strategic Plan for Women's Health Research. It specifically pertains to Objective 3.1, which relates to testing approaches to promote evidence-based interventions in community settings.

By testing the material with its target audience, the institute helps ensure that it resonates with consumers. This in turn could increase its uptake and use by the public and, more specifically, by women. The project also relates to Objective 3.2 ("Leverage partnerships to disseminate research that improves the health of women"), because NIDCR reached out to the TMJ Association to help recruit participants, and TMJA staff had the opportunity to listen in on the focus groups.

NIDCR Grand Rounds: Celebrating 35 Years of Sjögren's Syndrome Research at NIDCR

In 2019, NIDCR hosted a special Grand Round, "Celebrating 35 Years of Sjögren's Syndrome Research at NIDCR" at NIH. Sjögren's syndrome is a systemic autoimmune condition that commonly causes extreme dry mouth and dry eyes and affects up to 4 million people in the United States, the majority of whom are women. The event marked the establishment of what is now the NIDCR Sjögren's Syndrome Clinic, a bench-to-bedside program bringing basic and preclinical scientific discoveries to the clinical setting. The clinic started in 1984 as the Dry Mouth Clinic, launched by NIDCR investigators Phil Fox and Bruce Baum to evaluate people with salivary dysfunction and to better understand and find more effective treatments. The Grand Round consisted of several speakers, who together traced the past, present, and future of Sjögren's syndrome research, emphasizing the collaborations among researchers, NIH institutes and centers, and patients that were necessary for the progress made over the past 35 years and will be critical in the work toward better treatments.

This relates to Goal 3 ("Enhance dissemination and implementation of evidence to improve the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

RFA-OD-19-029: The Intersection of Sex and Gender Influences on Health and Disease

NIDCR is actively soliciting research on the role of sex and gender by signing onto the trans-NIH FOA, *the Intersection of Sex and Gender Influences on Health and Disease*.

NIDCR encourages applications that address the mechanisms underlying the manifestations of sex- and gender-based differences in dental-, oral-, and craniofacial-related diseases and conditions. These include studies aimed at understanding immune reactivity, genetic variation, environmental triggers, aging, and hormonal changes as they affect sex- and gender-based differences. Further, NIDCR encourages clinical research studies that address the influence of sex and gender on oral disease prevention, diagnosis, and management and studies that assess the influence of sex and gender on oral health outcomes.

This activity is aligned with Goal 1 ("Advance rigorous research that is relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

IV. Advancement of Women in Biomedical Careers

Administrative Supplement Programs to Advance Women in Biomedical Careers

NIDCR participates in three administrative supplement programs aimed at supporting, retaining, and advancing women at the postdoctoral, early career, and investigator career stages. NIDCR has historically participated in and remains active in the NIH program offering supplements to promote re-entry into biomedical and behavioral research careers (PA-18-592) to encourage and support individuals with high potential to re-enter an active research career after an interruption for family responsibilities or other qualifying circumstances. Between 2011 and 2019, NIDCR supported seven women and two men on re-entry supplements. After re-entry supplement support, these individuals have all remained in research positions. NIDCR participates in two new FY 2020 administrative supplement programs to support research continuity: (1) Administrative Supplements to Promote Research Continuity and Retention of NIH Mentored Career Development Award Recipients and Scholars (NOT-OD-20-054). The goals of this program are to support the transition and retention of investigators from mentored career development to research independence, to minimize departures from the biomedical research workforce, and to help sustain the investigator's research during critical life events. (2) Administrative Supplement for Continuity of Biomedical and Behavioral Research Among First-Time Recipients of NIH Research Project Grant Awards (NOT-OD-20-055). The goal of this program is to enhance the retention of investigators facing critical life events who are transitioning to the first renewal of their independent research project grant award or to a second new NIH research project grant. Two NIDCR awards were made in FY 2020 to women who are early-career faculty, one for each of the new FY 2020 programs.

Overall, programs are aligned with Objective 4.3 ("Enhance and develop programs to recruit, support, retain, and advance women at all stages of their research careers, from early career to leadership positions") of the Trans-NIH Strategic Plan for Women's Health Research.

NIDCR Mentoring Network to Support a Diverse Dental, Oral and Craniofacial Research Workforce

In FY 2020, NIDCR launched a new mentoring network program funded in response to RFA-DE-19-007: NIDCR Mentoring Network to Support a Diverse Dental, Oral and Craniofacial Research Workforce. The major goal of the program is to establish a mentoring network led by qualified principal investigators who will develop and direct activities aimed at fostering the research career advancement of early-career investigators (postdoctoral scientists and junior faculty) from groups underrepresented in the biomedical research workforce. Participation in the program is intended to advance the participants/mentees research careers, foster transition to the next career stage, and develop

a high-quality, independently funded dental, oral, and craniofacial research program. To accomplish these goals, the program supports creative educational activities with a primary focus on mentoring activities, skills development, and a grant writing experience. NIDCR made one award in FY 2020 to the American Association for Dental Research to support the AADR Mentoring an Inclusive Network for a Diverse Workforce of the Future (AADR MIND the Future). The program engages a cohort of 10 mentees per year who are paired with participating research mentors from across the NIDCR oral, dental, and craniofacial research community. The initial 2020–2021 mentee cohort includes nine female and one male participant from groups underrepresented in biomedical research. Half of the participating mentors in 2020–2021 are female researchers.

This program is directly related to Objective 4.4 ("Promote and support policies, mentoring and networks, collaborations, and infrastructure to retain and advance women in their careers") of the Trans-NIH Strategic Plan for Women's Health Research.

V. Implementation of the NIH Policy on Sex as a Biological Variable (SABV)

NIDCR extramural and intramural investigators are complying with NIH's SABV policy. SABV is addressed by reviewers during peer review, confirming that it is addressed in the research strategy of each extramural grant application. Intramural researchers individually ensure that they are complying with the SABV policy.

VI. Inclusion of Women in Clinical Research

The NIDCR is promoting inclusion of women and girls in clinical research by supporting clinical trials focused on oral health interventions in pregnant women to prevent caries development in their children.

CenteringPregnancy Oral Health Promotion (CPOP) Clinical Trial (U01DE027340)

Although largely preventable, maternal oral health problems are very common during pregnancy, and dental care utilization among pregnant women is low. These challenges in maintaining oral health and accessing and utilizing dental care during pregnancy are exacerbated in underserved, health disparities populations. Oral health promotion during pregnancy is critical and has the potential to improve women's oral health through improved prevention and receipt of dental treatment and improve children's future oral health through caregiver education and timely anticipatory guidance. CenteringPregnancy® (CP) is an innovative prenatal group care model that provides evidence-based prenatal care to women in a group setting. CP addresses general health education topics during group sessions but has not included oral health education. The CenteringPregnancy Oral Health Promotion (CPOP) clinical trial is a multi-site, cluster randomized controlled clinical trial that is evaluating the efficacy of the CPOP intervention, which adds maternal and infant oral health modules into the current CP curriculum, in improving maternal and infant oral health outcomes. The CPOP intervention is recruiting and enrolling 384 underserved pregnant women–infant dyads in the California Bay Area.

Great Beginnings for Healthy Native Smiles: An Early Childhood Caries Prevention Project (U01DE028508)

Early childhood caries (ECC) is the most common chronic disease among children. American Indian children are four times more likely to have untreated dental decay than White children. Previous research suggests that to prevent caries in American Indian children, interventions should start at birth, before dental caries develop; utilize behavioral strategies, such as motivational interviewing; and complement behavioral strategies with fluoride varnish application. The Great Beginnings for Healthy Native Smiles clinical trial is recruiting and enrolling 350 expectant mother–infant dyads in two American Indian communities (Hopi and Crow Tribes) and evaluating utilization of a bundled intervention consisting

of prenatal oral health education, motivational interviewing, and fluoride varnish applications in infants to reduce ECC. The oral health intervention will be delivered by trusted community health representatives who incorporate local and contextually relevant strategies for ECC prevention.

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National Institute of Diabetes and Digestive and Kidney Diseases

I. Executive Summary

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) conducts and supports biomedical and behavioral research to address some of the most common, costly, and chronic diseases and conditions affecting the U.S. and global populations, including diabetes, obesity, endocrine diseases, metabolic diseases, digestive diseases, nutritional disorders, kidney diseases, urologic diseases, and hematologic diseases. Many of the diseases and conditions within its research mission affect women solely, disproportionately, or in unique ways. For example:

- Only women develop gestational diabetes mellitus (GDM).
- Women lose their comparative cardiovascular and renal disease risk protection when they develop chronic diabetes.
- Obesity unmasks and increases risk for myriad health problems of special interest for women, including cardiovascular disease and GDM.
- Women are more prone to autoimmune disorders, including autoimmune thyroid and liver diseases.
- Bowel and bladder control problems and urinary tract infections are much more prevalent in women.
- Women are most highly affected by chronic pain syndromes associated with the bladder (interstitial cystitis/bladder pain syndrome) and gut (irritable bowel syndrome).

Many of these conditions also intersect with racial–ethnic health disparities that the NIDDK is committed to addressing. The scope of NIDDK women's health research crosses the institute's three extramural research divisions—the Division of Diabetes, Endocrinology, and Metabolic Diseases; the Division of Digestive Diseases and Nutrition; and the Division of Kidney, Urologic, and Hematologic Diseases—and its Division of Intramural Research. Their efforts are enhanced by multiple NIDDK offices and working groups, including a new Women's Health Working Group, which advises the NIDDK Director. Through its extramural and intramural programs, as well as collaborations across the NIH (including ORWH), the NIDDK supports and pursues research and other activities important to the health of women and girls, understanding of sex/gender influences in health and disease, reduction of health disparities, and women's progress in biomedical careers. Provided here are examples of just some of the many NIDDK-supported scientific advances, efforts, and plans the institute pursued in FY 2019–2020.

II. Scientific Advances

Diabetes and Pregnancy—Improving the Health of Mothers and Children

Reports showing longer-term metabolic impacts of maternal hyperglycemia during pregnancy have spurred new research efforts to improve the health of women and their children. The development of diabetes associated with pregnancy (gestational diabetes, or GDM) increases not only near-term health and delivery risks but also future risk for diabetes in mothers and for obesity and diabetes in children. In 2008, the NICHD-led Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study reported that elevated maternal blood glucose levels below those commonly used in the United States to diagnose GDM are associated with increased risk of adverse outcomes for the mother and child; based on the findings, many organizations adopted an alternate definition of GDM. *(Current U.S. criteria for GDM remain essentially the same as pre-HAPO.)* The NIDDK-led HAPO Follow Up Study (FUS), co-supported by the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, asked whether there are also long-term metabolic impacts of elevated maternal blood glucose levels that do not meet the traditional criteria for GDM. In 2018, HAPO-FUS reported that pregnancies that retrospectively met the alternate GDM definition were

associated with greater likelihood of type 2 diabetes in mothers and obesity in children 10 to 14 years post-delivery (Lowe et al., 2018). The children were also more likely to have risk factors for type 2 diabetes (Lowe & Scholtens et al., 2019). When examining the spectrum of maternal blood glucose levels seen in HAPO, HAPO-FUS researchers found significant associations with childhood adiposity (Lowe & Lowe et al., 2019), as well as with other metabolic dysfunctions associated with obesity and type 2 diabetes (Scholtens et al., 2019). In FY 2019, NIDDK established a clinical research consortium, Glycemic Observation and Metabolic Outcomes in Mothers and Offspring (GO MOMS), to perform a comprehensive, longitudinal description of the changes in glucose over the course of pregnancy. Data obtained from this study could help lay the foundation for research evaluating new approaches to GDM screening, diagnosis, and intervention, with the ultimate goal of improving the health of women and their children.

This clinical research aligns with Objectives 1.3 ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes"), 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health"), and 3.1 ("Design and test approaches to promote the adoption, adaptation, and integration of evidence-based interventions in public health, clinical practice, and community settings") of the Trans-NIH Strategic Plan for Women's Health Research.

Behavioral Interventions in Pregnancy Improve Maternal Weight Retention 1 Year Postpartum

Numerous observational studies have linked pre-existing overweight/obesity and/or excessive gestational weight gain (GWG) during pregnancy to short-term and long-term adverse health consequences in both mothers and offspring. However, additional research is needed to identify effective interventions that will improve weight, glucose levels, and other pregnancy-related outcomes in mothers and determine whether these interventions affect obesity and metabolic abnormalities in the offspring. The Lifestyle Interventions For Expectant Moms (LIFE-Moms) consortium, composed of seven clinical centers and a research coordinating unit, has sought to identify effective behavioral and lifestyle interventions that will improve weight, glycemic control, and other pregnancy-related outcomes in obese and overweight pregnant women and determine whether these interventions reduce obesity and metabolic abnormalities in their children. As summarized in prior Biennial Reports, the LIFE-Moms consortium conducted seven different clinical trials at its sites and found that comprehensive lifestyle interventions targeting dietary intake, physical activity, and other behavioral factors reduced excess GWG in geographically and socio-demographically diverse populations of women with overweight and obesity. The purpose of the latest study was to evaluate the effects of the LIFE-Moms prenatal lifestyle interventions on maternal and child anthropometric outcomes through 12 months postpartum. The study showed that compared with standard care, lifestyle interventions initiated in pregnancy and focused on healthy eating increased physical activity, and other behavioral strategies resulted in significantly less weight retention in the mothers at 12 months; anthropometric outcomes in infants were similar between the groups. These encouraging, if mixed, results will be used to inform next steps for research and can also inform clinical care for pregnant women with overweight and obesity (Phelan et al., 2020). (LIFE-Moms has been co-sponsored by the NIDDK (lead), NHLBI, NICHD, NCCIH, ORWH, ODP, and OBSSR.)

This clinical and translational research aligns with Objectives 1.3 ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes"), 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health"), and 3.1 ("Design and test approaches to promote the adoption, adaptation, and integration of evidence-based interventions in public health, clinical practice, and community settings") of the Trans-NIH Strategic Plan for Women's Health Research.

Advancing Bladder Health Research

Research findings and activities from an NIDDK research consortium have set the stage for a new study that could lead to improved bladder health and overall health for women and girls. Lower urinary tract symptoms (LUTS), such as those associated with urinary incontinence, urinary tract infections, and interstitial cystitis/bladder pain syndrome, are common in women, resulting in significant but underrecognized effects on quality of life, as well as public health and financial burdens. Stigma around LUTS and commonly

held beliefs about their inevitability frequently result in unreported and therefore untreated symptoms. Many women adopt unhealthy coping behaviors, such as limiting physical activity, restricting fluid intake, or social isolation. NIDDK has invested in multiple major research efforts to tackle LUTS. The Prevention of Lower Urinary Tract Symptoms (PLUS) Research Consortium—established in 2015 in collaboration with the National Institute on Aging, the Office of Behavioral and Social Sciences Research, and the Office of Research on Women's Health and renewed in 2020—has been undertaking studies necessary to establish the scientific basis for future prevention-intervention research targeting LUTS in women and girls. In FY 2019–2020, PLUS continued its work to establish this new area of scientific inquiry—promotion of bladder health—with a transdisciplinary process (Schmitz et al., 2020; Smith et al., 2020). In planning for a foundational longitudinal cohort study, PLUS investigators identified the need for and created four novel survey measures; developed a phone app for assessing toileting behaviors and environment "in the moment"; conducted a large focus group study including English- and Spanish-speaking adult women and adolescent girls (Hebert-Beirne et al., 2019; Low et al., 2019; Williams et al., 2020; Camenga et al., 2019); and used existing literature and databases to inform understanding of bladder health, normal bladder function, and risk and protective factors (Lowder et al, 2019; Lewis et al., 2020; Siegel et al., 2020; Sutcliffe et al., 2020; Brady et al., 2020; Wyman et al., 2020; Sutcliffe et al., 2019). This work has been brought together in a longitudinal cohort study, Assessments Taken over Time: Relationships Influencing Bladder and Urinary Tract Experiences, which should launch enrollment of English- and Spanish-speaking women in the summer of 2021.

This clinical and translational research aligns with Objectives 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes"), 1.3 ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes"), 2.1 ("Expand and develop advanced and innovative approaches for study design, data collection, and analysis to optimize data quality and the ability to detect the influences of sex and gender on health and disease"), 2.2 ("Develop and adapt reliable and valid measures relevant to the health of women"), 3.1 ("Design and test approaches to promote the adoption, adaptation, and integration of evidence-based interventions in public health, clinical practice, and community settings"), and 3.2 ("Identify collaborative opportunities and leverage partnerships to disseminate research that improves the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

Health Disparities and Women's Health

Several NIDDK mission diseases and disorders disproportionately affect U.S. racial and ethnic minority populations. Moreover, the intersection of race and ethnicity with sex and gender identity affects disease outcomes and contributes to health disparities. NIDDK is committed to combating these health disparities and supporting approaches toward advancing health equity in its mission areas, and its Office of Minority Health Research Coordination helps to implement the institute's efforts. Several recent advances relevant to health disparities in women of different racial and ethnic groups include findings from a retrospective cohort study that assessed the likelihood of living-donor kidney transplantation (LDKT) within a single-center kidney transplant waitlist by race and sex after implementation of an incompatible program. The implementation of the program resulted in the United States' longest single-center kidney chain, and the likelihood of LDKT increased by 100% for minorities, with the greatest improvement observed among minority women, whose pool of compatible family donors has been reduced by pregnancy-induced HLA-sensitization (Mustian et al., 2019). Findings have also emerged from The Federal Women's Study, a trial designed to assess racial and ethnic variations in the risk of diabetes and heart disease among Federal employees living in the Washington, D.C., metro area. Racial differences were observed, and Black premenopausal and postmenopausal women had a greater insulin response, as well as lower insulin clearance and greater β-cell function (Chung et al., 2019). A third study sought to better understand the effect of diabetes care processes on risk for diabetes complications and poor maternal and infant health outcomes in young women of reproductive age with type 1 or type 2 diabetes. Through a retrospective cohort study, researchers found that non-Hispanic Black women and Hispanic women were more likely to have poor diabetes control compared with non-Hispanic White women (Marshall et al., 2020).

This clinical and translational research aligns with Objectives 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes"), 1.3 ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes"), 3.1 ("Design and test approaches to promote the adoption, adaptation, and integration of evidence-based interventions in public health, clinical practice, and community settings"), and 3.2 ("Identify collaborative opportunities and leverage partnerships to disseminate research that improves the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

Addressing Facets of SARS-CoV-2/COVID-19 Important for Women

COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has multiple effects on health, and researchers have been racing to learn more about viral transmission, disease prevention, and impact on the human body—including effects specific to women. To better understand possible causes for sex-specific effects, intramural NIDDK researchers investigated the mechanisms that regulate the expression of Angiotensin-converting enzyme 2 (ACE2), a receptor that binds SARS-CoV-2 and facilitates its entry into cells, in mammary tissue. The study found that increased expression of ACE2 in mammary tissue of mice during pregnancy and lactation is controlled through the hormone-activated JAK/STAT5 signaling pathway. These findings, available through preprint, suggest the possibility of vertical transmission of SARS-CoV-2 through breast milk and non-pulmonary tissue damage (Hennighausen & Lee, 2020). New NIDDK-supported studies of SARS-CoV-2/COVID-19 may also lead to improved outcomes or prevention measures for both women and men. Based on observations thus far, obesity and diabetes appear to be associated with greater COVID-19 severity, and infection damages multiple organ systems. Also, COVID-19 may unmask or contribute to new-onset diabetes. Health disparities associated with many conditions within NIDDK's mission may be contributing to disparities in COVID-19 outcomes for certain racial and ethnic groups. In FY 2020, the NIDDK encouraged mission-relevant research to mitigate the pandemic's impact. For example, the NIDDK awarded several administrative supplements to existing research grants for study of COVID-19.

One addressing COVID-19 and women's health (3R01DK115545-03S1) will collect detailed information about the impact of COVID-19 and social distancing requirements on adolescents' diabetes management and maternal stress and coping. The study has the potential to inform understanding of how COVID-19 and social distancing influences maternal distress and family diabetes management; study results may be used to promote the most adaptive coping and parenting strategies during times of uncertainty. The NIDDK also issued a solicitation for mechanistic studies of the interaction between SARS-CoV-2/COVID-19 and diseases and organ systems of interest (RFA-DK-20-021). These future studies may also have the potential to reveal sex/gender differences.

This basic and clinical research aligns with Objectives 1.1 ("Discover basic biological differences between females and males"), 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes"), and 3.1 ("Design and test approaches to promote the adoption, adaptation, and integration of evidence-based interventions in public health, clinical practice, and community settings") of the Trans-NIH Strategic Plan for Women's Health Research.

III. Promotion of Women's Health Research

Enhancing Sex Differences Research—SCORE

To leverage opportunities to support research on sex differences in mission areas, the NIDDK participated in the Office of Research on Women's Health (ORWH)–led Specialized Centers of Research Excellence (SCORE) on Sex Differences (RFA-OD-19-013). As a result, the NIDDK, with ORWH, is newly supporting a SCORE project, "Sex related differences in Brain Gut Microbiome Interactions in Irritable Bowel Syndrome" (1U54 DK123755-01). Already, the researchers have published findings on the impact of the menopausal transition on IBS symptoms (Lenhart et al., 2020).

This aligns with Objectives 1.1 ("Discover basic biological differences between females and males"), 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and

outcomes"), 1.3 ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes"), 1.4 ("Promote research that explores the influence of sex and gender on the connection between the mind and body, and its impact on health and disease"), 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health"), and 3.2 ("Identify collaborative opportunities and leverage partnerships to disseminate research that improves the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

Pregnancy and Maternal Conditions that Increase Risk of Morbidity and Mortality Workshop

This meeting was held virtually (May 19–20, 2020) and co-sponsored by the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development; the Office of Research on Women's Health; the National Heart, Lung, and Blood Institute; and the Office of Disease Prevention. The meeting was organized in response to increasing U.S. maternal mortality rates, with a goal that the workshop participants will develop a research agenda targeted at the clinical causes of maternal morbidity and mortality. The NIDDK was invited to organize a session on maternal conditions that increase risk of morbidity and mortality. The following are summaries of the two NIDDK-supported presentations and recommendations arising from this session:

- *Pre-existing Chronic Kidney Disease and Acute Kidney Injury on Maternal Pregnancy Complications:* The rate of acute kidney injury (AKI) related to obstetric conditions has increased in recent years in the United States. These increases could be because of increased detection, modern infertility techniques that facilitate pregnancies in women with comorbidities (e.g., hypertension, diabetes), advanced maternal age, and increased incidence of hypertensive disorders of pregnancy and preeclampsia. AKI and preeclampsia affect long-term renal health and increase the risk for chronic kidney disease, albuminuria, and end-stage renal disease. Future studies should focus on exploring novel biomarkers for early detection of AKI in pregnancy.
- *Gestational Diabetes: A Metabolic Stress Test and Harbinger of Future Metabolic Dysfunction:* The development of gestational diabetes mellitus (GDM) increases the risk for long-term complications, such as type 2 diabetes and other metabolic disorders. The risk for developing glucose metabolism disorders increases when GDM is untreated; however, treatment of GDM lowers this risk and improves adverse pregnancy outcomes, including low birth weight and preeclampsia. A multicenter observational study (GO MOMS) focused on capturing the profile of glycemia across pregnancy could result in the identification of new biomarkers, use of new technologies, and identification of health care disparities associated with GDM.

This aligns with Objectives 1.3 (Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes), 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health"), and 3.2 ("Identify collaborative opportunities and leverage partnerships to disseminate research that improves the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

Obesity and Women's Health Symposium

This meeting was organized by NIDDK as part of the NIH Obesity Research Task Force Seminar Series and was held virtually on September 10, 2020. The symposium featured the research of distinguished scientists studying the many ways in which obesity has an impact on the health of women. The symposium presentations covered four topics: **obesity and cardiovascular disease in women**; **whether periconception weight management in women with obesity is harmful or futile**; **obesity and breast cancer**; and **obesity and lower urinary tract symptoms in women. Link:** https://www.niddk.nih.gov/news/meetings-workshops/2020/obesity-womens-health-virtual-symposium

This aligns with Objectives 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes"), 1.3 ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes"), and 3.2 ("Identify collaborative opportunities and leverage partnerships to disseminate research that improves the

health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

Special Issue on Maternal Morbidity and Mortality (MMM) for the Journal of Women's Health

Throughout FY 2019–2020, the NIDDK collaborated with institutes across NIH and the Office of Research on Women's Health in the effort to advance the conversation and research on MMM. One activity that resulted from this collaboration will be a collection of 21 review articles that will be published in the *Journal of Women's Health* in FY 2021, addressing various aspects of this critical public health issue from multiple vantage points. The topic that NIDDK covered was dysglycemia in pregnancy and maternal/fetal outcomes. Maternal dysglycemia—including diabetes, impaired glucose tolerance, and impaired fasting glucose—affects 1 in 6 pregnancies worldwide and represents a significant health risk to the mother and the fetus. Maternal dysglycemia is an independent risk factor for perinatal mortality, major congenital anomalies, and miscarriages. Furthermore, it increases the longer-term risk of type 2 diabetes, metabolic syndrome, cardiovascular morbidity, malignancies, and ophthalmic, psychiatric, and renal diseases in the mother. The most commonly encountered form of maternal dysglycemia is gestational diabetes mellitus (GDM). Currently, international consensus does not exist for diagnostic criteria defining GDM at 24–28 weeks gestation, and potential diagnostic glucose thresholds earlier in gestation require further investigation. *(See Scientific Advances.)* Likewise, recommendations regarding the timing and modality (e.g., lifestyle or pharmacological) of treatment vary greatly. Because a precise diagnosis determines the appropriate treatment and outcome of the pregnancy, it is imperative that a better definition of maternal dysglycemia and its treatment be achieved. The article addresses some of the controversies related to diagnosing and managing maternal dysglycemia and discusses the impact of maternal dysglycemia on complications experienced by the mother and infant, both at birth and in later life (Silva et al., 2021).

This aligns with Objectives 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health") and 3.2 ("Identify collaborative opportunities and leverage partnerships to disseminate research that improves the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

Public Outreach and Awareness for Women and Girls—Health and Science

In FY 2019–2020, NIDDK continued to support and promote activities important to women's health through public outreach and awareness efforts. For example:

- NIDDK joined with other NIH Institutes and Centers to promote the *International Day of Women and Girls in Science* (#WomenInScience, #IDWGS) on social media. NIDDK marked the event with messages on Twitter (https://twitter.com/search?q=(%23WomenInScience)%20(from%3ANIDDkgov)&src=typed_query&f=live).
- NIDDK also continued to raise awareness about diseases and conditions that affect women—such as diabetes, heart disease, and weight management—through various channels, including social media, its Healthy Moments radio episodes, electronic newsletters, the Diabetes Discoveries & Practice blog and the Sisters Together: Move More, Eat Better community program.

This aligns with Objective 3.2 ("Identify collaborative opportunities and leverage partnerships to disseminate research that improves the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

IV. Advancement of Women in Biomedical Careers

STEMM Careers—Training, Career Development, and Retention

The NIDDK supports numerous individual and institutional award programs along the biomedical research pipeline, from high school and undergraduates to the tenured faculty and from mentoring to grant support, that align with its research mission. (See https://www.niddk.nih.gov/research-funding/training-career-development.) In FY 2020, the NIDDK also engaged its National Advisory Council regarding the impact of COVID-19 on researchers and strategies for mitigation; noting the disproportionate effects on women, minority investigators, and scientists early in

their careers, the institute is seeking additional ways to foster and support these researchers during this challenging period. The NIDDK is also part of two NIH efforts that, though not exclusive to women, address obstacles that disproportionately affect women when at critical junctures in science, technology, engineering, mathematics, and medicine (STEMM) careers: (1) *Notice of Special Interest (NOSI): Administrative Supplement for Continuity of Biomedical and Behavioral Research Among First-Time Recipients of NIH Research Project Grant Awards* (NOT-OD-20-055), whose overarching goal is to enhance the retention of investigators facing critical life events who are transitioning to the first renewal of their first independent research project grant award or to a second new NIH research project grant award. In particular, it recognizes and seeks to mitigate the impact of pregnancy, childbirth, and caregiving responsibilities as contributors to underemployment of women scientists and engineers and consequent changes in career trajectories. (2) *Notice of Special Interest: Administrative Supplements to Promote Research Continuity and Retention of NIH Mentored Career Development (K) Award Recipients and Scholars* (NOT-OD-20-054), whose overarching goal is to support the transition and retention of investigators from mentored career development to research independence and to minimize departures from biomedical research workforce at this critical juncture. Childbirth, adoption, and certain primary caregiving responsibilities are critical life events that would qualify for consideration under this program.

This is aligned with Objectives 4.3 ("Enhance and develop programs to recruit, support, retain, and advance women at all stages of their research careers, from early career to leadership positions") and 4.4 ("Promote and support policies, mentoring and networks, collaborations, and infrastructure to retain and advance women in their careers") of the Trans-NIH Strategic Plan for Women's Health Research.

STEMM Career Development Focused on Underrepresented Populations

Ongoing research training initiatives developed by the NIDDK Office of Minority Health Research Coordination focus on developing and training new and young investigators. Specifically, efforts and programs focus on individuals who are underrepresented in biomedical research, including students with disabilities, those from disadvantaged backgrounds, and those from certain racial and ethnic minorities in the United States; while not focused solely on girls and women, these initiatives—Short Term Research Experience for Underrepresented Persons (STEP UP) (high school); STEP UP (undergraduate); and Diversity Summer Research Training Program (DSRTP)—encourage entry into NIDDK-relevant STEMM areas by girls and women who might not otherwise have an opportunity to do so. In FY 2019, girls and women constituted the majority of participants in all three programs; however, in FY 2020, both DSRTP and STEP-UP high school were canceled or curtailed because of the COVID-19 pandemic. The undergraduate STEP-UP program quickly transitioned to a hybrid year-round research experience in which 70% of the participants were women.

This is aligned with Objectives 4.3 ("Enhance and develop programs to recruit, support, retain, and advance women at all stages of their research careers, from early career to leadership positions") and 4.4 ("Promote and support policies, mentoring and networks, collaborations, and infrastructure to retain and advance women in their careers") of the Trans-NIH Strategic Plan for Women's Health Research.

V. Implementation of the NIH Policy on Sex as a Biological Variable (SABV)

SABV is a central tenet and principle of the Trans-NIH Strategic Plan for Women's Health Research, and NIDDK current and planned activities aligned with the plan include SABV. Scientific review groups run by NIDDK are ensuring that SABV is addressed as appropriate. NIDDK program staff members are also educated on the importance of considering SABV as part of their normal programmatic oversight roles. In addition, the newly established NIDDK Women's Health Working Group has worked to identify strategies to galvanize the impact of the NIDDK-supported research and address critical research gaps. In concert with the NIDDK Director, one of the strategies that was identified was to develop language to be included in all NIDDK-initiated funding opportunity announcements to emphasize the institute's interest in receiving more research applications that address, among other issues,

the health of women and sex/gender differences—recognizing that such research runs the gamut from fundamental biological studies to social constructs of identity. This effort aligns with and further supports the NIH SABV policy (NOT-OD-15-103). A draft of the proposed language is being circulated for appropriate approvals prior to implementation.

VI. Inclusion of Women in Clinical Research

Inclusion of women is a guiding principle for the Trans-NIH Strategic Plan for Women's Health Research, and NIDDK research activities aligned with the plan cover inclusion of demographically diverse populations of women in clinical research. For example, the renewal of the PLUS Consortium in FY 2020 will enable the initiation of a longitudinal study of bladder health in girls and women that builds upon the work done in the first phase of PLUS; it is anticipated the information gained from this study will enable researchers to identify questions that can be pursued in clinical studies and trials aimed at improving and maintaining bladder health—and, by extension, overall health—in women and girls. Similarly, the newly funded GO MOMS clinical study (FY 2020) will enroll pregnant women to learn more about the development of dysglycemia across the course of pregnancy. In addition to these specific examples, the NIDDK continues its proper stewardship in this area through compliance with NIH inclusion policies. NIDDK considers appropriate inclusion in funding decisions, monitors appropriate inclusion in ongoing research, and develops aggregate reports for regular congressionally required reports and considers these aggregate data to help assess inclusion within its research portfolio at a more general/higher level. *(Links to information: (1) the Inclusion of Women and Minorities in Clinical Research page [https://report.nih.gov/research/inclusion-women-and-minorities-clinical-research], which includes a link to the latest triennial report, and (2) NIDDK page in the NIH RCDC Inclusion Statistics Report [https://report.nih.gov/RISR/#/home?ic=NIDDK].)*

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National Institute of Environmental Health Sciences

I. Executive Summary

The mission of the National Institute of Environmental Health Sciences (NIEHS) is to discover how the environment affects people in order to promote healthier lives. The NIEHS vision is to provide global leadership for innovative research that improves public health by preventing disease and disability. The mission and vision of NIEHS are guided by the 2018–2023 Strategic Plan: Advancing Environmental Health Sciences Improving Health, comprising three highly interdependent, interactive, and inclusive themes:

- Advancing Environmental Health Sciences (EHS)
- Promoting Translation – Data to Knowledge to Action
- Enhancing EHS Through Stewardship and Support

The 2018–2023 Strategic Plan fulfills the 21st Century Cures Act requirement:

- Theme One: Goal 2—to examine sex differences in response to exposures.
- Theme Two: Goal 4—to uncover the exposure burdens that combine with other social determinants of health, such as age, gender, education, race, and income, to create health disparities, as well as working to ensure environmental justice.
- Theme Three: Goal 2—a commitment to developing an EHS workforce that consists of a wide range of characteristics, including race, ethnicity, gender, socioeconomic status, geographic location, and disability.

Advancing EHS encompasses the study of all levels of biological organization—molecular, biochemical pathway, cellular, tissue, organ, system, model organism, individual, and population—at all stages across the lifespan, from preconception through old age. EHS uses a rich, diverse, and constantly evolving set of observational, experimental, computational, and clinical approaches to explore the impacts of varying levels of exposure and susceptibility to such exposure. EHS research is aimed at discovering and explaining how factors, including chemical, physical, synthetic, and infectious agents; social stressors; diet and medications; and our own microbiomes, among others, affect biological systems. The knowledge generated by EHS—inclusive of interactions between humans, animals, and our natural and built environments—provides a critical component of our understanding of women's health and environmentally mediated disease.

II. Scientific Advances

Racial and Ethnic Disparities in Sleep Among Pregnant and Non-Pregnant Women

Poor sleep among pregnant women has been increasingly linked to suboptimal maternal health and birth outcomes. NIEHS scientists have identified higher short sleep prevalence in pregnant Black women compared with pregnant White women. Pregnant women overall were more likely than non-pregnant women to report trouble staying asleep, and advanced maternal age was associated with an increased prevalence of trouble staying asleep. These findings underscore the need for more research to assess sleep disorders in women (Feinstein et al., 2020).

This relates to Objectives 1.3 ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes") and 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health") of the Trans-NIH Strategic Plan for Women's Health Research.

Prenatal Exposure to Chemicals in Personal Care Products Linked to Earlier Puberty in Girls

Girls exposed to chemicals commonly found in personal care products before birth may hit puberty earlier, according to an NIEHS-funded study. The research found

that mothers who had higher levels of diethyl phthalate, a fragrance and cosmetics stabilizer, and triclosan, an antimicrobial agent, in their bodies during pregnancy had daughters who experienced puberty at younger ages. The results came from data collected as part of the Center for the Health Assessment of Mothers and Children of Salinas study, which followed 338 children from before birth to adolescence. Girls who had higher prenatal urinary concentrations of triclosan and one of its degradation products were associated with an earlier first occurrence of menstruation. Also, higher prenatal concentrations of the main metabolite of diethyl phthalate were associated with earlier onset of pubic hair development. The same trends were not observed in boys (Harley et al., 2019).

This relates to Objective 1.3 ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes") of the Trans-NIH Strategic Plan for Women's Health Research.

Racial Disparities in Chemical Exposures for U.S. Women

NIEHS grantees identified striking differences in markers of chemical exposure for women of different races and ethnicities, independent of other demographic factors. According to the authors, the findings shed light on the environmental factors that may drive racial disparities in disease outcomes. The researchers conducted a comprehensive analysis of chemical exposures by race and ethnicity in 38,080 U.S. women. They studied biomarker data for 143 chemicals collected by the National Health and Nutrition Examination Survey (NHANES) between 1999 and 2014. The scientists adjusted for age, socioeconomic status, smoking habits, and the cycle of NHANES data collection. Compared with non-Hispanic White women, they observed higher overall biomarker levels of several chemicals among non-Hispanic Black, Mexican American, other Hispanic, and other race or multiracial women. Specifically, these women had higher levels of pesticides and their metabolites, compounds associated with personal care and consumer products, such as parabens and monoethyl phthalate, and several metals, including mercury and arsenic. Average differences in chemical biomarker concentrations between racial and ethnic groups exceeded 400% for paraben metabolite comparisons between young non-Hispanic Black and non-Hispanic White women. Metals, pesticides, and chemicals in consumer products showed the highest disparities of the chemicals studied. Some, such as the metabolites of pesticides that contain dichlorophenol, persisted across age groups. According to the authors, the findings could help prioritize chemicals when designing studies and help guide public health interventions to reduce environmental and health disparities across populations (Nguyen et al., 2020).

This relates to Objective 1.3 ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes") of the Trans-NIH Strategic Plan for Women's Health Research.

NIEHS and NTP Report Life Experiences May Alter DNA Methylation

Scientists at NIEHS and Division of the National Toxicology Program (NTP), along with their collaborators, reported that DNA sequence may determine where methylation events occur and that life events such as pregnancy could alter DNA methylation patterns. The researchers used inbred mice to examine methylation, the addition of methyl groups onto DNA. Researchers intercrossed two inbred mouse strains and measured DNA methylation patterns in the livers of parents and offspring. They found that DNA methylation patterns were closely linked to the genetic makeup of the animal. These patterns were unchanged when passed to male and female offspring. However, in female animals that had experienced pregnancy, hundreds of DNA sites showed decreased methylation compared with virgin females. These findings suggest that genetics influence DNA methylation patterns and that major life events may leave a distinct methylation signature (Grimm et al., 2019).

This relates to Objective 1.3 ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes") of the Trans-NIH Strategic Plan for Women's Health Research.

Combined Phthalate and Stress Exposure May Lead to Preterm Birth

Phthalate exposure combined with high stress during pregnancy is associated with preterm birth, according to a team of researchers led by NIEHS scientists.

Phthalates, compounds that are present in personal care products and plastics, have been commonly found in pregnant women. Although exposures to phthalates or stress have been independently associated with increased risk for preterm birth, their joint impact was unknown before this study. Using data from 783 pregnant women participating in The Infant Development and the Environment Study (TIDES), researchers obtained questionnaire information about stressful events in each trimester and measured urinary phthalate metabolites from up to three trimesters. Team members found an increased risk of preterm birth associated with phthalate metabolites in urine during the third trimester but not the first trimester. Furthermore, adding the variable of stress to third-trimester data showed that the association between phthalate metabolites in urine and preterm birth risk was only significant for women who reported at least one stressful life event during pregnancy versus those who did not. This study paves the way for understanding how combined exposure to environmental and psychosocial factors affects pregnancy (Ferguson et al., 2019).

This relates to Objective 1.3 ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes") of the Trans-NIH Strategic Plan for Women's Health Research.

III. Promotion of Women's Health Research

Pregnancy as a Vulnerable Time Period for Women's Health

NIEHS developed a funding opportunity RFA-ES-20-003, *Pregnancy as a Vulnerable Time Period for Women's Health (R01 Clinical Trial Not Allowed)* in partnership with the Office of Research on Women's Health. The goal of the initiative is to accelerate multidisciplinary research projects studying the effects of environmental chemicals on maternal physiology and endocrine and metabolic functions during and shortly after pregnancy, as well as potential long-term maternal health effects caused by environmental exposures. NIEHS funded seven R01 research projects in FY 2020 for approximately $3 million of total costs from this initiative.

This RFA aligns with Goal 1 ("Advance rigorous research that is relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

Pediatric and Reproductive Environmental Health Scholars (PREHS) Program

NIEHS developed a funding opportunity RFA-ES-20-007, the Pediatric and Reproductive Environmental Health Scholars (PREHS) program, to provide new health care professionals with state-of-the-art environmental health training that blends academic research and practice-based applications in real-world settings. The goal of the PREHS program is to create a strong network of health care professionals who possess the skills and knowledge to address the complexities of pediatric and reproductive environmental health. The PREHS program will ensure scholars acquire advanced content in pediatric and reproductive environmental health and gain an understanding of the many interactions—biological, psychological, social, and cultural—that occur between children, pregnant women, and new mothers and their environment. With this newly acquired knowledge, scholars will be better equipped to assess and manage pediatric health conditions related to exposures in the child's environment. The PREHS program will bring together environmental health science research expertise at academic institutions with clinical and translational expertise at Pediatric Environmental Health Specialty Units (PEHSUs) to provide pediatric health care providers, obstetricians/gynecologists, nurses, and other interested health care professionals (PREHS Scholars) with research experiences that bridge clinical practice in environmental health, community-level engagement, and teaching. These K12 grant awards will generate well-qualified pediatric and reproductive environmental health leaders.

This RFA aligns with Goals 1 ("Advance rigorous research that is relevant to the health of women"), 3 ("Enhance dissemination and implementation of evidence to improve the health of women"), and 4 ("Promote training and careers to develop a well-trained, diverse, and robust workforce to advance science for the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

Women's Health Awareness Women's Wellness Conference: Transforming Communities by Enhancing Women's Health

NIEHS sponsored the 5th Women's Health Awareness Women's Wellness Conference on April 6, 2019, at North Carolina Central University in Durham, North Carolina. Women's Health Awareness is a community engagement conference that is free for the public. Since 2015, WHA has served more than 3,000 women who have participated in this community-level intervention. Women come from over 30 North Carolina counties, which include both urban and rural communities. In 2019, over 1,200 participants attended, with 81% of the participants being African American and 8% Hispanic/Latino. The goal of this conference is to inform and empower women to take responsibility for their health, understand their health options, and identify services, thereby increasing equal access to services, resources, and products that best help them prevent and reduce poor health. The conference's primary focus is on disease prevention, control, and management in Understudied, Underrepresented, and Underreported (U3) populations of women by providing health education, environmental health awareness, health resources, and free health screenings to develop healthier families and environmentally safer homes and communities.

Because of the emerging COVID-19 pandemic, the 6th annual Women's Health Awareness Conference was canceled in April 2020. During the pandemic, the WHA program has continued to stay engaged with its population through disseminating public health messaging that alerts the community of urgent public health and environmental concerns, scientific advances, and what people need to do to protect themselves from this deadly virus. Since April 2020, 10 health messages have been developed and disseminated to the community. The health messages are currently being narrated via a local television affiliate WTVD news by a popular female correspondent. Narration allows the public to have access to this important information. Also, the program has developed the Women's Health Awareness Newsletter to convey trending health topics with important health implications—e.g., the fall 2020 edition hot health topic: "The life you save could be your own. Don't delay medical care during COVID-19."

Primary care physicians have noticed an increase in heart attacks, strokes, and diabetes complications. On January 1, 2020, WHA released its inaugural podcast series to the community. This first podcast brings awareness to radon exposure and providing access to free radon test kits. Additionally, WHA is currently planning for a virtual commemorative Women's Health Awareness conference that will take place on Saturday, April 17, 2021.

This public outreach program aligns with Goals 1 ("Advance rigorous research that is relevant to the health of women"), 2 ("Develop methods and leveraging data sources to consider sex and gender influences that enhance research for the health of women"), 3 ("Enhance dissemination and implementation of evidence to improve the health of women"), and 5 ("Improve evaluation of research that is relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

The Basic Science of Uterine Fibroids Meeting

Scientists from multiple basic disciplines and an international group of physician-scientists from the field of obstetrics and gynecology presented recent studies and discussed new and evolving theories of uterine fibroid etiology, growth, and development at The Basic Science of Uterine Fibroids meeting, sponsored by the Campion Fund and NIEHS. The purpose was to share up-to-date knowledge, to stimulate new concepts regarding the basic molecular biology and pathophysiology of uterine fibroids, and to promote future collaborations. The meeting was held at NIEHS in North Carolina on February 28, 2020. Speakers reviewed recent advances in cellular and molecular processes that contribute to fibroid growth and new opportunities for treatment. At the conclusion of the conference, attendees identified important new directions for future research.

This RFA aligns with Goals 1 ("Advance rigorous research that is relevant to the health of women") and 3 ("Enhance dissemination and implementation of evidence to improve the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

IV. Advancement of Women in Biomedical Careers

NIEHS Scholars Connect Program

The NIEHS Scholars Connect Program (NSCP) is designed to provide a unique opportunity to highly motivated STEMM-focused undergraduate students to solidly connect with NIEHS and receive frontier-level training in biomedical research. Students in NSCP have an opportunity for hands-on mentored research experiences, as well as professional and personal development. The program is committed to encouraging students to pursue careers in scientific investigation, both basic and clinical. NSCP also is committed to increasing diversity in environmental health science, and applications from underrepresented populations in STEMM are strongly encouraged. In FY 2019–2020, across two cohorts of the program (as the program begins in June and ends in April of the following year), seven African American women, seven White women, one Latina woman, and three Asian women participated.

Undergraduate Research Education Program (UP) to Enhance Diversity in the Environmental Health Sciences (RFA-ES-19-010): EMPOWER Summer Research Program

Fostering diversity, including efforts to address underrepresentation in the scientific research workforce, is a key component of the NIH strategy to identify, develop, support and maintain the quality of our scientific human capital. Enhancing diversity in the extramural scientific workforce is critical to the success of the NIH mission and is consistent with the mandates of the 21st Century Cures Act.

The NIH Research Education Program supports research education activities in the mission areas of the NIH. The overarching goal of this R25 program is to support educational activities that encourage individuals from diverse backgrounds, including those from groups underrepresented in the biomedical and behavioral sciences, to pursue further studies or careers in research. To accomplish the stated overarching goal, this funding opportunity will support creative educational activities, with a primary focus on research experiences for undergraduate students, to provide hands-on exposure to research, to reinforce their intent to graduate with a science degree, and/or to prepare them for graduate school admissions and/or careers in research.

NIEHS funds the Engaging Multi-Disciplinary Professional Opportunities for Women in Environmental Research (EMPOWER) summer research experience program, which includes 10 research scholars who are African American or Hispanic girls or women in grades 10–12 attending four urban Atlanta high schools and four teaching fellows who are teachers that provide science instruction in these schools. This intensive, 8-week summer fellowship provides hands-on research experience focused on in-depth understanding of how exposures to toxic environmental insults in the urban environment impact health and alter biologic processes. The research experience will consist of three interlocking research projects, incorporating laboratory and field experience and led by faculty with expertise in a range of urban environmental exposures and their health effects. These projects are all united by the overarching theme of collecting and interpreting data on urban environmental exposures and their related health effects. The fellowship experience will also encompass training in scientific rigor, support for scientific development, engagement with women-of-color role models in the sciences, engagement with current college students, and learning about pathways to college admission and college success. (LINK)

V. Implementation of the NIH Policy on Sex as a Biological Variable (SABV)

NIEHS follows a protocol in which grants are evaluated for consideration of SABV. SABV is discussed in the grant review process, and feedback is solicited as to whether it is acceptable. If a grant NIEHS is considering is deemed unacceptable, NIEHS discusses that with the principal investigator prior to award.

SABV is encouraged through the publication of funding opportunity announcements that include review criteria such as:

- Have the investigators presented adequate plans to address relevant biological variables, such as sex, for studies in vertebrate animals or human subjects?
- If the project involves human subjects and/or NIH-defined clinical research, are the plans to address the protection of human subjects from research risks and address inclusion (or exclusion) of individuals on the basis of sex/gender, race, and ethnicity, as well as the inclusion or exclusion of individuals of all ages (including children and older adults), justified in terms of the scientific goals and research strategy proposed?

RFA-ES-20-008

NIEHS is committed to emphasizing the importance of using both male and female vertebrate model organisms, as well as the inclusion of women in human studies, in support of SABV.

VI. Inclusion of Women in Clinical Research

NIEHS Clinical Research Unit

NIEHS supports very few clinical trials. However, NIEHS and NTP conduct a great deal of animal research, almost all of which is analyzed by sex. The NIEHS Clinical Research Unit currently actively recruits men and women for 19 clinical studies. Several studies have a specific focus on women's health. Researchers are studying the health effects of an herbal supplement taken by some women to treat hot flashes, cramps, or other symptoms in the Black Cohosh Study. To examine whether overweight girls are truly entering puberty before girls whose weight is normal, researchers have recruited girls between the ages of 8 and 14 to participate in the Body Weight & Puberty Study. Efforts to determine the physiologic and pathophysiologic underpinnings of irregular menstrual cycles among adolescents in the early postmenarchal period are being made in the A Girl's First Period – Why Is It So Unpredictable? Study, which enrolls girls ages 8–14.

The Calorie Restriction, Environment, and Fitness: Reproductive Effects Evaluation Study recruited women participants to understand how nutrition and exercise affect women's reproductive cycles. Additional components of this study are determining the effect of the menstrual cycle and caloric restriction on sleep, the metabolic hormone responses to caloric restriction, and the effect of caloric restriction on thyroid function. In complementary studies in patients with hypothalamic amenorrhea, the investigators are exploring the question of whether genetic susceptibility plays a role in the variable response of women to physiologic stressors in the development of amenorrhea. The Ovarian Health Study recruited women participants for developing assays to measure anti-müllerian hormone in the urine as a promising biomarker for ovarian health. The NIEHS-EPA Pilot Study of Exposure to Chemicals in Consumer Products actively recruited healthy stay-at-home women to improve the way data are gathered for studies that examine chemical exposure from consumer products.

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National Institute of General Medical Sciences

I. Executive Summary

The National Institute of General Medical Sciences (NIGMS) supports basic research that increases understanding of biological processes and lays the foundation for advances in disease diagnosis, treatment, and prevention. The institute also supports research in certain clinical areas, primarily those that affect multiple organ systems. In addition, NIGMS supports research training, career development, diversity, and capacity-building activities through a variety of programs at the undergraduate, graduate, postdoctoral, and faculty levels. The focus of these programs is to train the next generation of scientists, enhance the diversity of the scientific workforce, and develop research capacities throughout the country.

In FY 2019–2020, NIGMS supported research in a broad range of areas related to women's health, including topics of specific interest to the NIH Office of Research on Women's Health (ORWH). This support includes projects that increase our understanding of basic biological processes that may lead to improved diagnosis and treatment of conditions specific to (or that disproportionately affect) women. Key areas of research involved (and continue to involve) maternal health during and after pregnancy, as well as pregnancy-related complications such as preterm birth. NIGMS also supported projects aimed at improving women's STEMM education and training and those aimed at reducing the disparities in career advancement and leadership for women in academic medicine. Finally, NIGMS has sought to promote women's health research in underrepresented populations and in rural areas, where women typically have less access to robust health care.

NIGMS' projects align with several goals and objectives in the Trans-NIH Strategic Plan for Women's Health Research. Several NIGMS-funded projects, for instance, align to Goal 1, including a study on the relationship of the vaginal microbiome and preterm birth. Similarly, several NIGMS-funded projects align with Goal 3, including developing a culturally relevant smoking cessation program for American Indian women. Other projects align with Goals 2 and 4, as described below.

II. Scientific Advances

Quantitative Metagenomics and the Vaginal Microbiome of Preterm Birth (R35GM133745)

This project is focused on developing methods of quantitative analyses of genetic material (i.e., metagenomics) to better understand the vaginal microbiome and the role it can play as a biomarker or influence in diseases such as preterm birth. Through microbiome genetic sequencing experiments, this NIGMS-funded project has developed methods to accurately evaluate and categorize naturally occurring microbiomes. Progress has also been made to consistently determine the relationship of the vaginal microbiome to preterm birth using different metagenomic sequencing methodologies. The project's current focus is on evaluating different factors that could influence the consistency between study results, including cohort characteristics, the definition of the preterm birth phenotype, and technical differences in microbiome sequencing methodology (Berman et al., 2020).

This is a basic/translational research project and relates to Objective 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health") of the Trans-NIH Strategic Plan for Women's Health Research.

Center for Biomedical Research Excellence (COBRE) for Reproductive Health (P20GM121298)

NIGMS-funded researchers at the COBRE for Reproductive Health (at the Women and Infants' Hospital, Rhode Island) have worked to develop an infrastructure that supports women's reproductive health. This group uses computational approaches such

as preclinical and human models to understand the mechanisms and identify the biochemical pathways responsible for preeclampsia (PE), gestational diabetes, and other pregnancy-related complications. These types of complications arise from the dysregulation of protein signaling networks. Researchers at the center have made correlations to other protein-based disorders, such as Alzheimer's disease (AD), leading to the creation of a noninvasive and sensitive blood test for the detection of protein aggregates in serum. This is the first step in the development of predictive assays for the diagnosis of PE, AD, and potentially other ailments caused by protein dysregulation. This work has been submitted to *Proceedings of the National Academy of Sciences* for publication.

This is a basic research project and relates to Objective 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health") of the Trans-NIH Strategic Plan for Women's Health Research.

Cigarette Smoking among American Indian Women Experiencing Intimate Partner Violence (S06GM123544)

Despite the high levels of intimate partner violence (IPV) and smoking experienced by American Indian (AI) women, there have been no smoking cessation interventions designed for this population. In this study, NIGMS-funded researchers engaged qualitative research methods to inform the development of a culturally relevant and trauma-informed smoking cessation intervention for AI women experiencing IPV. Results from this study outline the AI cultural values, teachings, and traditional medicine fundamental to developing a culturally centered, trauma-informed smoking cessation intervention. Women and service providers identified cultural and traditional practices promotive of cessation and healing, including smudging, sweats, and the power of intergenerational storytelling to overcome trauma. Mentorship and social support among women were believed to support behavior change. In conclusion, smoking cessation interventions for AI women experiencing IPV must recognize the multilayered mechanisms of violence and trauma specific to the indigenous experience. In addition, AI values, traditional teachings, and knowledge are vital intervention components to foster healing and smoking cessation among AI women experiencing IPV. Data collected from the qualitative analysis informed a newly developed smoking cessation curriculum, "Healing Within: Smoking Cessation for American Indian Women." The results were presented at the American Public Health Association's 2020 Virtual Annual Meeting and Expo.

This is a clinical research project and relates to Objective 3.1 ("Design and test approaches to promote the adoption, adaptation, and integration of evidence-based interventions in public health, clinical practice, and community settings") of the Trans-NIH Strategic Plan for Women's Health Research.

III. Promotion of Women's Health Research

Addressing Sex as a Biological Variable in Preclinical Pharmacology and Neuroscience Research: Accounting for Neglected Factors and Applying Practical Solutions to Enhance Rigor and Reproducibility (R25GM133017)

As part of NIH's initiative to enhance rigor and reproducibility in research, NIGMS, along with nine other NIH institutes and centers, issued a funding opportunity announcement (FOA) to develop, pilot, and disseminate training modules to enhance data reproducibility. This FOA was reissued in 2018 (RFA-GM-18-002). Several of the awards address the issue of sex as a biological variable, including R25GM133017, a project to develop a training module to educate the preclinical pharmacology and neuroscience research community about this issue. The material will provide preclinical researchers with the practical knowledge and guidance they need to conduct rigorous and reproducible research that is applicable to both sexes. This award was issued in 2019, and the project will end in 2022.

This relates to Objective 4.1 ("Enhance knowledge of sex and gender influences on health and disease among all scientists, clinicians, and other health professionals to accelerate the translation of that knowledge into practice") of the Trans-NIH Strategic Plan for Women's Health Research.

Research on Women's Health in IDeA States

(Notice of Special Interest [NOSI]: Administrative Supplements for Research on Women's Health in the IDeA States, NOT-GM-20-017)

NIGMS supports research related to the specific health needs of unique populations through several programs, including the Institutional Development Award (IDeA) program. Residents in IDeA States, especially those living in rural areas, often have less access to health care and therefore tend to suffer from poorer health outcomes. Several IDeA States, for instance, are among States with the highest maternal and infant mortality rates. To address this critical issue, NIGMS and the NIH Office of Research on Women's Health, in conjunction with several other NIH institutes, are providing administrative supplements to IDeA grants to increase research directed toward women's health and health disparities, with a special interest in maternal and infant morbidity and mortality. In so doing, NIGMS seeks to expand the capacity of IDeA States to conduct research that addresses women's health.

This relates to Goal 1 ("Advance rigorous research that is relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

Native American Research Centers for Health: White Mountain Apache Tribe/Johns Hopkins University (S06GM123547)

The goal of this NIGMS-funded project is to test the feasibility of implementing a novel mother–daughter intervention to enhance cultural protective factors (identified through previous research) and to reduce risk for substance use and risky sex among American Indian (AI) girls as they transition through puberty. NIGMS-funded investigators aim to conduct a pilot evaluation of the intervention for impacts on girls' substance use initiation and associated sexual behaviors common during this developmental stage and relevant impacts among their mothers or other participating female caregivers. This research is being conducted by long-standing tribal–academic research partners: the White Mountain Apache (Apache) Tribe and Johns Hopkins Center for American Indian Health. The investigator team began recruitment and consenting of participants in June 2019 to determine the feasibility and acceptability of the mother–daughter intervention and evaluation measures and structure. However, because of the COVID-19 pandemic, there has been a pause in all study activities, per Johns Hopkins research guidance. Given the sensitive nature of the evaluation, the Apache team determined it was not appropriate to conduct evaluations via phone. Investigators intend to complete 6-month assessments as soon as COVID-19 restrictions on in-person evaluation data collection are lifted. The project was initiated in the past 2 years.

This relates to Objective 3.1 ("Design and test approaches to promote the adoption, adaptation, and integration of evidence-based interventions in public health, clinical practice, and community settings") of the Trans-NIH Strategic Plan for Women's Health Research.

IV. Advancement of Women in Biomedical Careers

Maximizing Opportunities for Scientific and Academic Independent Careers (MOSAIC)

The MOSAIC program is part of NIGMS' efforts to enhance diversity within the academic biomedical research workforce and is designed to facilitate the transition of promising postdoctoral researchers from diverse backgrounds (e.g., individuals from groups historically underrepresented in the biomedical research workforce, including women) into independent faculty careers in research-intensive institutions. The program has two components: an institutionally focused research education cooperative agreement (UE5) and an individual postdoctoral career transition award (K99/R00) to enhance diversity. The objective of the MOSAIC Postdoctoral Career Transition Award to Promote Diversity (K99/R00) is to enhance workforce diversity by facilitating a timely transition of promising postdoctoral researchers from diverse backgrounds from their mentored postdoctoral research positions to independent tenure-track or equivalent faculty positions at research-intensive institutions. The first UE5 awards were issued in FY 2020, and the first MOSAIC K99/R00 awards are set to be issued in FY 2021.

This program relates to Objectives 4.2 (“Develop the next generation of researchers to advance science on the health of women”), 4.3 (“Enhance and develop programs to recruit, support, retain, and advance women at all stages of their research careers, from early career to leadership positions”), and 4.4 (“Promote and support policies, mentoring and networks, collaborations, and infrastructure to retain and advance women in their careers”) of the Trans-NIH Strategic Plan for Women’s Health Research.

Peer Mentoring to Overcome Obstacles for Midcareer Women Clinician-Scientists in Academic Medicine (R01GM139842-01)

NIGMS recognizes that there is a need for more hypothesis-driven research to test biomedical training, mentoring, and networking interventions for efficacy and replicability across career stages and at a range of institution types. The purpose of the Research on Interventions program is to support research that will enhance the evidence base for effective, high-impact, scalable interventions and to improve our understanding of the factors contributing to success, including the social and behavioral factors involved in the advancement of individuals pursuing independent academic biomedical research careers. In 2020, NIGMS funded an ongoing research project that centers on reducing the disparities in career advancement and leadership for women in academic medicine. This research addresses barriers faced by mid-career women scientists, including the intersection of race and LGBTQ+ status.

This project relates to Objective 4.4 (“Promote and support policies, mentoring and networks, collaborations, and infrastructure to retain and advance women in their careers”) of the Trans-NIH Strategic Plan for Women’s Health Research.

V. Implementation of the NIH Policy on Sex as a Biological Variable (SABV)

Pediatric Persistent Post-Surgical Pain: From Animals to Application (K23GM123372-04)

This NIGMS-funded project incorporates sex as a biological variable in research design, with the goal being to develop an animal model exploring how gene–environmental interactions, age, and biological sex contribute to presurgical and postsurgical

pain thresholds. This would serve as a first step to functionally assaying genetic mechanisms in the gene association arm of proposed human studies. One of the aims of this project is to explore whether animal model data are relevant to human surgical models and explore whether gene–environmental interactions and female sex can reliably predict persistent postsurgical pain. One hypothesis is that a history of stress and female sex will exacerbate postsurgical pain in an observational cohort study. Another hypothesis is that the relative risk profile of known pain genes may substantially vary in altered environments. A history of stress and female sex may exacerbate the role of the gene GCH1 in chronic pain etiology. The data collection from these studies is ongoing.

This project relates to Objective 2.1 ("Expand and develop advanced and innovative approaches for study design, data collection, and analysis to optimize data quality and the ability to detect the influences of sex and gender on health and disease") of the Trans-NIH Strategic Plan for Women's Health Research.

VI. Inclusion of Women in Clinical Research

Mississippi Center of Excellence in Perinatal Research (P20GM121334)

NIGMS-funded researchers at the Mississippi Center of Excellence in Perinatal Research are studying multiple aspects of perinatal research, ranging from the metabolic effectors responsible for the manifestation of polycystic ovary syndrome (PCOS) to prenatal screening for congenital heart disease. In the area of PCOS, a center researcher previously determined that hyperandrogenemia, a hallmark of this disorder, also increases the risk of developing postmenopausal cardiometabolic sequelae. The researchers published a manuscript detailing that "Lira" a peptide-1 receptor agonist, can mitigate cardiometabolic risk factors (Fernandez et al., 2019). This information led to the mechanistic conclusion that androgens play an important role in mediating increases in blood pressure in postmenopausal women with PCOS. Most recently, the principal investigator of this center was awarded an administrative supplement to study the complications that arise in the aftermath of a hypertensive pregnancy. The investigators designed an approach that tracks the blood pressure of women treated at the center by telemetry with the goal of making improvements in maternal morbidity related to postpartum preeclampsia.

This is a clinical research study that relates to Objective 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health") of the Trans-NIH Strategic Plan for Women's Health Research.

Pathways to Teen Rapid Repeat Pregnancy and Adverse Birth Outcomes (P20GM109097)

NIGMS-funded researchers are studying the biobehavioral pathways affecting the incidence and timing of rapid repeat pregnancy (RRP) and its adverse birth outcomes. Their work focuses on maternal adverse childhood experiences (ACEs; e.g., emotional, physical, or sexual abuse; exposure to domestic violence; substance abusing, mentally ill, or incarcerated household member; or absent parent) as a trigger launching a trajectory for RRP and heightened risk for adverse birth outcomes. Specifically, this study seeks to (1) delineate variation in the incidence and timing of RRP by maternal ACEs and determine whether this relationship is mediated by reproductive attitudes and behaviors and (2) determine behavioral and physiological pathways leading to disparities (e.g., age, race and ethnicity, and socioeconomic status) in adverse birth outcomes (e.g., perinatal loss, pregnancy and birth complications, preterm birth, and low birth weight) following RRP. This clinic-based longitudinal, multi-ethnic cohort study uses a multimethod (e.g., survey, biomarker, bioinformatics) strategy to include mothers following the birth of their first or second child. Recruitment of women into the study continued at the two participating perinatal clinics: University of Oklahoma Health Science Center and Oklahoma State University Center for Health Sciences.

Preliminary data have shown that maternal ACEs are associated with greater ambivalence about pregnancy and greater likelihood of unintended pregnancy. Prenatal attachment, previously linked to healthy behaviors during pregnancy and early mother–infant bonding, is also reduced by maternal ACEs (Shreffler et al., 2019). These preliminary findings provide initial evidence that reducing the proportion of unintended pregnancies and/or increasing prenatal attachment

when unintended pregnancies occur will reduce the risk of adverse birth outcomes. Further, health care providers who assess patients' ACE scores can target women with high ACE scores before they become pregnant and intervene, for example, by offering long-acting reversible contraception.

This is a clinical research study that relates to Objectives 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health") and 2.2 ("Develop and adapt reliable and valid measures relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

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National Institute of Mental Health

I. Executive Summary

The National Institute of Mental Health (NIMH) is the lead Federal agency for research on mental illnesses. The mission of NIMH is to transform the understanding and treatment of mental illnesses through basic and clinical research, paving the way for prevention, recovery, and cure. To carry out this mission, NIMH conducts and supports biomedical and behavioral research, health services research, research training, and health information dissemination with respect to the causes, diagnosis, treatment, management, and prevention of mental illnesses.

In accordance with the 21st Century Cures Act, NIMH staff members work closely with the Office of Research on Women's Health (ORWH) and other NIH Institutes, Centers, and Offices (ICOs) to ensure activities take into account the health needs of minorities and women and are focused on reducing health disparities. NIMH fosters interdisciplinary research to improve diagnosis, treatment, and prevention of mental disorders in women. NIMH prioritizes research in mental health disparities, global mental health, and training opportunities for women in mental health research. These efforts lay the groundwork for interventions to meet the needs of women from diverse socioeconomic, racial, ethnic, and geographic backgrounds in a variety of treatment settings. In addition, NIMH funds research aimed at increasing scientific understanding of sex and gender differences in mental illnesses that either affect women exclusively (e.g., postpartum depression) or predominantly (e.g., eating disorders). Differences in the detection, diagnosis, and treatment of mental illnesses in females compared with males vary from childhood to adulthood. Understanding sex differences in the neurobiological mechanisms and other health determinants underlying mental illnesses, including those in which rates do not differ for males and females, is critical for identifying key targets for intervention.

This report, spanning fiscal years 2019 and 2020, highlights published findings from NIMH-funded research on sex and gender differences and women's mental health; webinars and initiatives to promote and disseminate research on women's mental health; and efforts to advance women in biomedical careers.

II. Scientific Advances

First FDA-Approved Drug for Postpartum Depression: According to the Centers for Disease Control and Prevention (CDC), approximately 1 in 8 women in the United States experience symptoms of postpartum depression, a depressive episode occurring in the period following childbirth (Bauman et al., 2020). In 2019, the Food and Drug Administration (FDA) approved brexanolone, the first drug specifically designed to treat postpartum depression. Brexanolone is an analog of the endogenous human steroid hormone allopregnanolone. FDA approval represents the final phase of a bench-to-bedside journey for this drug—a journey that began in the NIMH Intramural Research Program (IRP). In the 1980s, NIMH IRP researchers found that neurosteroids, such as allopregnanolone, play a role in the brain's response to stressful events. They also found that these neurosteroids, which are synthesized from the hormone progesterone, fluctuate and steadily increase during pregnancy. After a mother gives birth, these neurosteroid levels drop rapidly. These findings led to the hypothesis that this drop in neurosteroids could trigger the depression and anxiety-like symptoms in women following childbirth that may lead to a postpartum depression diagnosis. Researchers tested this hypothesis in animals and found that stress was observed to induce behavioral changes in the early postpartum period. Stabilizing some of these neurosteroids—by, for example, providing supplemental allopregnanolone—reversed the behavioral changes in these animals. These key insights into how neurosteroids might help alleviate postpartum depression symptoms led to the development of the new drug brexanolone (Gordon, 2019).

This relates to Objective 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health") of the Trans-NIH Strategic Plan for Women's Health Research.

Sex Differences in Brain Anatomy Across Human Development: Investigators in the NIMH IRP Section on Developmental Neurogenomics are combining neuroimaging, genomic, and bioinformatic techniques to better understand the architecture of human brain

development in health and in neurogenetic disorders that increase risk for psychiatric symptoms. These researchers examined more than 2,000 brain scans from the Human Connectome Project (U54MH091657) and found evidence for highly reproducible sex differences in the volume of certain brain regions. This pattern of sex-based differences in brain volume corresponds with patterns of sex-chromosome gene expression observed in samples from the brain's cortex. These findings suggest that sex chromosomes may play a role in the development or maintenance of sex differences in brain anatomy. Future research may build on these findings to elucidate the causes and consequences of sex differences in the human brain (Liu et al., 2020). In another study from this group, researchers uncovered sex-based differences in the development of the hippocampus and amygdala—brain areas that have been implicated in the biology of several mental illnesses that impact males and females differently. To learn more about the growth trajectories of these two structures from childhood through early adulthood, researchers examined structural magnetic resonance imaging (sMRI) scans collected from healthy participants between the ages of 5 and 25. These results bring greater resolution to the spatiotemporal understanding of amygdalo-hippocampal development in healthy males and females and uncover focal sex differences in the structural maturation of the brain components that may contribute to differences in behavior and psychopathology that emerge during adolescence (Fish et al., 2020).

This relates to Objectives 1.1 ("Discover basic biological differences between females and males"), 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes"), and 2.3 ("Leverage secondary data sources for research on the health of women through a big data enterprise that includes data sharing and analytic strategies") of the Trans-NIH Strategic Plan for Women's Health Research.

Sex-Specific Genetic Differences in the Prefrontal Cortex of Women with Depression: Depression affects women at almost twice the rate that it affects men (NSDUH, 2019). NIMH-funded researchers investigated a gene (LINC00473, expressed only in primates) that is commonly lower in the prefrontal cortex of women with depression but not in depressed men. The researchers hypothesized that LINC00473 would promote resilience to stress selectively in female mice. To test this idea, LINC00473 was expressed in the prefrontal cortex of adult male and female mice. Indeed, LINC00473 promoted resilience to stress in female mice but had no effect in male mice. LINC00473 expression also produced changes in the functional properties of prefrontal cortical neurons selectively in female mice. These changes that occurred only in female mice may further implicate LINC00473 as a female-specific driver of stress resilience that is aberrant in female depression (Issler et al., 2020).

This relates to Objectives 1.1 ("Discover basic biological differences between females and males") and 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes") of the Trans-NIH Strategic Plan for Women's Health Research.

DNA Methylation Biomarkers Prospectively Predict Both Prenatal and Postpartum Depression: In an effort to identify a biomarker for postpartum depression, NIMH-funded researchers administered the Edinburgh Postnatal Depression Scale and collected blood samples from pregnant women both with and without a prior psychiatric history. They looked for epigenetic changes such as DNA methylation, a biological process where methyl groups are added to DNA, which changes the expression of a gene; such changes may result in the development of various disorders. The researchers found that two epigenetic biomarkers (HP1BP3 and TTC9B) correlated with both prenatal depression and postpartum depression. Consideration of additional information, such as prenatal mood status or previous psychiatric history, may help improve prediction of postpartum depression based on scores on the Edinburgh Scale. Findings from this study confirm that blood collected throughout pregnancy might be useful to help identify pregnant women at future risk for postpartum depression who may benefit from early clinical intervention (Payne et al., 2020).

This relates to Objective 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health") of the Trans-NIH Strategic Plan for Women's Health Research.

A Machine Learning Algorithm for Predicting Risk of Postpartum Depression Among Pregnant Women: NIMH-funded researchers aimed to develop and validate a machine learning framework to identify risk for developing postpartum depression by using data extracted from electronic health records (EHRs). The researchers found that the best-performing algorithm to predict diagnosis of postpartum depression within 1 year of childbirth used EHR information such as clinical features related to mental health history, medical comorbidity, obstetric complications, medication prescription orders, and demographic characteristics. Results of this study indicate that integrating information from EHRs with machine learning technology may facilitate scalable and timely intervention for women at risk for postpartum depression (Zhang et al., 2021).

This relates to Objectives 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health") and 2.1 ("Expand and develop advanced and innovative approaches for study design, data collection, and analysis to optimize data quality and the ability to detect the influences of sex and gender on health and disease") of the Trans-NIH Strategic Plan for Women's Health Research.

An App-Based Genetic Study of Postpartum Depression: Genome-wide association studies require a large number of participants to achieve statistical power to test a hypothesis. In an effort to create a database to power genome-wide association studies on postpartum depression, NIMH-funded researchers developed an app to facilitate recruitment, consent, and screening of research participants. Using this app, researchers recruited over 7,000 women with a history of postpartum depression and collected nearly 3,000 saliva samples, which were stored at the NIMH Repository and Genomics Resource Biologic Core. The researchers ensured the reliability of the screening tool with a 6–9-month follow-up assessment of those participants who initially met criteria for postpartum depression. The researchers also performed a clinical validation of a subset of participants to assess sensitivity of the app. This study demonstrated the effectiveness of using an app for recruitment of a global sample of women with postpartum depression and the importance of collaboration among researchers, app developers, ethicists, and participants (Guintivano et al., 2018).

This relates to Objectives 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health"), 2.1 ("Expand and develop advanced and innovative approaches for study design, data collection, and analysis to optimize data quality and the ability to detect the influences of sex and gender on health and disease"), and 2.4 ("Expand and refine methodologies to improve the recruitment and retention of women underrepresented in clinical research") of the Trans-NIH Strategic Plan for Women's Health Research.

III. Promotion of Women's Health Research

Notice of Special Interest in High Priority Research Areas for Sex and Gender Influences on the Adolescent Brain and the Mental Health of Girls and Young Women (Ages 12–24):

Global epidemiological data show that up to 20% of children and adolescents suffer from a disabling mental illness, and up to 50% of all adults with mental illnesses experience symptom onset in adolescence. Gender differences in the development and onset of mental illnesses emerge at young ages, and gender is a modifier of the illness risks and protective factors that can be identified at the genetic, neurobiological, and psychosocial levels. NIMH published a notice of special interest to solicit applications to explore sex and gender influences on the development of the adolescent brain and mental health of girls and young women. NIMH encourages multidisciplinary research projects to examine biological, social, cultural, and behavioral contributions of sex and gender influences on mental health and illnesses. Research is needed to identify biomarkers and behavioral indicators that predict risk trajectories of mental illnesses. Additionally, translational research is needed that applies recent basic research discoveries and identifies opportunities to advance clinical research and mental health services research. Prevention and intervention projects that consider the impact of biological as well as social, cultural, and gender-based target mechanisms on mental health outcomes are also encouraged (NOT-MH-19-039).

This relates to Objective 1.4 ("Promote research that explores the influence of sex and gender on the connection between the mind and body, and its impact on health and disease") of the Trans-NIH Strategic Plan for Women's Health Research.

Implementing a Maternal health and PRegnancy Outcomes Vision for Everyone (IMPROVE): In an effort to address increasing rates of maternal mortality in the United States, NIH solicited applications for administrative supplements to active grants and cooperative agreements to improve the understanding of leading causes of pregnancy-related and pregnancy-associated mortality. These supplements encourage researchers to investigate the biological, behavioral, sociocultural, and structural factors contributing to maternal mortality and severe maternal morbidity by building an evidence base for improved care and outcomes in specific populations and regions of the country. NIMH is specifically interested in studies to identify determinants of risk or protection to detect the most vulnerable populations and provide points of intervention in mental health. The institute is also interested in research to develop and/or test interventions addressing stress, perinatal and postpartum depression, and harmful substance use (e.g., peer support, complementary health approaches, strategies to coordinate or integrate obstetrics and gynecology, mental health, and substance use treatment services) and assess their impact on maternal health outcomes (NOT-OD-20-104).

This relates to Objective 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health") of the Trans-NIH Strategic Plan for Women's Health Research.

Concept Clearances for Potential New Women's Mental Health Research Initiatives: A *concept* describes the basic purpose, scope, and objectives of a potential solicitation of grants or contracts. *Concept clearance* is the process by which NIH Institutes and Centers receive public input from a National Advisory Council on the merits of concepts. NIMH posts concepts approved by the National Advisory Mental Health Council on the NIMH website to alert researchers to NIMH interests and potential future funding opportunity announcements (FOAs). Concept approval by the council does not ensure that a concept will be developed into a FOA; their publication and timing are not certain and depend on sufficient funding and other priorities. Furthermore, the actual FOAs may differ in certain details from their originating concepts.

- ***Mood and Psychosis Symptoms During the Menopause Transition.*** The menopause transition is a window of vulnerability for the development of mood and psychotic symptoms, and the mechanisms underlying this vulnerability are largely unknown. In May 2020, NIMH staff presented a concept proposing to encourage comprehensive interdisciplinary research to identify biological, genetic, and environmental factors that could be used to identify women at risk of new or recurring mood and psychotic disorders during the menopause transition. This concept clearance also aims to encourage research to better understand the mechanistic links between the menopause transition and these disorders. The goal of such potential research is to improve women's health outcomes by identifying therapeutic targets for future development of novel treatment interventions.

  This relates to Objective 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health") of the Trans-NIH Strategic Plan for Women's Health Research.

- ***Prevention of Perinatal Depression: Improving Intervention Delivery for At-Risk Individuals.*** Perinatal depression, or depression that develops during pregnancy or after childbirth, affects as many as 1 in 7 women and is one of the most common complications of pregnancy and the postpartum period. NIMH is committed to identifying women at increased risk for perinatal depression and determining ways to improve intervention delivery, particularly for underserved populations. In September 2020, NIMH staff presented a concept proposing to encourage research that includes strategies for identifying women at risk for perinatal depression; evidence-based, service-ready, and scalable treatments and preventive interventions; and strategies that support the delivery of interventions with fidelity in the health care setting or other settings where women receive mental health services in the community. Further, NIMH

is interested in studies conducted in real-world settings that leverage patient information from electronic health record data to determine which interventions are predicted to work best for which individuals. Identifying risk factors and developing appropriate screening, treatment, and preventive interventions has the potential to optimize care and improve public health outcomes and the health of women and their children.

This relates to Objective 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health") of the Trans-NIH Strategic Plan for Women's Health Research.

Preventing Perinatal Depression Now: A Call to Action: In September 2020, NIMH staff and NIMH-supported researchers published a commentary, *Preventing Perinatal Depression Now: A Call to Action*, to address the rise in perinatal depression in pregnant women and postpartum women. An estimated 11.5% of pregnant women and postpartum women are affected by perinatal depression each year in the United States, yet just over half of women with perinatal depression are undiagnosed. Although there are several screening tools for perinatal depression, there is no consensus on which tool is most accurate or a gold standard for screening. In 2019, to address the growing rates in perinatal depression, the U.S. Preventive Services Task Force (USPSTF) recommended that clinicians provide or refer pregnant women and postpartum women at increased risk of perinatal depression to counseling interventions (e.g., cognitive behavioral therapy and interpersonal therapy). This landmark recommendation was one of the first guidelines to recommend that such preventive measures for perinatal depression be included in standard clinical care. Building on this recommendation, NIMH staff and NIMH-supported researchers developed three strategies to guide investigators: (1) establish a standard combination of multicultural perinatal depression screenings with evidence-based timepoints for screening administration; (2) introduce an evidence-based definition of perinatal depression that accurately captures the prevalence and incidence of this mental illness; and (3) improve the understanding of perinatal depression by incorporating the psychosocial context in routine clinical practice for pregnant women and postpartum women. The ultimate goal of these strategies is to increase the number of pregnant women and postpartum women who are screened and receive support to prevent perinatal depression and get women into treatment (Lewis Johnson et al., 2020).

This relates to Objective 3.2 ("Identify collaborative opportunities and leverage partnerships to disseminate research that improves the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

Let's Play Ball – How Sex and Gender Effects Influence Sports Involvement, Hippocampal Volume, and Depressive Symptoms in Children: On July 31, 2019, the NIMH Office for Disparities Research and Workforce Diversity hosted a webinar with NIMH grantee Deanna Barch, Ph.D., of the Washington University School of Medicine in St. Louis. Recent studies have found that higher levels of exercise are significantly associated with lower depression among both adults and young people. One reason exercise has a positive relationship with mental health may be that engagement in team sports has the potential to lead to increased social support. In addition, research suggests that exercise may modify the volume of the hippocampus, a region of the brain that has been found to be altered in depression. However, it is not clear whether this relationship emerges as early as preadolescence. During the webinar, Dr. Barch summarized her research findings from a nationwide sample of over 4,000 children ages 9–11 who completed surveys, interviews, and MRI scans for the Adolescent Brain and Cognitive Development (ABCD) Study®. Data were gathered on each child's participation in 23 different sport-related activities. Dr. Barch described how involvement in sports was positively correlated with hippocampal volume in both boys and girls and was related to fewer depressive symptoms for boys but not girls. Moreover, these relationships held even when correcting for family income, maternal education, race, ethnicity, age, and total brain volume. These findings may help illuminate a potential neural mechanism for the impact of exercise on the developing brain and the differential effects.

This relates to Objective 3.2 ("Identify collaborative opportunities and leverage partnerships to disseminate research that improves the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

A Woman's Voice: Understanding Autistic Needs: According to the Centers for Disease Control and Prevention, autism spectrum disorder (ASD) is 4.3 times more common in boys than in girls (Maenner et al.,

2020). On April 23, 2019, the NIMH Office of Autism Research Coordination (OARC) hosted a special event to recognize National Autism Awareness Month. The event featured a panel presentation from female autistic self-advocates Barb Cook, Liane Holliday-Willey, Ed.D., and Dena Gassner, M.S.W. The three women are editors and authors of the book *Spectrum Women: Walking to the Beat of Autism*. The panel also included autistic self-advocate Jennifer O'Toole, author of *Autism in Heels: The Untold Story of a Female Life on the Spectrum*. Panelists discussed their books, their perspectives on research, and their lived experience, thus shedding light on the real-world challenges of being a woman with ASD.

This relates to Objective 3.2 ("Identify collaborative opportunities and leverage partnerships to disseminate research that improves the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

IV. Advancement of Women in Biomedical Careers

Diversity in the scientific workforce enhances excellence, creativity, and innovation. Thus, increasing diversity, including the number of women, in the scientific workforce remains an important goal for NIMH. As such, NIMH participates in a number of activities available to individuals, from high school students to junior faculty, to encourage the inclusion of women in the NIMH workforce in both the intramural and extramural research communities.

In fiscal year 2020, NIMH, along with other NIH partners, issued two requests for applications (RFAs) through the Brain Research through Advancing Innovative Neurotechnologies® (BRAIN) Initiative's Advanced Postdoctoral Career Transition Award to Promote Diversity (RFA-NS-19-043, RFA-NS-19-044). The purpose of these awards is to enhance and maintain a strong cohort of new, talented NIH-supported independent investigators from diverse backgrounds in BRAIN Initiative research areas. The awards facilitate a timely transition of outstanding postdoctoral researchers to independent tenure-track or equivalent faculty positions. Eligibility is limited to applicants from groups underrepresented in the biomedical, clinical, behavioral, and social sciences, including women.

This relates to Objectives 4.2 ("Develop the next generation of researchers to advance science on the health of women") and 4.3 ("Enhance and develop programs to recruit, support, retain, and advance women at all stages of their research careers, from early career to leadership positions") of the Trans-NIH Strategic Plan for Women's Health Research.

Also, in fiscal year 2020, NIMH signed on to participate in the Maximizing Opportunities for Scientific and Academic Independent Careers (MOSAIC) Program, which is part of NIH's efforts to enhance diversity within the academic biomedical research workforce and is designed to facilitate the transition of talented postdoctoral researchers from diverse backgrounds into independent faculty careers in research-intensive institutions. The MOSAIC K99/R00 program aims to provide independent NIH research support before and after this transition to help awardees launch successful independent research careers (PAR-19-342, PAR-19-343). Additionally, MOSAIC K99/R00 scholars will be part of organized scientific cohorts and will be expected to participate in mentoring, networking, and professional development activities coordinated by MOSAIC Institutionally Focused Research Education Award to Promote Diversity (UE5) grantees.

This relates to Objectives 4.2 ("Develop the next generation of researchers to advance science on the health of women"), 4.3 ("Enhance and develop programs to recruit, support, retain, and advance women at all stages of their research careers, from early career to leadership positions"), and 4.4 ("Promote and support policies, mentoring and networks, collaborations, and infrastructure to retain and advance women in their careers") of the Trans-NIH Strategic Plan for Women's Health Research.

In June 2019, NIH Director Francis Collins, M.D., Ph.D., issued a statement on NIH's commitment to changing the culture and climate of biomedical research to create an inclusive and diverse workforce. He noted that too often, women and members of other groups underrepresented in science are noticeably missing from speaker panels at scientific meetings and other high-level conferences. Dr. Collins announced that it is time to end the tradition in science of all-male speaking panels and that he will decline speaking opportunities if they are not inclusive of scientists of all backgrounds. NIMH Director Joshua Gordon, M.D., Ph.D., immediately

stood by this pledge. Furthermore, Dr. Gordon issued a statement describing what he expects and how he will implement an even playing field for scientists of diverse backgrounds when he evaluates an invitation to attend and present at events. He also encouraged scientific leaders across the biomedical enterprise to support all of the talented minds engaged in research.

This relates to Objective 4.4 ("Promote and support policies, mentoring and networks, collaborations, and infrastructure to retain and advance women in their careers") of the Trans-NIH Strategic Plan for Women's Health Research.

V. Implementation of the NIH Policy on Sex as a Biological Variable (SABV)

In 2015, NIH published the SABV policy (NOT-OD-15-102). This policy outlines NIH's expectation that sex as a biological variable will be factored into research designs, analyses, and reporting in vertebrate animal and human studies. As such, NIMH encourages the inclusion of both biological sexes in NIMH-funded extramural and intramural studies as appropriate.

NIMH has worked to educate applicants and reviewers on this policy and provide guidance on its implementation. NIMH directs reviewers to include sex as a biological variable as an independent review factor in all funding applications considered by the institute. Additional monitoring is carried out by NIMH program staff to ensure that applications selected for funding are compliant with the SABV policy. Such efforts include examination of statistical plans in study applications that include both sexes to ensure they are well powered to detect sex differences.

NIMH has promoted the SABV policy in multiple announcements and publications across basic and clinical research. For example, in September 2019, NIMH released a notice outlining guidelines and priorities for potential applicants considering animal neurobehavioral approaches in basic and preclinical research relevant to mental illnesses (NOT-MH-19-053). In section D of the notice, researchers are encouraged to factor sex as a biological variable into proposed research designs, analyses, and reporting. Studies using this approach may lead to the identification of sexually dimorphic outcomes and may inform future research opportunities. In addition, NIMH staff, including the NIMH director, published a commentary that describes the institute's priorities in stress research and notes that sex should be considered a biological variable (Simmons et al., 2020). By including both biological sexes in research studies, investigators may identify sex-related pathophysiology caused by environmental and biological stressors, which may inform novel treatment approaches (Bale, 2019).

In addition to the above efforts, NIMH participates in the Trans-NIH SABV Working Group. As a member, NIMH contributes to the development of resources and tools for extramural and intramural investigators to improve and comply with the SABV policy during preparation of an NIH application for funding or for reporting of a study in scientific publications. For example, sex and gender differences in mental disorders are addressed in module 6 in the *Bench to Bedside: Integrating Sex and Gender to Improve Human Health* course. This working group also engages on the refinement of the current policy and evaluation of SABV implementation in NIH-funded research.

VI. Inclusion of Women in Clinical Research

NIMH follows several steps to ensure compliance with inclusion guidelines for recruitment of participants in both extramural and intramural clinical research. Grant applications are evaluated for the appropriateness of proposed plans for meeting sex, gender, racial, and ethnic minority enrollment goals and how the investigator will meet these goals. For NIH-defined Phase III clinical trials, enrollment goals are further assessed for proposed analyses of intervention effects among sex, gender, racial, and ethnic groups. For extramural clinical research studies, the NIMH Office of Clinical Research monitors the entry of inclusion data, performs quality assurance tasks, prepares aggregate reports for the National Advisory Mental Health Council and the NIH Office of Research on Women's Health (ORWH), and provides up-to-date training on procedures for ensuring the accuracy of inclusion data, as well as on the use of the electronic Human Subjects System.

All NIH Intramural Research Program (IRP) clinical research studies require investigators to provide plans for the appropriate inclusion of women and minorities and/or a justification whenever representation is limited or absent, as part of their NIH protocol reviews. NIMH IRP investigators recruit for active studies girls and women nationwide, as well as regionally in the greater Washington, D.C., area. Recruitment activities include direct mail, digital and social media, radio and podcast advertisement, and print ad campaigns, as well as outreach in person and digitally via webinars and events to advocacy groups, provider groups, and the general public. Intramural institutional review boards review intramural research protocols for compliance with inclusion guidelines and conduct annual monitoring. The NIH Clinical Center's Office of Protocol Services (OPS) maintains centralized systems for capturing participant data, including sex, gender, ethnic, and racial status. OPS coordinates annual reporting of demographic participant data to the NIH Office of Extramural Research and ORWH.

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National Institute on Minority Health and Health Disparities

I. Executive Summary

Women's health remains an important area of research interest for the National Institute on Minority Health and Health Disparities (NIMHD) in fulfilling its mission to improve minority health and reduce health disparities and in complying with the 21st Century Cures Act requirement to ensure that the institute's activities "take into account women and minorities and are focused on reducing health disparities" [Public Law 114–255, Sec. 2031(c)].

Racial and ethnic minority women are disproportionately affected by several diseases and health conditions compared with White women. Even among racial and ethnic minority women, disparities exist in certain diseases and conditions for some women compared with others of different race and ethnicities, such as lupus in African American or Black and Hispanic or Latina women. While women of racial and ethnic minority backgrounds continue to experience disparities in diseases such as diabetes and cardiovascular disease, cancers—especially breast and cervical—remain a stubborn health disparity of increasing concern. In recent years, research findings have highlighted the critical need for enhanced research and outreach activities to understand and address the stark disparities in maternal morbidity and mortality. African American and American Indian and Alaska Native women, for example, not only have higher rates of pregnancy-related complications but are two to three times more likely than White women to experience maternal mortality.

During fiscal years (FY) 2019–2020, NIMHD gave increased focus to the issue of maternal morbidity and mortality and issued the *Addressing Racial Disparities in Maternal Mortality and Morbidity* funding opportunity announcement (RFA-MD-20-008) to support multidisciplinary research examining the efficacy and/or effectiveness of multilevel interventions to reduce health and health care disparities in maternal morbidity and mortality experienced by racial and ethnic minority women. NIMHD funded the following five grants through this initiative:

- **Minding the Gap: A Multidisciplinary Approach to Reduce Maternal Health Disparities in Georgia** will analyze Georgia linked vital records, hospital discharge, and claims data to assess the extent, location, and determinants of differences in severe maternal morbidity (SMM) among African American or Black and White women at delivery and 3 to 12 months postpartum. 1R01MD016031-01
- **Meeting Women Where They Are: Multilevel Intervention Addressing Racial Disparities in Maternal Morbidity and Mortality** is testing the effectiveness and cost-effectiveness of a multilevel intervention to address African American maternal morbidity and mortality in two Michigan counties by expanding access to enhanced prenatal and postnatal care services (e.g., home visiting programs, Healthy Start programs) using telehealth and flexible scheduling. R01MD016003
- **Improving Health Outcomes and Equity by Targeting Postpartum Mothers at Highest Risk** aims to better identify African American or Black and Hispanic or Latina women most at risk for poor outcomes following delivery, determine the problems they experience, and adapt an evidence-based intervention to improve quality of postpartum care for high-risk women. 1R01MD016029-01
- **Hospital Quality, Medicaid Expansion, and Racial and Ethnic Disparities in Maternal Mortality and Morbidity** will examine to what extent hospital quality contributes to maternal racial and ethnic disparities in eight U.S. States, societal- and individual-level maternal factors associated with using versus bypassing high-quality hospitals, and whether Medicaid expansion has impacted hospital quality and maternal outcomes. 1R01MD016012-01
- **Reducing Racial Disparities in SMM Post COVID-19: Assessing the Integration of Maternal Safety Bundles and Community Based Doulas to Improve Outcomes for Black Women** will examine perinatal care, maternal outcomes, and health care utilization

of African American or Black women at increased risk of severe maternal morbidity and mortality compared with White women. 1R01MD016026-01

Additionally, in FY 2020, NIMHD funded the *Maternal and Developmental Risks from Environmental and Social Stressors (MADRES)* project in collaboration with the National Institute of Environmental Health Sciences to examine prenatal environmental exposures and social stressors in relation to depression and cardiovascular risk factors postpartum. Another collaboration with the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, the *Maternal and Infant Environmental Riskscape (MIEHR) Research Center*, is studying the contributions of exposures in the biological, physical, social, and built environments of the environmental risk scape to environmental health disparities in pregnant women and their infants.

In FY 2019 and FY 2020, NIMHD, in collaboration with the other NIH Institutes and Centers, developed the NIH Minority Health and Health Disparities Strategic Plan (2021–2025). The plan includes goals and strategies that will help to (1) address inclusion of racial and ethnic minorities, women, older adults, and children in clinical research to meet the requirements of the 21st Century Cures Act; (2) support the implementation of the NIH Policy on Sex as a Biological Variable (SABV); and 3) advance implementation of the 2019–2023 Trans-NIH Strategic Plan for Women's Health Research—for example, with research that will aim to:

- Uncover contributors and develop interventions to reduce maternal mortality and severe maternal morbidity in the United States over the next 10 years in order to address the disparities between African American or Black and American Indian and Alaska Native women compared with White women; and
- Understand the underlying etiologic pathways for the higher rates of systemic lupus among African American women and Latinas compared with White women by 2030.

This report also provides an overview of select NIMHD FY 2019 and FY 2020 extramural and intramural research, research findings, and other activities that align with the goals of the Trans-NIH Strategic Plan for Women's Health Research. Topics covered in the report include breast cancer, cervical cancer, pregnancy-related conditions, preterm birth, lupus, pre-exposure prophylaxis (PrEP) uptake, lung cancer, sleep disparities, and the impact of COVID-19 on incarcerated women.

II. Scientific Advances

Rural–Urban Differences in Neuroimmune Biomarkers and Health Status among Women Living with Breast Cancer

Breast cancer survivors are at risk of neuroimmune dysfunction in survivorship because of chronic emotional and psychosocial stressors following breast cancer treatment. An NIMHD-funded research project studied relationships between neuroimmune activity and perceived health in rural and urban breast cancer survivors. The study found differences in immune activity between rural and urban breast cancer survivors. There were no observable differences between the rural and urban group in neuroendocrine activity. Among rural breast cancer survivors, the results showed relationships between perceptions of mental health and salivary amylase, an enzyme in saliva, while among urban women, it found an association between perceptions of mental health and interleukin-6, a protein produced in response to an infection or injury. Interleukin-6 was positively associated with perceptions of physical health in rural breast cancer survivors. Results suggests that rural–urban residence may be a factor in relationships between neuroimmune function and perceived health status, particularly social functioning in women with breast cancer (Hulett et al., 2021).

This translational research supports Goal 1 ("Advance rigorous research that is relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

Trans-ethnic Meta-analysis of Genome-wide Association Studies Identifies Maternal ITPR1 as a Novel Locus Influencing Fetal Growth during Sensitive Periods in Pregnancy

Abnormal fetal growth is a risk factor for infant morbidity and mortality and is associated with

cardiometabolic diseases in adults. Genetic influences on fetal growth can vary at different gestation times, but genome-wide association studies have been limited to birth weight. An NIMHD intramural scientist led a trans-ethnic genome-wide meta-analysis and fine mapping to identify maternal genetic loci associated with fetal weight estimates using ultrasound measures taken during pregnancy. The investigators identified a novel genome-wide significant association of the inositol 1,4,5-trisphosphate receptor type 1 (ITPR1) gene with reduced fetal weight from 24 to 33 weeks gestation. Single-nucleotide polymorphism (SNP), the most common type of genetic variation among people, was associated with head circumference but not with abdominal circumference or length of the bones in the arms and legs. Decreased placental expression of ITPR1 was correlated with increased placental epigenetic age acceleration, a risk factor for reduced fetal growth, among male fetuses. The results of this study highlight the role of common maternal genetic variants in the inositol receptor signaling pathway on fetal growth from late in the second trimester until early in the third trimester (Tekola-Ayele et al., 2020).

This translational research supports Goal 2 ("Develop methods and leverage data sources to consider sex and gender influences that enhance research for the health of women) of the Trans-NIH Strategic Plan for Women's Health Research.

Direct and Vicarious Racial Discrimination at Three Life Stages and Preterm Labor: Results from the African American Women's Heart & Health Study

The relationship between racial discrimination and preterm labor, a key measure of maternal health, is an understudied area in research. This study examined the associations between preterm labor and direct and vicarious racial discrimination among African American women at three life stages: childhood, adolescence, and adulthood. Findings showed a 48% increase in the odds of preterm labor with each unit increase in adolescent direct racial discrimination. Each unit increase in childhood vicarious racial discrimination was associated with a 45% increase in the odds of preterm labor. The results reveal an association between life-stage racial discrimination and preterm labor risk among African American women, which underscores the need for further research to understand how direct and vicarious racial discrimination at different developmental periods impact racial disparities in birth outcomes (Daniels et al., 2020).

This translational research supports Goal 1 ("Advance rigorous research that is relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

Neighborhood Social Determinants of Triple-Negative Breast Cancer

Triple-negative breast cancer (TNBC) is an aggressive, heterogeneous subtype of breast cancer that is more frequently diagnosed in African Americans or Black women than in White women. This study investigated the role of neighborhood social determinants of racial disparities in TNBC. Controlling for age, African Americans or Black women had 2.21 times the incidence of TNBC incidence compared with White women. The incidence of TNBC was independent of neighborhood concentrated disadvantage index (CDI). Neighborhood environment did not impact the observed racial disparity. African American or Black women were more likely to be diagnosed at later stages, and CDI was associated with more advanced stages of TNBC at diagnosis. CDI was also significantly associated with poorer stage-specific survival. Results suggest that neighborhood disadvantage contributes to racial disparities in stage at diagnosis and survival among TNBC patients but not to disparities in incidence of the disease. To improve overall survival, additional research is needed to explore the mechanisms through which social determinants affect the promotion and progression of TNBC (Hossain et al., 2019).

This translational research supports Goal 1 ("Advance rigorous research that is relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

Racial Disparities in Prematurity Persist among Women of High Socioeconomic Status

Persistent racial disparities in preterm birth (PTB) exist among African American or Black women compared with White women in the U.S., but the influence of sociodemographic factors remains unclear. An NIMHD-

funded study evaluated the persistence of disparities in PTB among African American or Black women of high socioeconomic status (SES). According to the results, the PTB rate at each gestational age cutoff was higher for women of "mixed" White and African American or Black race and highest for women who were African American or Black only. Among women with insurance and prenatal care their entire pregnancy, maternal race was associated with higher odds of PTB at each gestational age cutoff, with the highest odds among women at less than 28 weeks. Rates of preterm birth at each gestational age cutoff remained highest for women who identified as African American or Blacks, intermediate for women identifying as both African American or Black and White, and lowest for White women. Racial disparities in prematurity persist even among college-educated women with private insurance who are not receiving Special Supplemental Nutrition Program for Women, Infants, and Children benefits. The findings suggest that factors other than socio-demographics are important in the underlying pathogenesis of PTB (Johnson et al., 2020).

This translational research study supports Goal 1 ("Advance rigorous research that is relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

Fetal Macrosomia in a Hispanic/Latinx Predominant Cohort and Altered Expressions of Genes Related to Placental Lipid Transport and Metabolism

Fetal overgrowth, also referred to as fetal macrosomia when birth weight is more than 4,000 grams, is a major concern in the treatment of gestational diabetes mellitus (GDM), a key pregnancy complication. Fetal overgrowth may lead to increased risk of cesarean delivery, birth trauma, and other maternal and fetal outcomes. Researchers studied whether fatty acid transport and metabolism in the placental tissue is impaired in Hispanic or Latina GDM women, dependent on fetal sex. Results showed higher incidence of GDM and obesity in Hispanic or Latina women compared with women of other ethnicities, but not in fetal macrosomia. The presence of GDM, fetal macrosomia, and fetal sex did not alter expressions of most genes related to placental lipid transport and metabolism. In obese women with GDM, the fatty acid–binding protein 4 (FABP4) was elevated in male placentas, which resulted in a higher incidence of fetal overgrowth in male, compared with female, fetuses. While the findings showed racial disparity in GDM, investigators did not find any racial disparity in fetal macrosomia. Changes in the ability of the placenta to supply nutrients, including lipids, to the growing fetus may contribute to fetal overgrowth in obese women with GDM, pointing to the need for further research to tackle fetal macrosomia (Yang et al., 2020).

This translational research supports Goal 1 ("Advance rigorous research that is relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

III. Promotion of Women's Health Research

This section highlights select examples of NIMHD's FY 2019 and FY 2020 research and activities that support the promotion of research on women's health. These include a funding opportunity announcement on maternal health disparities, a research project to understand the impact of COVID-19 on imprisoned African American women, research to address the low rate of cervical cancer screening among American Indian and Alaska Native women, a study testing the effectiveness of a chronic disease management evidence-based intervention to address lupus, and research on measures to assist with data collection and accurate sexual orientation and gender identification.

Addressing Racial Disparities in Maternal Mortality and Morbidity

At its February 2020 meeting, the National Advisory Council on Minority Health and Health Disparities approved a concept for the NIMHD to develop an initiative focused on maternal morbidity and mortality disparities. In FY 2020, NIMHD released the *Addressing Racial Disparities in Maternal Mortality and Morbidity* funding opportunity announcement to support multidisciplinary research examining the efficacy and/or effectiveness of multilevel interventions to reduce health and health care disparities in maternal morbidity and mortality experienced by racial and ethnic minority

women. A total of five awards were made in FY 2020 through this initiative.

This initiative aligns with Goal 1 ("Advance rigorous research that is relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research. (RFA-MD-20-008)

Assessing the Impact of the COVID-19 Outbreak on Women with Experience in the Criminal Probation System

In FY 2020, NIMHD supported several research supplements to address the COVID-19 pandemic among populations experiencing health disparities, including women. One example of this research is the *Assessing the Impact of the COVID-19 Outbreak on Women with Experience in the Criminal Probation System*. Women in prison are often overlooked, and their health is compromised by inadequate availability of health care, as well as sexism and racism for women of racial and ethnic minority backgrounds. This study seeks to determine the medical and social effect of COVID-19 on a predominantly African American sample of incarcerated women. Approximately 82% of the women have one or more chronic health conditions, which are characteristics linked with disparities in COVID-19 risk, infection, and mortality. This study is conducting rigorous analyses to (1) assess changes in health care access and utilization associated with the COVID-19 outbreak and related local public health mandates such as shelter in place and (2) examine how health literacy and social determinants, such as housing and income, are associated with adherence to public health mandates and participation in COVID-19 screening (3R01MD010439-04S1).

This research aligns with Goal 1 ("Advance rigorous research that is relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

Characterizing Disparities and Elucidating Opportunities across the Cervical Cancer Continuum among Native American Women

American Indian and Alaska Native (AI/AN) women have significantly lower cervical cancer screening rates, have disproportionately higher cervical cancer incidence rates, and are more often diagnosed at late stages of the disease than women of other racial and ethnic backgrounds. In FY 2019, the *Characterizing Disparities and Elucidating Opportunities across the Cervical Cancer Continuum among Native American Women* study began. Linking data for AI/AN women in the Indian Health Epi Data Mart with data for women in the New Mexico HPV Pap Registry (NMHPVPR), the study aims to characterize cervical cancer screening coverage, rates and intensity, failures in cervical cancer screening, diagnosis and treatment, and correlates of cervical screening with HPV vaccination among AI/AN women. The overarching goal of this study is to elucidate the specific pathways through which failures to screen for cervical cancer occur among AI/AN women across the cervical cancer continuum to inform cost-effective and data-driven strategies for intervention that can mitigate the pervasive health disparities witnessed among AI/AN women (5R21MD014662-02).

This research aligns with Goal 1 ("Advance rigorous research that is relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

A Widespread Self-Management Education Program to Reduce Health Disparities in African American Women with Systemic Lupus Erythematosus

Systemic lupus erythematosus (SLE) is a chronic disease that disproportionately affects young African American women. This study will examine whether an established self-management program for people with chronic illnesses can improve self-management behaviors and reduce the negative medical and psychosocial consequences of SLE among African American women. The study aims to assess the effectiveness and cultural relevance of the Chronic Disease Self-Management Program (CDSMP) in African American women with SLE, including differential effects of the CDSMP on outcomes by sociodemographic and health factors (5R01MD010455-05).

This research supports Goal 3 ("Enhance dissemination and implementation of evidence to improve the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

Identifying, Refining, and Testing Sexual Orientation and Gender Identity Measures to Detect and Delineate Sexual and Gender Minority Populations for Research

To enhance research for the health of women, it is important to consider sex and gender influences and for researchers to have reliable and efficient methods to measure sexual and gender minority (SGM) status. This helps researchers to accurately capture and better understand the health of sexual and gender minority individuals. One example of NIMHD's work in this area is the *Identifying, Refining and Testing Sexual Orientation and Gender Identity Measures to Detect and Delineate Sexual and Gender Minority Populations for Research* project. The proposed research will develop a high-performing, efficient strategy for identifying SGM people.

The study uses a mixed-methods approach to develop and describe the performance characteristics of a reliable, low-burden, community-acceptable SGM status screening question. Leveraging two large national cohorts, the study will apply iterative quantitative testing among both SGM and non-SGM individuals to measure response accuracy, as well as participant understanding and acceptability. This strategy will evaluate performance characteristics and demographic differences in answer choice patterns. This research will contribute to enhancing research on women's health and cultivate accurate identification and inclusive data collection, which are critical to improving health outcomes and reducing health disparities for women.

This research supports Goals 1 ("Advance rigorous research that is relevant to the health of women") and 2 ("Develop methods and leverage data sources to consider sex and gender influences that enhance research for the health of women") of the Trans-NIH Strategic Plan for Women's Health Research (1R21MD015878-01).

IV. Advancement of Women in Biomedical Careers

In FY 2020, NIMHD hired a woman scientist for the position of Deputy Director. She joined other women already in scientific senior leadership roles at NIMHD, such as the first woman Scientific Director of the NIMHD intramural research program, who is also the first Latina Scientific Director at NIH, and another Latina serving as Director of the Division of Clinical and Health Services Research. NIMHD supports training and career development for the next generation of minority health and health disparities researchers, including women, using several mechanisms, such as fellowships for predoctoral students, and career development awards, such as K awards for early-stage investigators. In addition, the Loan Repayment Program supports more than 100 talented scientists each year from racial and ethnic minority backgrounds and other scientists interested in health disparities or clinical research.

In FY 2019 and FY 2020, women who received mentored research scientist development awards (K01s) from NIMHD proposed research in several areas related to women's health, such as:

- *Mindfulness-intervention to Address PTSD in Trauma-exposed Homeless Women*, a randomized clinical trial of a modified-MBSR intervention that aims to reduce post-traumatic stress disorder (PTSD) symptoms in homeless women and to explore physiological correlates of treatment response in participants with clinically significant PTSD (K01MD013910).
- *Understanding Racial and Ethnic Disparities in Preterm Birth: A Systems Science Approach* will support the awardee in developing skills in systems dynamic modeling to understand how structural and intermediary determinants generate and perpetuate racial and ethnic preterm birth disparities and to inform strategies to address these disparities (5K01MD013911-02).
- *Using Implementation Science to Increase PrEP Uptake among African American Women in the South* seeks to develop, pilot-test, and evaluate a pre-exposure prophylaxis (PrEP) Implementation Toolkit within two community health care clinics to increase PrEP uptake among African American women, address IPV as a barrier to PrEP uptake, and ultimately combat racial disparities in women's HIV diagnoses (1K01MD015005-01A1).

The **NIMHD Health Disparities Research Institute** (HDRI) is another example of the institute's activities to foster

the advancement of women in biomedical research. This yearly 1-week program is aimed at early-career investigators from diverse backgrounds interested in becoming independent researchers. The program seeks to support research career development of promising research scientists conducting minority health or health disparities research and stimulate research in the disciplines supported by health disparities science. Eligible early-stage investigators include individuals who completed their doctorate level or equivalent degree or postgraduate clinical training within the past 10 years. Participants attend lectures and seminars on various topics related to minority health and health disparities research, have mock grant review sessions, and have small group discussions, including consultation on preparing a grant application. More than 270 scholars have attended the HDRI summer program since 2016, and more than 60% have been from underrepresented backgrounds. In FY 2019, women made up 80% of the participants, and in FY 2020, they made up 76% of participants.

V. Implementation of the NIH Policy on Sex as a Biological Variable (SABV)

NIH's SABV policy calls for ICs to consider sex as a biological variable in research designs, analyses, and reporting in vertebrate animal and human studies as scientifically appropriate. During FY 2019 and FY 2020, NIMHD led the development of the NIH Minority Health and Health Disparities Strategic Plan (2021–2025). The plan includes a research-sustaining goal to ensure appropriate representation of minority and other health disparity populations in NIH-funded research (Goal 7), which supports the implementation of NIH's SABV policy. A specific strategy within this goal that further promotes implementation of the SABV policy suggests that the ICs provide guidance, recommendations, and technical assistance for NIH-funded researchers in appropriate study design and best practices for recruitment to ensure compliance with laws, regulations, and policies regarding the inclusion of minorities and other health disparity populations in research.

VI. Inclusion of Women in Clinical Research

To generate the best evidence possible and to ensure that all communities benefit equally from advances in prevention, treatment, or management of disease, it is important for clinical research and trials to include participants who adequately represent those with the disease or condition under study. The inclusion of racial and ethnic minorities, including women, is inherent in the mission and work of the NIMHD. In developing the NIH Minority Health and Health Disparities Strategic Plan (2021–2025) in collaboration with the ICs, NIMHD included the following research-sustaining goal and specific strategies to promote the inclusion of individuals from racial and ethnic minority groups and other populations that experience health disparities, such as sexual and gender minorities, rural residents, and individuals of less privileged socioeconomic backgrounds, including women, in research with human participants:

Goal 7: Ensure appropriate representation of minority and other health disparity populations in NIH-funded research

- Strategy 7.1: Provide guidance, recommendations, and technical assistance for NIH-funded researchers in appropriate study design and best practices for recruitment to ensure compliance with laws, regulations, and policies regarding the inclusion of minorities and other health disparity populations in research.
- Strategy 7.2: Promote and enforce accountability for inclusion of diverse populations by tracking of originally proposed recruitment strategies and objectives to ensure sufficient samples for analyses of sub-population data.
- Strategy 7.3: Promote inclusion of minorities and other health disparity populations in big data sets, clinical research, and future big science initiatives.

Below are examples of NIMHD's intramural and extramural research from FY 2019 and 2020 to address the inclusion of women in clinical research.

Elucidating Lung Cancer Etiology among Asian American Female Never Smokers

Lung cancer in never smokers (LCINS) disproportionately affects Asian American females. Although the incidence rates of lung cancer are declining in most racial and ethnic groups, the incidence of lung cancer, especially adenocarcinoma, has been increasing in most Asian ethnic groups. This population-based case–control study will assemble the largest population-based lung cancer case–control dataset, with associated genetic and tumor genomic data, for never-smoking Asian women. The study aims to identify risk factors for LCINS among Asian females, determine the independent and joint contributions of multilevel risk factors, characterize the mutational landscape of LCINS among Asian females, and identify multilevel risk factors associated with the major mutational tumor features.

Perinatal Attentional Retraining Intervention for Smoking (PARIS) for Minority Women

Maternal smoking is the leading cause of cancer mortality in pregnant women and is associated with adverse pregnancy outcomes and increased infant morbidity and mortality. Many women have high rates of relapse to smoking following childbirth, but there are no effective treatments to treat relapse among postpartum racial and ethnic minority women. Attentional retraining (AR) is effective at reducing anxiety related to transition stress, such as that experienced by women postpartum. This randomized clinical trial uses smartphones to administer AR to determine whether AR can prevent smoking relapse in postpartum African American or Black and Hispanic or Latino women.

Gene Regulation May Influence Racial Disparities in Breast Cancer Survival

In the United States, African American women are more likely than White women to die from breast cancer, although White women are more likely to get diagnosed with the disease. The survival gap is widest among women with breast cancer that is associated with receptors for hormones causing the uncontrolled growth of breast cells. Researchers analyzed the pattern of genes expressed in the breast tissue samples to uncover biological factors underlying this disparity. African American women had a higher frequency of triple-negative breast cancer compared with White women. The study found no significant racial difference in gene regulators associated with the development of these inner cells. The authors suggest that other factors in the genetic pathway in breast tissue might play a role in the worse breast cancer survival outcomes for African American women compared with White women. The results of this study highlight genetic markers that clinicians may use to predict breast cancer survival based on race. The study also indicates potential targets for therapy and promotes further investigation to enable researchers to understand the biological processes that may contribute to racial disparities in breast cancer survival (Byun et al., 2020).

Nuevo Amanecer-II: Results of a Randomized Controlled Trial of a Community-based Participatory, Peer-delivered Stress Management Intervention for Rural Latina Breast Cancer Survivors

Nuevo Amanecer is a 10-week stress management program for rural, low-literacy Hispanic or Latina breast cancer survivors. Trained peers delivered Nuevo Amanecer-II to Spanish-speaking Hispanic or Latina women with breast cancer that had not spread, in three rural communities. Women were randomized to receive the program immediately or wait 6 months. Assessments were conducted at baseline, 3 months, and 6 months. Primary outcomes were breast cancer–specific quality-of-life domains. Secondary outcomes included general distress symptoms and stress management skills. Compared with women in the control group, intervention group women reported greater improvements in anxiety at 6 months, in relaxation at 3 months and 6 months, in awareness of tension at 3 months and 6 months, and in coping confidence at 3 months. The findings highlight the potential of stress management programs delivered by trained peers in rural community settings to reduce anxiety and improve stress management skills among Hispanic or Latina breast cancer survivors (Napoles et al., 2020).

Racial and Ethnic Disparities in Sleep Duration and Sleep Disturbances among Pregnant and Non-Pregnant Women in the United States

Sleep disturbances among pregnant women are increasingly linked to suboptimal maternal or birth outcomes. Despite worsening disparities in adverse birth outcomes in the U.S., few studies investigating sleep by pregnancy status have included racially or ethnically diverse populations. This study investigated relationships between self-reported pregnancy and six sleep characteristics stratified by race and ethnicity. Researchers also examined associations between race and ethnicity and sleep stratified by pregnancy status. Pregnant women were less likely than nonpregnant women to report short sleep and more likely to report long sleep and trouble staying asleep. Among White women, sleep medication use was less prevalent among pregnant women than it was among nonpregnant women, but this association was not observed among African American or Black women and was less pronounced among Hispanic or Latina women. Compared with pregnant White women, pregnant African American or Black women had a higher short sleep prevalence. Given disparities in maternal and birth outcomes and sleep, expectant mothers, particularly racial or ethnic minorities, may need screening followed by treatment for sleep disturbances (Feinstein et al., 2020).

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National Institute of Neurological Disorders and Stroke

I. Executive Summary

The mission of the National Institute of Neurological Disorders and Stroke (NINDS) is to seek fundamental knowledge about the brain and nervous system and to use that knowledge to reduce the burden of neurological disease. This burden is borne by every age group, every segment of society, and people all over the world. Most disorders of the nervous system affect men and women equally, but some have specific health implications for women or disproportionately affect women. NINDS supports basic, preclinical, and clinical research to understand sex differences in neurological disorders and in normal development and function of the nervous system. In addition, NINDS supports efforts to increase the inclusion of women in research and their representation in the biomedical research workforce.

Basic research supported by NINDS often focuses on how sex-specific mechanisms influence normal neurological functioning. In some conditions, such as chronic pain, investigators are trying to understand the reasons for the higher burden observed among women and how sex hormones may play a role in disease mechanisms. Diseases associated with aging, such as dementia, are associated with higher burden in women, in part because of the longer life expectancy among women, and researchers are working to understand how sex interacts with age and other biological and social factors to influence risk and outcomes of the disease. Other conditions that have both social and biological differences related to sex include spinal cord and traumatic brain injury, and investigators are working to understand factors that lead to different rates and symptoms of injury, as well as how sex influences injury recovery and outcomes. Women with epilepsy face special problems during pregnancy because of potential effects of anti-seizure medications on the fetus and during phases of the menstrual cycle. NINDS also supports research relevant to women in its rare disease portfolio. Researchers are exploring mechanisms and potential therapeutic targets for autism spectrum disorders, which often affect females and males differently. Finally, NINDS supports research to understand disparities, most notably in stroke and dementia, among racial and ethnic minority populations, and some of this work also explores differences by sex and how these relate to race and ethnicity to influence risk and outcomes.

II. Scientific Advances

Sex and Race Differences in the Association of Incident Ischemic Stroke with Risk Factors. Race-specific and sex-specific stroke risk varies across the lifespan, but few reports describe sex differences in stroke risk separately in Black individuals versus White individuals. To better understand these differences, NINDS's Reasons for Geographic and Racial Differences in Stroke (REGARDS) study—a prospective cohort study following more than 25,000 individuals across the U.S—is assessing the incidence and risk for stroke and cognitive decline, with a special focus on disparities in health outcomes across racial and ethnic groups, urban versus rural populations, and in women versus men (U01NS041588). In their most recent report, REGARDS investigators found sex differences in the association of several risk factors with stroke incidence in White individuals, specifically diabetes, systolic blood pressure, use of antihypertensive medications, and heart disease (e.g., traditional stroke risk factors); however, the explanation for male–female differences in Black participants was much less clear. On one hand, male–female differences in overall stroke risk were quite similar between the White participants and Black participants; both White female and Black female participants between the ages of 45 and 64 had anywhere between 28% and 32% lower stroke risk than men of the same race. However, the difference in risk between Black men and Black women could not explained by differences in traditional risk factors. Therefore, more research is needed to understand sex differences in stroke risk in Black Americans. The research team concluded that sex-specific risk factor management to prevent stroke could be beneficial for White individuals but not necessarily for Black individuals (Howard et al., 2019).

This clinical research study is related to Objective 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes") of the Trans-NIH Strategic Plan for Research on Women's Health.

Changes in Seizure Frequency and Antiepileptic Therapy during Pregnancy. Several recent NINDS-funded publications on epilepsy in pregnant women have provided actionable insights for improving health outcomes. Women with epilepsy face special problems during pregnancy because of potential effects of anti-seizure medications on the fetus and during phases of the menstrual cycle. Additionally, women with epilepsy may also experience lower birth rates than women without epilepsy; however, the evidence is mixed. To better understand these health risks, NINDS-funded investigators from the long-standing Maternal Outcomes and Neurodevelopmental Effects of Antiepileptic Drugs (MONEAD) study conducted a clinical trial to determine whether women with epilepsy have a higher seizure frequency during pregnancy than those who are not pregnant. In 2020, results from the trial were published in *The New England Journal of Medicine* and showed that there was no meaningful difference between pregnant women and nonpregnant women in seizure frequency. At the same time, however, the researchers observed more frequent increases in doses of antiepileptic drugs taken by pregnant versus nonpregnant women in the study, which is a potential cause of concern and an area for future research (Pennell et al., 2020).

This clinical study is related to Objective 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecological health") of the Trans-NIH Strategic Plan for Women's Health Research.

Small Study Suggests Botox May Be Potential Treatment for Chronic Pelvic Pain. NINDS-funded investigators are investigating pelvic pain associated with endometriosis, which often becomes chronic, persisting long after surgical and hormonal interventions. A recent small clinical study conducted by scientists at the NINDS Division of Intramural Research suggested that treating pelvic floor muscle spasm with botulinum toxin (frequently sold under the brand name Botox) may be effective for reducing and improving quality of life of women with chronic pelvic pain. Published in *Regional Anesthesia & Pain Medicine*, the study enrolled 13 women with chronic pelvic pain. Within 2 months of receiving the first botulinum toxin injections, pain decreased in all of the participants, with 11 out of 13 reporting that their pain was mild or had disappeared altogether. Additionally, usage of pain medication was reduced in more than half of the participants. Prior to receiving toxin injections, eight participants reported moderate or severe disability and after treatment, six of those patients noted an improvement. Larger clinical studies will need to confirm the current findings. In addition, future research will focus on the mechanisms underlying chronic pelvic pain and better understanding of ways in which botulinum toxin may help treat those disorders (Tandon et al., 2019).

This clinical study is related to Objective 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecological health") of the Trans-NIH Strategic Plan for Women's Health Research.

Basic Research on Sex Differences in Autism Spectrum Disorders. Autism spectrum disorders (ASD) are more prevalent in males; however, the underlying reasons for this sex difference are not altogether clear. A new study in *Neuron* from NINDS's Division of Intramural Research offers clues to why some autism spectrum disorders (ASD) are more common in boys than in girls. The research team found that a single amino acid change in the *NLGN4* gene, which has been linked to autism symptoms, may drive this difference in some cases. Every cell in the human body contains two sex chromosomes. Females have two X chromosomes; males have one X and one Y. Until now, scientists assumed that the version of *NLGN4* gene on the Y chromosome functioned the same as the one on the X chromosome. Using a variety of advanced research technologies—including biochemistry, molecular biology, and imaging tools—the research team found that the proteins encoded by these genes do function differently. The Y chromosome version produces a protein that is not able to move to the cells' surface as easily as the X chromosome version, which results in synaptic dysfunction and makes it more difficult for neurons in the brain to send signals to one another. When the researchers fixed the error using genetic methods in cells in a dish, they restored much of its correct function. The research team concluded that they

may have discovered a new mechanism that explains male bias in *NLGN4*-associated ASD (Nguyen et al., 2020).

This basic study is related to Objective 1.1 ("Discover basic biological differences between males and females") of the Trans-NIH Strategic Plan for Women's Health Research.

III. Promotion of Women's Health Research

CCRWH COVID-19 Work Group. NINDS Deputy Director Nina F. Schor, M.D., Ph.D., co-chairs (with Program Director Marrah Lachowicz-Scroggins, Ph.D., of the National Heart, Lung, and Blood Institute) the COVID-19 Work Group of the Coordinating Committee on Research on Women's Health, initiated in 2020. This work group has completed a funding opportunity and awarded grant landscape analysis for NIH related to the intersection between COVID-19 and women's health. Using this information, work group members are in the process of conducting a gap analysis to identify and implement initiatives that address research issues underrepresented in the current portfolio, which relates broadly to Goal 1 of the Trans-NIH Strategic Plan for Women's Health Research ("Advance rigorous research that is relevant to the health of women"). In addition, the work group is collaborating with the NIH Working Group on Women in Biomedical Careers to discern the unique needs of women in the biomedical workforce related to the COVID-19 pandemic.

NeuroCOVID database. Relevant to Goal 2 of the Trans-NIH Strategic Plan for Women's Health Research ("Develop methods and leverage data sources to consider sex and gender influences that enhance research for the health of women") and planned during FY 2020, NINDS recently launched a new database to collect information from clinicians about COVID-19-related neurological symptoms, complications, and outcomes, as well as COVID-19 effects on pre-existing neurological conditions. The COVID-19 Neuro Databank/Biobank (NeuroCOVID), which was created and will be maintained by NYU Langone Health, will be a resource of clinical information, as well as biospecimens from people of all ages who have experienced neurological problems associated with SARS-CoV-2 infection. NeuroCOVID can be accessed by scientists for research studies on preventing, managing, and treating neurological complications associated with COVID-19. The database will provide insight into how COVID-19 affects the nervous system and how common such complications are. Data will be made freely available to the research community and will enable scientists to examine women's health and racial and ethnic group disparities in COVID-19-related neurological outcomes.

Understanding Traumatic Brain Injury in Females: A State-of-the-Art Workshop Summary and Future Directions. In 2020, NINDS published findings from the "Understanding Traumatic Brain Injury (TBI) in Women" workshop held in 2017, which brought together researchers and clinicians to identify knowledge gaps, best practices, and target populations in research that focuses on females and/or sex differences within the field of TBI. The workshop was held in partnership with the Uniformed Services University of the Health Sciences in Bethesda, MD, and the Defense and Veterans Traumatic Brain Injury Center of Excellence. The workshop and the current literature underscore that females have been underrepresented in TBI studies and clinical trials and have often been excluded in preclinical studies. Such an absence in research on females has led to an incomplete and sometimes inaccurate understanding of TBI in females. Workshop participants concluded that overall, despite some progress, there remains an overabundance of research focused on males and relatively little on females.

This workshop and publication are related to Goals 1 ("Advance rigorous research that is relevant to the health of women") and 2 ("Develop methods and leverage data sources to consider sex and gender influences that enhance research for the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

IV. Advancement of Women in Biomedical Careers

Leveraging the NIH BRAIN Initiative to Support an Appropriate Gender Balance in Biomedical Engineering Sciences. NIH is concerned about the large loss of talented researchers during the transition from postdoctoral training to junior faculty positions, particularly those from underrepresented groups, including women. NINDS is leveraging existing initiatives

to address women's health research and biomedical workforce goals—for example, through the NIH BRAIN Initiative. Promoting diversity, including gender diversity, in the scientific workforce is critical to the success of the NIH mission and consistent with the mandates of the 21st Century Cures Act, which provides targeted support for the NIH BRAIN Initiative. The NIH BRAIN Initiative Advanced Postdoctoral Career Transition Award to Promote Diversity (K99/R00) program is designed to facilitate a timely transition of outstanding postdoctoral researchers from diverse backgrounds from mentored postdoctoral research positions to independent tenure-track or equivalent faculty positions (PAR-18-814). NINDS now includes women as an eligible group, as women are underrepresented in the disciplines pertinent to the BRAIN Initiative, including neuroscience, engineering, computer science, mathematics, and beyond. In the first 2 years of this program, NIH funded 30 exceptional women among the awardees.

NINDS Original Research: The Dearth of Women in Medical School Leadership Positions & Implications for Research. Although the absolute numbers of women trained to conduct neuroscience research have steadily increased over decades, several recent studies confirm that the fraction of leadership positions at U.S. medical schools occupied by women remains chronically low. To examine this phenomenon, NINDS Deputy Director Nina F. Schor, M.D., Ph.D., conducted a qualitative research study, which was published in the *Annals of Neurology* in 2019. The study found, for example, that for institutions in which women were in top leadership positions, the institutional research portfolio was dominated (60% ± 10%) by funding for public health and community-based research, as well as research-sustaining topics such as biomedical workforce training and infrastructure/facilities; conversely, for institutions in which men were in top leadership positions, the institutional portfolio was dominated by funding for basic and clinical research. It was not possible to determine whether women were chosen as research leaders at certain institutions or women choose to pursue research leadership positions at said institutions because of the nature of the institutional research portfolio. Indeed, there is evidence that women tend to make career choices away from academia altogether or away from leadership positions for several systemic reasons. More research is needed to better understand the role women in leadership play as drivers of the nature of institutional research portfolios.

NINDS's Research Program Award (aka the "R35 Award") is one of the institute's signature programs, which provides a unique opportunity of up to 8 years of grant funding versus the standard 2–5-year NIH grant. In recent years, however, less than 30% of R35 investigators have been women. To promote a balance of male and female awardees, NINDS is assessing how to encourage more female scientists to apply for the R35 award and has rolled out several outreach efforts to the extramural neuroscience community (e.g., revamped web and social media content). Going forward, NINDS's goal is to successfully diversify the applicant pool for the R35 award—with respect to research methodology and area of study, as well as investigator background and career stage.

V. Implementation of the NIH Policy on Sex as a Biological Variable (SABV)

NINDS program staff members ensure compliance with the SABV policy through detailed guidance to grant awards, as well as rigorous review of grant applications and award progress reports. In the pre-application stage, NINDS's program directors discuss with applicants the rationale for the policy and provide guidance on how best to incorporate SABV principles into their study design, including reference to the ORWH website. During review, Scientific Review Officers emphasize standard guidance as needed and make sure that the study section chairpeople encourage all reviewers to cover SABV during the application discussion. After peer reviews are completes, program staff members then consider all reviewers' SABV-related comments and factor that information into the institute's decision of whether an application is fundable. After awards are made, grantees must submit annual progress reports, which detail the steps they have taken to apply SABV principles during the course of the research project. Program staff members then follow up with awardees if it is not clear whether sufficient progress has been made.

VI. Inclusion of Women in Clinical Research

NINDS uses several approaches to facilitate and monitor inclusion of women in clinical research. During the peer review process for grant applications, the inclusion plan for clinical research is examined. Phase III clinical trials are required to have inclusion analysis plans to inform enrollment targets. Peer reviewers assess the inclusion plans, and prior to each NINDS Advisory Council meeting, program directors examine the reviewers' comments on unacceptable inclusion goals and resolve issues in writing with the investigators. Program directors also review enrollment data submitted in the annual progress reports and determine whether the enrollment targets for gender inclusion are scientifically appropriate. NIH monitors inclusion through a centralized system and allows access to institute-specific records and cumulative reports, enabling program staff members to track enrollment data.

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National Institute of Nursing Research

I. Executive Summary

The mission of the National Institute of Nursing Research (NINR) is to promote and improve the health of individuals, families, and communities. NINR strives to conduct, foster, and support research and research training using a holistic perspective to improve health outcomes and eliminate health inequities by bridging biomedical science with the realities of people's lives and living conditions, biological and social determinants, health care and community interventions, and scientific breakthroughs with their implementation in nursing practice and policy across a wide variety of clinical and community settings.

NINR promotes the study of women's health and sex/gender influences on health and disease through research on health topics across the lifespan, among a variety of communities, and with a commitment to advancing the careers of women scientists. The institute's support of women's health research is reflected in NINR's Strategic Plan, which describes NINR's interest in research on sex and gender differences, health disparities, social determinants of health, and emphasizing scientific program partnerships with underrepresented and minority communities.

Throughout FY 2019–2020, NINR continued to support many research efforts relevant to women's health, with specific attention to issues surrounding pregnancy, management of chronic conditions, promotion of wellness, and identifying and ameliorating health disparities. Through these efforts, NINR seeks to strengthen research specific to women, whether as patients, caregivers, or community members. The institute actively ensures that research it supports includes a diversity of women and that it addresses racial and ethnic disparities in health experienced by women. Finally, because of the demographics of the nursing field, most of the investigators supported by NINR are women. NINR promotes these scientists across the span of their careers through extramural grants, intramural grants, and training programs, and the institute remains dedicated to the growth of current and future nurse scientists.

II. Scientific Advances

Microbiome Study Identifies Possible Causes and Protectors Against Preterm Birth

Spontaneous preterm births (sPTB) are the leading cause of morbidity and mortality in neonates. In a retrospective analysis comparing women with sPTB and term births, researchers characterized the cervicovaginal microbiota of pregnant women to understand the potential influence of the microbial environment. Variation in the categories of microbial species were observed at different stages of pregnancy. Further analysis identified a handful of cervicovaginal microbial species associated with increased risk of sPTB overall, with different species associated with sPTB in African American and non–African American women. High levels of Lactobacillus, a class of bacteria associated with positive reproductive and health outcomes, appeared to counteract the effects of some microbe-associated sPTB risk. The Lactobacillus effects were also dependent on high levels of β-defensin, an antimicrobial protein produced by the immune system. However, the interactions of these factors are complex, and more research is needed. These findings show a potential use of prenatal profiles of microbiota, immune molecules, and other potential biomarkers and modifiers to identify women at risk for sPTB (Elovitz et al., 2019).

This clinical research relates to Objective 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health") of the Trans-NIH Strategic Plan for Women's Health Research.

Racial and Ethnic Disparity Trends in Severe Maternal Morbidities

Severe maternal morbidities (SMMs)—such as hemorrhage, embolism, and stroke—have been increasing in the United States since 1997, and women from racial–ethnic minorities have been affected more than non-Hispanic White women. To better understand contributing factors, researchers analyzed more than 8 million birth records in California from 1997 to 2014

using the Centers for Disease Control and Prevention's index for SMM during delivery hospitalization. The index includes clinical criteria associated with severe events such as blood transfusions, acute respiratory distress, and acute renal failure (Leonard et al., 2019). They found higher prevalence for SMMs in racial–ethnic minorities, reflecting national statistics, with the highest in non-Hispanic Black women (1.63%) and the lowest in non-Hispanic White women (0.84%). There was a nearly threefold increase across all racial–ethnic minorities during the study period. The elevated risk for SMMs in non-Hispanic Black, Hispanic, and American Indian/Alaska Native women was attenuated with adjustments for sociodemographic and clinical factors, such as anemia, pre-pregnancy body mass index (BMI), and chronic comorbidities but were persistently higher than in non-Hispanic White women. The researchers concluded patient-level risk factors did not fully explain the racial and ethnic disparities in SMM incidence, and explanations for these disparities could be explored in future research into topics such as health care delivery, community environment, and chronic stress. A separate analysis of more than 6 million California birth records from 1999 to 2011 revealed a fourfold increased risk for SMM associated with stillbirths in comparison with live births, and this risk for stillbirth-associated SMM was 5.4-fold after 29 weeks of gestation. Hypertensive disorders, infections of the fetal or placental tissues, disrupted placentas, and fetal malformations were among the stillbirth conditions that could contribute to the increased risk for SMMs (Wall-Wieler et al., 2019).

This clinical research relates to Objective 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health") of the Trans-NIH Strategic Plan for Women's Health Research.

Community Nursing Approach to Improve Management of Pelvic Inflammatory Disease

Pelvic inflammatory disease (PID) is a common condition in young women. Post-acute care for mild to moderate PID is done through outpatient treatment rather than hospitalization. Poorly managed PID can lead to infections, such as *Neisseria gonorrhoeae* and *Chlamydia trachomatis*, with subsequent development of chronic pelvic pain in approximately 40% of cases and increased incidence of impaired fertility. In a randomized controlled trial, researchers assessed the impact of a technology-enhanced community health nursing intervention to improve self-management in females ages 13–25 with PID in comparison with usual care. The participants were recruited from clinics at a large urban academic medical center; over 90% were African American, and 86% received Medicaid coverage. The intervention included automated text message reminders to take medication and adhere to the treatment regimen, as well as follow-up with a community health nurse for clinical assessment, a detailed self-management education session, and an in-home visit. At the 90-day follow-up, the differences in positives tests of sexually transmitted infection (STI; specifically, *N. gonorrhoeae* and *C. trachomatis*) between the intervention and control groups (6 out of 135 and 13 of 125, respectively) were not statistically significant. However, with more *C. trachomatis*–positive tests at baseline in the intervention group, the differential decrease in STI-positive tests was greater for the intervention group (48 of 140 at baseline and 6 of 135 at 90 days for the intervention group, compared with 34 of 133 baseline and 13 out of 112 at 90 days for the control group). These findings suggest that a technology-supported community health nurse intervention can enhance the management of post-PID outcomes in young women (Trent et al., 2019).

This clinical research relates to Objective 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health") of the Trans-NIH Strategic Plan for Women's Health Research.

Influence of Family Environment and Acculturation in Latina Mothers' Dietary Behaviors

The diets of U.S. Latinx individuals who adopt U.S. culture generally change from healthy to unhealthy, with consumption of fewer fruits and vegetables, more salt and sugar, and more food prepared outside of the home. Acculturation of children in Latinx households has been shown to influence the quality of their mothers' diets. A longitudinal sociocultural study evaluated the purchase of fruits and vegetables, the quality of family interactions, and patterns of mothers' away-from-home eating in households of Mexican origin near California's border with Mexico. In families with traditional (maintaining Latinx culture) or bicultural

(maintaining traditional and U.S. culture) mothers and bicultural children, expressiveness and positive interactions around food were associated with the purchase of more fresh produce, healthier maternal diet (e.g., more vegetables, less fat), and fewer away-from-home meals (although this increased over time). Households with traditional or bicultural mothers and assimilated (which the authors described as rejecting traditional culture and adopting U.S. culture) children had less positive family interactions regarding food, purchased fewer fruits and vegetables, and consumed more away-from-home meals. These findings indicate that interventions to encourage healthy diets should address family interactions and discussions (Soto et al., 2019).

This clinical research relates to Objective 1.3 ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes") of the Trans-NIH Strategic Plan for Women's Health Research.

III. Promotion of Women's Health Research

- NINR conducted a virtual workshop September 29, 2020, titled "Innovative Models of Care for Reducing Inequities in Maternal Health." Co-sponsors included the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, the National Institute on Minority Health and Health Disparities, the Office of Research on Women's Health (ORWH), and the Tribal Health Research Office. The workshop explored how nurses, midwives, and birth companions can improve maternal and infant health for women in U.S. communities affected by racial discrimination, socioeconomic inequality, and other system-level factors that contribute to maternal health disparities.
- NINR's current research initiatives include one on maternal nutrition and pre-pregnancy obesity. *Maternal Nutrition and Pre-pregnancy Obesity: Effects on Mothers, Infants and Children (Clinical Trial Optional)* (PA-18-776) encourages applications to improve health outcomes for women, infants, and children by stimulating interdisciplinary research focused on maternal nutrition and pre-pregnancy obesity. Maternal health significantly impacts not only the mother but also the intrauterine environment and subsequently fetal development and the health of the newborn. (Open date: September 5, 2018. Expiration date: September 8, 2021.)
- NINR participates in RFA-OD-19-029 (*The Intersection of Sex and Gender Influences on Health and Disease [R01 Clinical Trial Optional]*), which is led by ORWH. This funding opportunity promotes research that examines sex and gender factors and their intersection in health and disease and addresses Goal 1 of the Trans-NIH Strategic Plan for Women's Health Research, to advance rigorous research that is relevant to the health of women. NINR states a particular interest in applications that propose research on sex/gender influences in HIV/AIDS research. (Open date: October 25, 2019. Expiration date: November 27, 2021.)
- In addition, NINR participates in important trans-NIH initiatives focused on women's health, including:
  - NIH Maternal Morbidity Task Force
  - Coordinating Committee on Research on Women's Health (CCRWH)
  - NIH Pediatric Research Consortium (N-PERC)
  - NIH Working Group on Women in Biomedical Careers

IV. Advancement of Women in Biomedical Careers

- NINR supports a larger proportion of female scientists than male scientists. A working group of the National Advisory Council of Nursing Research recently produced a report with information and recommendations that identify strengths, limitations, challenges, and opportunities to enhance nursing research education and training and diversify the nursing scientist workforce. In its report, the working group stated that NINR has an important role in advocating for enhancements across NIH that would improve opportunities and outcomes for women scientists and that NINR's support would greatly enhance the desirability and

realistic possibility of successfully pursuing a nurse scientist career.

- NINR promotes individual predoctoral and postdoctoral trainees through the F31 and F32 mechanisms and supports mentored career development through the K01, K23, and K99/R00 mechanisms. Women's health is among the topics of current training and career awards. A few examples include:
  - F31 NR018363, Neighborhood Disorder and Epigenetic Regulation of Stress Pathways in Preterm Birth
  - K01 NR016984, Metabolomics of Labor Dysfunction in African-American Women
  - R00 NR017101, Influence of Diet, Iron Stores, and Toxic Metals on Uptakes and Effects on Uterine Fibroid Risk in African American Women; and
  - F31 NR18588, Biomarkers of Long-Term Fatigue in Breast Cancer Survivors Treated with Radiation

V. Implementation of the NIH Policy on Sex as a Biological Variable (SABV)

NINR has implemented the following practices to comply with NIH's policy to consider SABV in research design, analysis, and reporting:

- NINR has added language to funding opportunity announcements (FOAs) and notices of special interest (NOSIs) stating that investigators should present adequate plans to address relevant biological variables, such as sex, for studies in vertebrate animals or human subjects.
- NINR program staff members discuss incorporating SABV with potential grant applicants prior to submission.
- In the review of all applications assigned to NINR that have gone through peer review, program staff members work with principal investigators to ensure all concerns with how SABV is incorporated into the research design are addressed prior to resubmission or funding of the application.

VI. Inclusion of Women in Clinical Research

NINR actively supports research that examines the effect that sex and gender differences have on health. For example, adverse symptom experiences can differ between men and women with the same disease or condition. Additionally, NINR supports research on sex and gender differences in response to treatment. Understanding how both symptoms and treatment responses vary over time and across the lifespan is also an important area of study.

Among individuals who presented at the emergency department with possible acute coronary syndrome (ACS), men and women who reported higher symptom distress were more likely to be "ruled in" for ACS. Women, whether ruled in or ruled out for ACS, reported more chest pressure, and chest pressure was a significant predictor for ACS diagnosis in women (Mirzaei et al., 2020).

Engagement with health care providers (HCPs) is an important component in medication adherence and management of psychological distress for people living with HIV (PLWHs). Male PLWHs with depressive symptoms had lower levels of HCP engagement. Male PLWHs with good medication adherence had higher levels of engagement with HCPs, suggesting that HCP interaction could mitigate psychological symptoms. Female PLWHs did not have either of these associations, and other studies have shown that female PLWHs have low levels of HCP engagement and poor medication adherence (Baik et al., 2020).

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National Library of Medicine

I. Executive Summary

The National Library of Medicine (NLM) is a leader in biomedical and health data science research and the world's largest biomedical library. NLM research and information services support scientific discovery, health care delivery, and public health decision-making. NLM's efforts in this space support and advance women's health and help create a more diverse and data-skilled workforce.

NLM supports projects that provide health information to populations experiencing health disparities, including women, children, and sexual and gender minorities. Through its more than 8,000 organizational members of the Network of the National Library of Medicine (NNLM), NLM deploys community-relevant strategies to meet the needs of stakeholders. This network provides a trusted local platform for outreach and engagement in support of major NIH initiatives.

NLM strives to improve the diversity of the biomedical information science workforce, both within NLM and across the larger scientific community, to ensure rigorous research that benefits all. NLM supports research grants to apply computational and information science approaches to reduce bias in health data and health communication. For example, NLM-funded researchers have developed a data science–enabled approach to better manage endometriosis and improve the effectiveness of clinically useful risk prediction approaches by mapping human genome data to different types of clinical data predicting risks, including those associated with gender.

NLM-supported researchers use informatics tools to assist in automated interpretation of cervical visualizations and create models to predict preterm births.

II. Scientific Advances

Researchers at NLM and researchers supported by NLM grants use computational approaches and information science to understand and improve the health of women and girls and develop computational methods and tools to support research on the influences of sex and gender on health and disease.

Computational Biology and Information Science Approaches to Address Women's Cancers

In collaboration with the National Cancer Institute (NCI), NLM has conducted research since 2003 using medical image processing, machine learning, and artificial intelligence (AI) methods to develop an automated visual evaluation (AVE) algorithm for reliable prediction of cervical precancer. The AVE algorithm was trained and validated using image data and other clinical data from women participants in population-based longitudinal studies conducted by the NCI and microscopy images of cervical cytology and histopathology (Guo, Xue, Long, & Antani, 2020; Guo, Xue, Mtema, et al., 2020; Hu et al., 2019; Schiffman et al., 2020; Sornapudi et al., 2019; Sornapudi et al., 2020; Zou et al., 2020; Ganesan et al., 2019; Xue et al., 2019). In FY 2019–2020, NLM:

- Evaluated the use of smartphones or similar devices to provide high-quality point-of-care cervical screening. Results were used to improve reliability of the AI and minimize adverse impact caused by getting data from various clinical settings and devices.
- Developed a new algorithm to classify treatability by thermal ablation.
- Developed a novel direct metric learning algorithm that does not require region of interest localizations on the cervical image and maintains sensitivity while improving specificity over the AVE algorithm.
- Devised a new algorithm to study the morphology of cervical cells in the biopsied tissue images with unknown magnification captured using a smartphone affixed to a common optical microscope.
- Conducted pilot studies to study performance of the AVE algorithm in detecting cervical precancer in women living with HIV.

NLM used network biology to study breast cancer resistance. NLM researchers developed a method to uncover a network-level association of mutational

signatures and dysregulated molecular pathways. The pathways identified with this method provide novel insights into mutagenic processes in breast cancer that have the potential to become steppingstones for developing personalized drug therapies (Choobdar et al., 2019; Kim et al., 2020).

This relates to Objective 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes") of the Trans-NIH Strategic Plan for Women's Health Research.

PhendoPHL: A Data-Science Enabled Personal Health Library to Manage Endometriosis

Endometriosis is a chronic condition estimated to affect 10% of women of reproductive age. It has a very high burden on quality of life and productivity, and the self-management needs of women living with this disorder are multiple. NLM-funded researchers are working to design, develop, and evaluate a data science–enabled personal health library, PhendoPHL, to support the self-management needs of women living with endometriosis. Grounded in self-determination theory and informed by user-centered design methods, PhendoPHL aims to enable women to explore their own health patterns through interactive visualizations of integrated clinical and self-tracked data, identify temporal personalized patterns and compare with population norms through novel data-science methods, and see actionable visualizations of data for shared decision-making during patient–provider encounters. In FY 2019–2020, researchers identified themes about facilitators and obstacles for carrying out tasks for endometriosis care (e.g., establishing goals, values, identifying treatments). To understand what timeline visualization functions are preferred by patients and providers, researchers developed working prototypes to convey longitudinal self-tracking data from a single patient record. Partnering with an existing menstrual self-tracker application, researchers analyzed the deidentified data of 378,000 users and 4.9 million natural cycles of user-tracked observations across a wide range of categories to better understand variation of menstrual experience within and across individuals. A dataset of self-tracked endometriosis daily symptoms, treatments, self-management strategies was generated for nearly 11,000 research participants. The researchers also identified indicators of retention in remote digital health studies (Ensari et al., 2020; Li et al., 2020; Pratap et al., 2020; Urteaga et al., 2020).

This relates to Objectives 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health"), 2.1 ("Expand and develop advanced and innovative approaches for study design, data collection, and analysis to optimize data quality and the ability to detect the influences of sex and gender on health and disease"), and 2.3 ("Leverage secondary data sources for research on the health of women through a big data enterprise that includes data sharing and analytic strategies") of the Trans-NIH Strategic Plan for Women's Health Research.

Toward Improved Understanding of Sex Differences in Drug Response: Developing Gene and Pathway-based Informatics Methods to Examine Sex-Differential Genetic Effects

Women are at more than 1.5-fold higher risk for adverse drug events, such as drug-induced liver injury. Between 1997 and 2000, eight out of the ten drugs withdrawn from the market posed greater health risks to women. Some risks were associated with dosing, but other mechanisms related to biological sex differences are poorly understood. Throughout the drug development pipeline, sex is rarely considered, and labels are routinely left out of analysis, even at the computational level. An often-cited reason for not studying women is within-sex variability caused by the menstrual cycle. Genetic data from genome-wide association studies (GWAS) and gene expression levels provide opportunities for analyzing the effects of sex—allowing for insights into biological function and examination of unlabeled data because sex can be imputed. Additionally, network-based analysis of these data has the benefit of increasing the signal-to-noise ratio by relying on prior information about gene–gene interactions and pathways, and it aids in the biological interpretation of results. To improve understanding of sex-differential effects, NLM-funded researchers are using genetic and gene expression data to (1) investigate the molecular effects of between-sex differences at the organ level and within-sex differences caused by menstrual cycle hormone variability, (2) develop network-based methods for detecting sex-differential

effects in GWAS, and (3) link identified between- and within-sex variability to drug response. In FY 2019–2020, researchers developed meta-analytical methods to impute sample sex from expression, applied the sex labeling method to publicly available human and mouse data, and conducted a comprehensive analysis of sex bias, cell line sex, and sample mis-annotation in gene expression data (Flynn et al., 2021; Wang et al., 2020).

This relates to Objective 1.1 ("Discover basic biological differences between females and males") of the Trans-NIH Strategic Plan for Women's Health Research.

Prediction of Preterm Birth in First Time Mothers (Nulliparous Women)

Preterm birth (PTB) is the leading cause of mortality and long-term disability among neonates, with heavy emotional and financial consequences to families. Prediction of PTB risk is exceedingly challenging for first-time mothers (nulliparous women) because of a lack of prior pregnancy history. The challenge of improving PTB prediction is because of the inherent complexity of its multifactorial etiology and the lack of approaches capable of integrating and interpreting large multidisciplinary data. NLM-funded researchers developed predictive models for PTB based on nongenetic maternal attributes. An important research question is whether factors other than history of PTB can be used to identify a nulliparous patient at risk. The researchers are working to devise longitudinal risk prediction methods for PTB that integrate all available data. This work is addressing risk for PTB by combining genetic factors with other clinical factors to determine risk and using longitudinal data and models to optimize scheduling of patient visits, testing, and treatment. They contributed data science expertise to improve data preparation for the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development dataset called nuMoM2b, which is a prospective cohort study of a racially, ethnically, and geographically diverse population of 10,038 nulliparous women with singleton gestation. In FY 2019–2020, they identified high-level groups of risk factors and variables, calculated summary statistics for features measured, examined the distribution of gestational ages (and thus the distribution of preterm birth and full-term birth) for patients in certain risk groups, and collected statistics to build a sequential decision model to improve patient care as it relates to visits and diagnostics tests (Joseph et al., 2020; Shenhav et al., 2019).

This relates to Objective 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health") of the Trans-NIH Strategic Plan for Women's Health Research.

Decision-Making Modeling for Treating Intimate Partner Violence

Approximately 1 in 4 women experience severe intimate partner violence (IPV) during their lifetime, and many of these situations result in serious injury or death. Gender-specific group therapy is widely considered the standard treatment for IPV, but some participants of these groups do not experience a decrease in violence in response to these treatments. Reports on the effectiveness of standard treatments and research findings suggest that different treatments may be more effective in reducing violence recidivism in certain situations. Factors such as demographics, types of violence, and treatment delivery influence how participants respond to treatment. Standard IPV treatment does not reflect this variability and does not provide equal opportunity for recovery to all who are struggling with IPV. In FY 2019–2020, researchers conducted a systematic review and meta-analyses of existing evidence of the treatment of intimate partner violence perpetrators and victims. They created an integrated dataset representing more than 1,500 individuals by combining data from existing studies, electronic health records, and national data sources. Using this integrated dataset, the researchers used data mining approaches, to characterize subgroups of victims and perpetrators based on patterns such as conflict tactics, as well as types and degree of violence. They also observed synergistic health correlate terms that, when found in a woman's electronic health record, indicated that pregnancy and IPV will occur together in that record. The researchers developed several possible explanations for this co-occurrence. They also began work on a conceptual framework for the dynamic systems modeling in combination with agent-based modeling to identify patterns that could be used to develop predictive models to assess potential effectiveness of treatment for IPV (Karakurt et al., 2019; Liu et al., 2020; Yilmaz et al., 2020).

This relates to Objective 1.3 ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes") of the Trans-NIH Strategic Plan for Women's Health Research.

III. Promotion of Women's Health Research

Information Resources

NLM funds many health information resources with information in support of women's health research and care delivery. MedlinePlus, produced by the NLM, provides content specific to women's health issues, including pregnancy, breast cancer, cervical cancer, and bone density screenings, as well as topical issues such as body image and menopause. MedlinePlus also features health topics about HIV/AIDS in women, heart disease in women, sexual problems in women, and women's health exams and tests. The recent addition of MedlinePlus Genetics enhances coverage of women's health issues with several genetic disorders specific to women, including Turner syndrome, primary ovarian insufficiency, and triple X syndrome. The MedlinePlus pages provide links to relevant journal articles, key statistics, and research relevant to women's health. Research indicates that most online health information seekers are women; the MedlinePlus audience is estimated to be two-thirds women.

The LactMed® drugs and lactation database includes information about drugs and other chemicals to which breastfeeding mothers may be exposed, the levels of such substances in breast milk and infant blood, and the possible adverse effects in the nursing infant. Suggested therapeutic alternatives to those drugs are provided when appropriate. All data presented in this database are derived from the scientific literature and fully referenced. A peer review panel reviews the data to ensure scientific validity and currency.

NLM's Genetic Testing Registry (GTR) includes information on tests for numerous conditions that relate to women's health. GTR currently includes information on nearly 700 clinical tests for conditions such as ovarian cancer, premature ovarian failure, ovarian insufficiency, breast cancer, uterine growth restriction and three research tests for breast and/or ovarian cancer. In 2019, 147 tests for these women's health–related phenotypes were registered in GTR, and 328 were registered in 2020. There are four laboratories registered that specialize in women's health, two of which are in the United States. NLM's ClinVar database aggregates information about genomic variations and their relationship to human health. ClinVar extensively expanded its offerings related to women's health, adding more than 7,400 new variants related to the BRCA1 and BRCA2 genes and more than 19,000 submitter reports about the clinical significance of those variations.

NLM's Bookshelf provides free online access to books and documents in the life sciences, including systematic reviews and clinical guidelines. In FY 2019–2020, the Bookshelf added 65 new systematic reviews, as well as guidelines related to women's health. Included among the many topics are screening, genetic testing, and treatments for breast cancer, screening for hepatitis B virus and HIV in pregnant women, treatments for urinary incontinence, and telehealth services designed for women.

This relates to Objective 3.2 ("Identify collaborative opportunities and leverage partnerships to disseminate research that improves the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

Women's Health Technologies Coordinated Registries Network Project

NLM partnered with the Food and Drug Administration and the Office of the National Coordinator for Health Information Technology for the Patient-Centered Outcomes Research Trust Fund (PCORTF) project, Developing a Strategically Coordinated Registry Network (CRN) for Women's Health Technologies, which developed and tested a standards-based approach to establishing a CRN allowing data exchange among three registries (Office of the Assistant Secretary for Planning and Evaluation, 2017). NLM supported the informatics working group, recommended the use of clinical terminologies and health data standards, facilitated consensus on a minimum core set of common data elements across three registries, and supported the development of the HL7 Fast Healthcare Interoperability Resources (FHIR) Implementation Guide.

This relates to Objectives 2.3 ("Leverage secondary data sources for research on the health of women through a big data enterprise that includes data sharing and

analytic strategies"), 3.1 ("Design and test approaches to promote the adoption, adaptation, and integration of evidence-based interventions in public health, clinical practice, and community settings"), and 3.2 ("Identify collaborative opportunities and leverage partnerships to disseminate research that improves the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

Outreach Initiatives to Reduce Health Disparities and Improve Women's Health

The NLM's Network of the National Library of Medicine (NNLM) leverages more than 8,000 academic health sciences libraries, hospital and public libraries, and community-based organizations across the United States and coordinates health sciences information services regionally through Regional Medical Libraries (RMLs). In FY 2019–2020, the RMLs funded projects to improve access to health information, increase engagement with research and data, expand professional knowledge, and support outreach that promotes awareness and use of NLM resources in local communities. Many projects address women's health issues and seek to mitigate health disparities in a culturally sensitive manner. Projects are developed with community partners and grantees and are delivered in customized ways to reach diverse communities. NNLM fosters relationships with public health organizations that serve women and girls. With the Black Girl Health Foundation, NNLM provided dialogue and resources for young women's mental health (Black Girl Health, 2021). The February Health Heart Gathering and the Go Red for Women's Health Walk and Chronic Disease Health Screening provided nutrition information and family-friendly physical activity for Native American elders and families in community intergenerational celebrations of women's health. The Superwoman Project helped women of color cope with the needs and challenges of mothering in the wake of the COVID-19 pandemic and provided mothers of color with up-to-date and medically sound information related to COVID-19. This project also provided general support to moms and information about child mortality, parenting, mental and holistic health, marriage and relationships, leadership, and navigating the workforce. A series of film screenings and discussions were held for women in underserved areas with the director of *Life Interrupted*—a documentary featuring empowering stories of breast cancer survivors told from the survivors' perspectives.

This relates to Objective 3.2 ("Identify collaborative opportunities and leverage partnerships to disseminate research that improves the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

NLM Portfolio of Exhibitions about Women's Health and Women in Medicine

NLM's four traveling exhibitions about women's health and women in medicine traveled to 43 sites across the country in FY 2019–2020. A reported 85,804 visitors experienced the exhibitions before this program was put on hold because of COVID-19. Online adaptations of these exhibitions garnered nearly 160,000 page views.

- *Confronting Violence: Improving Women's Lives* examines the history of domestic violence and the medical community during the 1970s–1980s.
- *The Literature of Prescription: Charlotte Perkins Gilman and "The Yellow Wall-Paper"* explores mental health and gender through the lens of one woman's experience during the late 19th century.
- *Pictures of Nursing: The Zwerdling Postcard Collection* looks at cultural representations of nurses over the past 100 years.
- *Rise, Serve, Lead! America's Women Physicians* recognizes the legacy of women physicians.

An additional online-only exhibition, *Changing the Face of Medicine: Celebrating America's Women Physicians*, launched in 2003, acknowledges the accomplishments of over 300 women physicians and garnered 1,015,641 page views during the same time.

This relates to Objective 3.2 ("Identify collaborative opportunities and leverage partnerships to disseminate research that improves the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

IV. Advancement of Women in Biomedical Careers

NLM supports efforts to advance career development for women in biomedical sciences through unique

training opportunities to bolster inclusion of women underrepresented in biomedical informatics and data science.

NLM's University-Based Training Programs for Biomedical Informatics and Data Science

NLM is committed to building a workforce for data-driven research and health and is improving the pipeline of young scholars from groups underrepresented in the field of biomedical information science. NLM is a leading funder of Ph.D.-level training in biomedical informatics and data science, which ensures data science and open science proficiency, expands research methods that support rigor and reproducibility, promotes and increases workforce diversity, and engages the next generation of researchers.

NLM's university-based research training program supports 16 universities across the country that enroll approximately 200 predoctoral and postdoctoral fellows and trainees to enhance recruitment of women and other groups underrepresented in biomedical informatics and data science. The program leverages NLM's long-term investment strategy to help shape the field of biomedical informatics and data science. Graduates serve as leaders in academia and industry. NLM encourages its university-based programs to share curriculum materials and use-case examples with other graduate-level training programs to accelerate data science training in other universities. NLM provides awards to sponsor summer research experiences for undergraduates and others interested in careers in biomedical informatics and data science. In FY 2020, supplemental funding enabled training programs to work with a coalition of 12 faculty members from minority-serving institutions who designed a 10-week data science research internship program incorporating data science skills focused on machine learning, statistics, and clinical informatics; ethical considerations in data science; and core skills for academic success and career development related to the analysis and presentation of scientific literature and findings. NLM trained 89 women in these programs in 2019 and 75 in 2020. In FY 2020, NLM also supported three NIH National Research Service Award predoctoral fellowships.

This relates to Objectives 4.1 ("Enhance knowledge of sex and gender influences on health and disease among all scientists, clinicians, and other health professionals to accelerate the translation of that knowledge into practice"), 4.3 ("Enhance and develop programs to recruit, support, retain, and advance women at all stages of their research careers, from early career to leadership positions"), and 4.4 ("Promote and support policies, mentoring and networks, collaborations, and infrastructure to retain and advance women in their careers") of the Trans-NIH Strategic Plan for Women's Health Research.

Innovative Programs to Enhance Pathways for Women in Biomedical Careers

NLM leverages its position as both a hub of data science and a leader in the history of science to develop innovative programming to enhance pathways for women in biomedical careers. In so doing, NLM works to further NIH-wide efforts to foster a culture that not only advances science but also ensures the development and retention of a diverse, safe, and respectful workforce for the future. In October 2019, the NLM hosted a women-led codeathon on the NIH campus (NCBI Insights, 2019; NLM In Focus, 2019). This first-of-its-kind event brought together 46 women representing NIH, academia, and the private sector. Over the course of three days, attendees worked collaboratively to tackle various scientific problems while taking advantage of networking opportunities and instructional sessions. Several teams continued to collaborate after the codeathon concluded, and their work has resulted in manuscripts and posters submitted to conferences. That same month, NLM also hosted science journalist Angela Saini, who presented a special lecture on gender, race, and power in science (Bock, 2019). Over the course of the lecture, Saini systematically dispelled several sexist and racist myths that have been promulgated through non-rigorous scientific research, underscoring how systemic biases have informed the conduct of science. With nearly 1,000 views, the lecture has seeded conversations across NLM on how to both mitigate the impacts of implicit bias and promote a more diverse workforce to enhance research rigor.

NLM established the Ada Lovelace Computational Health Lecture Series to highlight the research of women in computational sciences. In 2020, speakers

presented talks titled "Implications of Poetical Science for Advancing Health Equity through Information Visualization," "Sequence-Structure-Function Modeling for the 3D Genome," and "Dynamic Genome Rearrangements in the Ciliate *Oxytricha*."

This relates to Objectives 4.1 ("Enhance knowledge of sex and gender influences on health and disease among all scientists, clinicians, and other health professionals to accelerate the translation of that knowledge into practice"), 4.3 ("Enhance and develop programs to recruit, support, retain, and advance women at all stages of their research careers, from early career to leadership positions"), and 4.4 ("Promote and support policies, mentoring and networks, collaborations, and infrastructure to retain and advance women in their careers") of the Trans-NIH Strategic Plan for Women's Health Research.

V. Implementation of the NIH Policy on Sex as a Biological Variable (SABV)

The Database of Genotypes and Phenotypes (dbGaP) Supporting Sex-Based Research

Through its publicly accessible databases, NLM enables researchers to analyze results of studies by sex/gender. Inclusion of this field allows users to sort study results rapidly and effectively by sex/gender, which enhances study analysis and the design of follow- on studies. The Database of Genotypes and Phenotypes (dbGaP) archives and distributes data from studies that investigate the interaction of genotype and phenotype in humans. This database contains more than 1,700 studies with deidentified genomic and phenotypic (clinical observation) data on more than 2.8 million study participants. Approximately 54% of participants in studies submitted to dbGaP with a gender designation are female.

This database provides summary information of study results to the public. Researchers can request datasets in dbGaP to conduct their own analyses—for instance, looking across multiple studies for a common genetic feature associated with a certain condition. Because sex is a phenotype measure in virtually all studies, approved researchers can conduct analyses that examine hypotheses related to biological and medical differences that might exist between the sexes. For example, researchers could request large datasets from studies that include cholesterol measurements and then analyze whether certain genotypes thought to be related to elevated LDL (low-density lipoprotein) differed between males and females. The ability of researchers to analyze genotype and phenotype data in dbGaP by sex/gender of study participants is an important way that NLM enables research to address sex/gender differences.

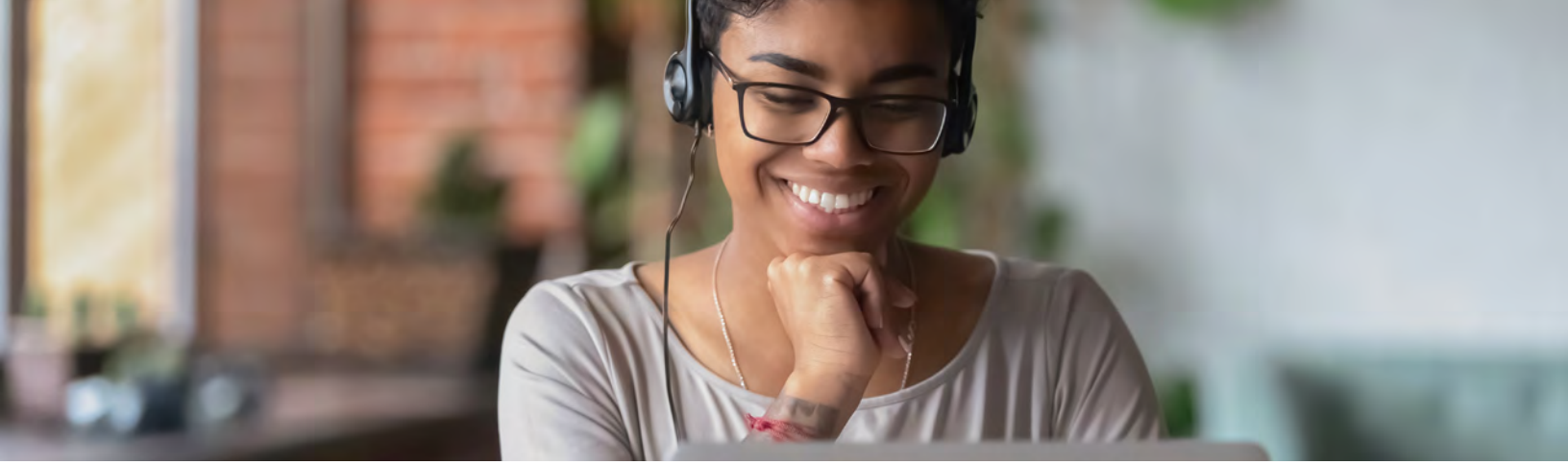
The dbGaP archives also include data from numerous studies that specifically relate to women's health, such as the Women's Health Initiative and the Women's Interagency HIV Study.

This relates to Objectives 1.1 ("Discover basic biological differences between females and males"), 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes"), 2.1 ("Expand and develop advanced and innovative approaches for study design, data collection, and analysis to optimize data quality and the ability to detect the influences of sex and gender on health and disease"), and 2.3 ("Leverage secondary data sources for research on the health of women through a big data enterprise that includes data sharing and analytic strategies") of the Trans-NIH Strategic Plan for Women's Health Research.

VI. Inclusion of Women in Clinical Research

ClinicalTrials.gov Enhances Capabilities Related to Women's Health Data

NLM supports the NIH Policy on the Inclusion of Women and Minorities as Subjects in Clinical Research through its information resources that include the eligibility of women in clinical research studies. ClinicalTrials.gov, a resource provided by the NLM, is a public database of privately and publicly funded clinical studies conducted around the world. Reporting requirements help ensure that information about the sex/gender of trial participants is publicly accessible and transparent,



which is an important step in facilitating the monitoring of the participation of women in clinical trials. Federal regulations require submitted registration information to include the sex/gender of participants who may enroll in the clinical trial. After the trial is completed, results information must include the number of participants enrolled in each arm of the clinical trial by sex/gender, and summary results must be submitted with valid analyses by sex/gender, race, and ethnicity for applicable NIH-defined Phase III clinical trials to ClinicalTrials.gov.

NLM is engaged in ongoing efforts to enhance the manner in which information on ClinicalTrials.gov (including sex/gender information) is searched, displayed, accessed, and analyzed to enable increased monitoring of the participation of women in trials and their results.

This relates to Objectives 2.3 ("Leverage secondary data sources for research on the health of women through a big data enterprise that includes data sharing and analytic strategies") and 2.4 ("Expand and refine methodologies to improve the recruitment and retention of women underrepresented in clinical research") of the Trans-NIH Strategic Plan for Women's Health Research.

Community Engagement Partnership with All of Us *Research Program*

Community centers and libraries are poised to serve populations underrepresented in biomedical research (UBR), including women and children. The NLM community engagement partnership with the NIH *All of Us* Research Program began in FY 2018 to reach library audiences to raise awareness and educate the public about the ability to participate in a national research data collection effort. *All of Us* strives to enroll 50% of research participants belonging to at least one UBR population. The NLM partnership includes activities that engage women and girls in health literacy activities, as well as programs aimed to increase awareness of the *All of Us* Research Program. In FY 2019–2020, programs hosted with public libraries and community partners and designed to serve women and girls included book clubs on Black maternal health; diversity in the medical profession; inherited disease, including BRCA breast cancer, cystic fibrosis, and sickle cell; and other topics by women authors (Network of the National Library of Medicine, NNLM Reading Club). During the COVID-19 pandemic, most in-person activities were canceled and shifted to virtual health programming.

This relates to Objectives 2.4 ("Expand and refine methodologies to improve the recruitment and retention of women underrepresented in clinical research") and 3.2 ("Identify collaborative opportunities and leverage partnerships to disseminate research that improves the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

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Office of AIDS Research

I. Executive Summary

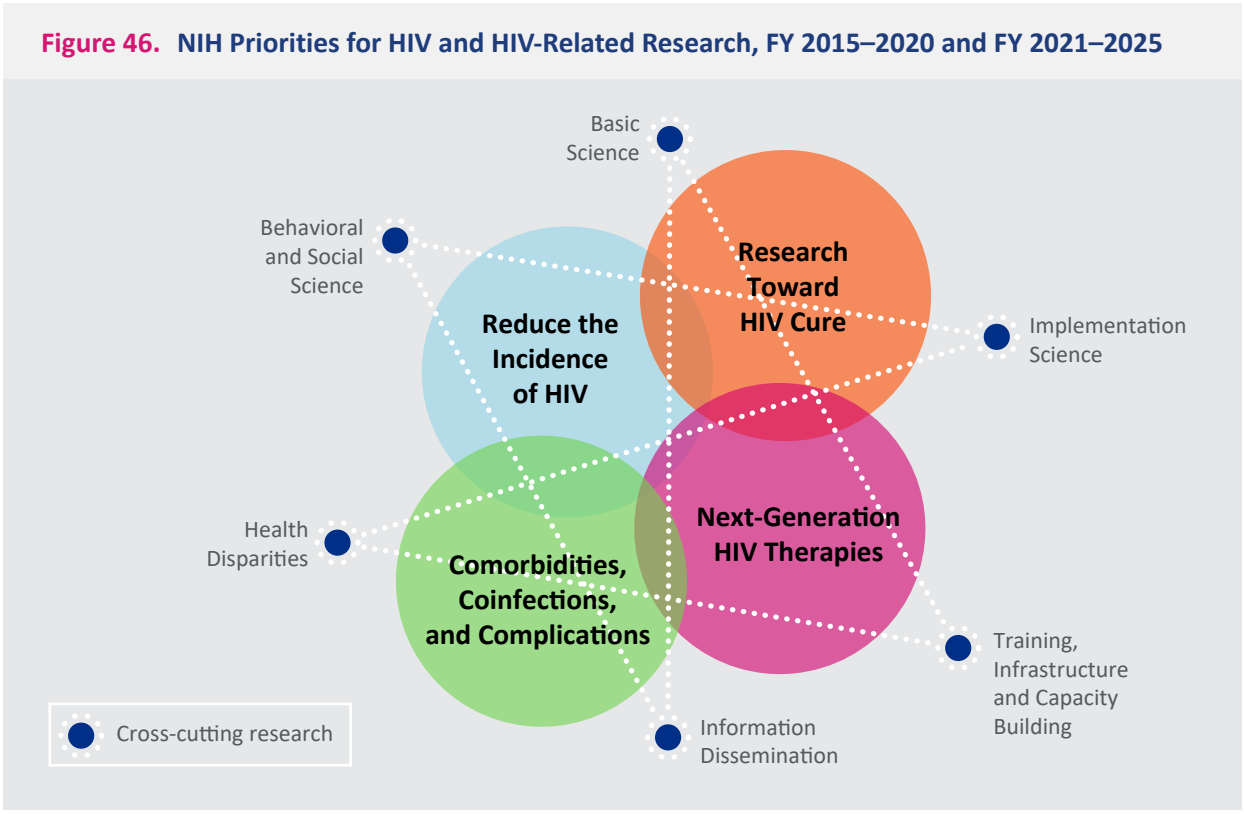
The NIH Office of AIDS Research (OAR)—located within the Office of the Director's Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI)—coordinates the scientific, budgetary, legislative, and policy elements of a diverse HIV/AIDS research program across the NIH. OAR's mandate is to oversee NIH's vision for HIV/AIDS research, to end the HIV pandemic, and to improve the health outcomes of people with HIV (PWH). To accomplish this goal, the OAR establishes the NIH HIV/AIDS research priorities (Figure 46) and develops the *NIH Strategic Plan for HIV and HIV-Related Research*, which serves as a road map for HIV/AIDS research across almost every NIH Institute and Center (IC). The OAR also ensures that HIV/AIDS research funds are allocated across the ICs based on the strategic plan.

In FY 2019 and FY 2020, more than $3 billion of HIV/AIDS funding was distributed annually across ICs, representing the largest public investment in HIV/AIDS research globally. Approximately $500 million per year of this investment supported research related to HIV and women.

Globally, women remain at significant risk for HIV. Approximately 5,500 young women ages 15 to 24 become infected with HIV every week; in sub-Saharan Africa, women in this age group are twice as likely to have HIV as their male counterparts. In the United States and dependent areas, 19% of the 37,832 new HIV diagnoses in 2018 were among women (UNAIDS, 2020; CDC, 2020; HIV.gov, 2020).

HIV poses unique challenges for women. Some may be unaware of their male partner's risk factors for

Figure 46. NIH Priorities for HIV and HIV-Related Research, FY 2015–2020 and FY 2021–2025



Implications for research concerning HIV and women intersect all priority and cross-cutting areas under the Plan.

HIV (including injection drug use, multiple sexual partnerships, and having sex with other men) and may not use barrier protection or other protection, putting

them at a higher risk for exposure to HIV. Other sexually transmitted infections (STIs) and history of sexual abuse pose additional risk factors.

II. Scientific Advances

» Results from **HIV Prevention Trials Network** (HPTN) studies 083 and 084 demonstrated that a long-acting injectable pre-exposure prophylaxis (PrEP) regimen is safe and effective for preventing HIV acquisition in women and men who have sex with men. These findings contribute to the development of new PrEP options for women that may be more compatible with various lifestyles and empower women to directly reduce their HIV risk, thus helping to overcome barriers and challenges to adherence to daily oral PrEP.

- The HPTN 084 study was launched in late 2017 and enrolled over 3,000 cisgender women, ranging in age from 18 to 45, in 20 clinical research sites in sub-Saharan Africa. An investigational long-acting form of the HIV drug cabotegravir, injected once every 8 weeks, was safe and superior to a daily oral PrEP regimen with tenofovir/emtricitabine (Truvada) at preventing HIV acquisition among a group of African cisgender women. In November 2020, an independent data and safety monitoring board (DSMB) overseeing the trial determined that the study indicated the long-acting injectable cabotegravir had superior efficacy to oral tenofovir/emtricitabine at preventing HIV in the study population. In response to these findings, the DSMB recommended that the National Institute of Allergy and Infectious Diseases discontinue a phase of the trial and share these results (NIAID, Nov. 9, 2020).
- These promising results for women build on findings announced earlier in 2020 from a companion HPTN 083 study, which enrolled about 4,500 cisgender men and transgender women who have sex with men and was carried out in multiple countries. The study demonstrated that the long-acting injectable cabotegravir was superior to daily oral PrEP at preventing HIV among these subpopulations (Lancet, 2020).
- The studies are key examples of the expanded inclusion of women in health research as required by the 21st Century Cures Act.

» An intravaginal ring with the topical microbicide dapivirine was evaluated for HIV prevention in two recent studies among women in Africa. Results from the **Dapivirine Ring Extended Access and Monitoring** (DREAM) and **HIV Open-Label Prevention** (HOPE) studies suggest a reduced risk of acquiring HIV infection, based on statistical modeling. The intravaginal ring passed regulatory review by the European Medicines Agency in July 2020 for its use among women age 18 or older in developing countries and received World Health Organization prequalification in November 2020. IPM, the regulatory sponsor, plans to apply for regulatory approval in eastern and southern African countries and in the United States. This is a significant step toward expansion of the HIV prevention options available to women—specifically, the first discreet, self-initiated, and long-acting HIV prevention option for women. In addition to the oral PrEP and vaginal delivery systems, there is a need for HIV prevention and contraceptive dual protection technologies, or multipurpose prevention technologies (MPTs), utilizing alternative delivery routes targeting adolescent girls and young women who are at a higher risk of HIV infection (NIAID, 2020; MTN Microbiocide Trials Network, 2020; EurekAlert!, 2020).

» CD4 cells are infection-fighting white blood cells targeted by HIV. As people on combined antiretroviral therapy (cART) with poor CD4 cell recovery may have continued immune impairment and an increased risk of health complications, an increase of peripheral blood CD4 lymphocyte counts (CD4 cell recovery) is a key goal of cART for HIV. In a recent study under the umbrella of the **MACS-WIHS Combined Cohort Study**, researchers examined specific genetic factors associated with the extent of CD4 recovery in HIV-infected women. The researchers identified women in the cohort who were on cART with viral load below 400 copies and drew racially and ethnically matched samples of those with improved or diminished CD4 response over 2 years. The study compared the genetic sequences of women on cART to look for genetic factors that may predict recovery of CD4 cell

counts in women with HIV. After adjustment for age and genomic estimates of race and ethnicity, the researchers identified 41 genes that were associated with differences in CD4 cell recovery. Many of the genes identified are known to regulate the production, survival, death, and proliferation of CD4 cells and other white blood cells. Some of the genes associated with CD4 cell recovery are responsible for the production of cellular components known to interact with HIV. The identification of new genes may influence the recovery of immune function in treated HIV infection and could ultimately support the identification of new factors that contribute to HIV disease development and health complications in women (Greenblatt et al., 2019; WIHS, 2019).

III. Promotion of Women's Health Research

The OAR allocated over $1.05 billion to support research related to HIV and women across the NIH ICs in FY 2019 and FY 2020. The National Institute of Allergy and Infectious Diseases (NIAID), the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), the National Institute on Drug Abuse (NIDA), the National Institute of Mental Health (NIMH), and the National Cancer Institute (NCI) were the largest contributors to this research during the 2-year period. (See Figure 47)

A growing number of projects were focused on HIV-related comorbidities, which reflects the evolving nature of the HIV pandemic. Examples of research projects related to HIV and women across the NIH that were supported by HIV/AIDS dollars include:

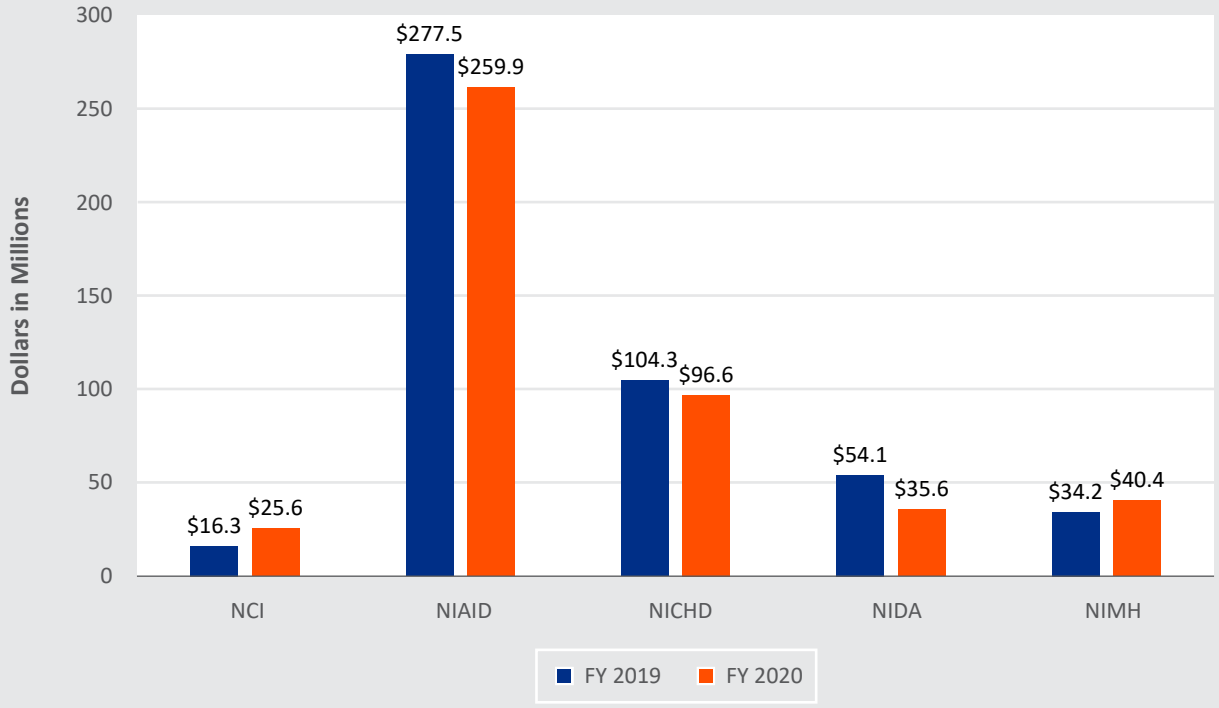
NIAID:

- PrEP and PEP: Doxycycline Post-Exposure Prophylaxis for Prevention of Sexually Transmitted Infections among Kenyan Women Using HIV Pre-Exposure Prophylaxis
- Optimizing Viral Suppression for Pregnant and Postpartum Women Living with HIV through HIV Resistance Testing

NICHD:

- Iron and Folic Acid Supplementation Strategies During Pregnancy and Adverse Pregnancy Outcomes in Botswana

Figure 47. FY 2019-20 Women and HIV Funding by IC



- The Impact of Vaginal Microbiota on Cervical Dendritic Cells: An Observational Study of Women from Sub-Saharan Africa at High Risk for HIV Acquisition

NIDA:

- Sisters Informing Sisters About Topics on AIDS and Prevention (SISTA-P): Adaptation of the SISTA Intervention to Include PrEP Information and Skills Building for Black Women Who Are at Risk for HIV
- Implementation of PrEP for Women Who Inject Drugs through Practice Facilitation in Primary and Reproductive Health Care

NIMH:

- Peer PrEP Referral and HIV Self-Test for PrEP Initiation among Young Kenyan Women
- Stigma, Cohesion and HIV Outcomes among Vulnerable Women across Epidemic Settings

NCI:

- Prognostic Value of Quantitative HPV Viral Load in Determining Cervical Cancer Treatment Response and Recurrence
- A Novel Cervical Cancer Screen-and-Treat Demonstration Project with HPV Self-Testing and Thermocoagulation for HIV-Infected Women in Malawi

The National Heart, Lung, and Blood Institute; the National Institute on Aging; and the National Institute on Alcohol Abuse and Alcoholism (NIAAA):

- Arterial Inflammation and Coronary Microvascular Dysfunction among Women with HIV: Missing Pieces to the MI Risk Puzzle
- Emerging Factors in the Pathophysiology of Endothelial Dysfunction in HIV+ Women
- Assessing the Role of Alcohol and Intimate Partner Violence on HIV Care and Viral Suppression in Uganda

This OAR activity is aligned with Goal 1 ("Advance rigorous research that is relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

OAR Innovation Fund: Each year, OAR sets aside a portion of its annual appropriated budget to fund innovative, high-priority HIV/AIDS research activities and workshops submitted by the ICs for OAR funding. In FY 2019–2020, this funding included direct OAR support of women-centric research projects, administrative supplements, and workshops through the ICs. Some examples include:

- Integrating Counseling to Transform HIV Family Planning Services (NICHD)
- Examining PrEP Use, Implementation Preferences and the Potential for Social Support to Improve PrEP Delivery and Persistence Among Female Sex Workers in Durban, South Africa (National Institute of Nursing Research)
- Reducing Tobacco Smoke Exposures Among Low Income Children and Women Caregivers in the Arkansas Delta Region (National Institute on Minority Health and Health Disparities)
- Pharmacokinetic and Safety of Antiretroviral and Related Drugs in Lactating Women and Breastfed Infants Study (NICHD)

This OAR activity is aligned with Goal 1 ("Advance rigorous research that is relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

Sexual and Gender Minority Administrative Supplements: In FY 2019–2020, OAR provided partial funding to the Sexual and Gender Minority Research Office (SGMRO) to co-fund two administrative supplements related to sexual and gender minorities:

- **Impact of Social Cohesion and Social Capital in PrEP Uptake and Adherence Among Transwomen of Color:** This project seeks to use real-time geospatial methods to investigate associations between relationships, networks, and neighborhoods in relation to HIV pre-exposure prophylaxis (PrEP) uptake and other HIV-related outcomes among Asian transgender women (TW) in the New York City metropolitan area. As the largest study of HIV disparities and risk in Asian transgender women, an understudied population in the United States, the supplement will accelerate the science and impact of the parent grant, fostering cross-cultural comparisons and analyses of health disparities and

HIV prevention among Asian, Black, and Latina TW. This research will provide a context-specific and nuanced understanding of how social contextual factors may contribute to HIV prevention behaviors in transgender women of color, which will in turn inform contextually appropriate HIV prevention interventions.

- **Transgender Men and HIV in Uganda: PrEP Uptake and Persistence:** Research is needed to better understand HIV risk behaviors among transgender men, who face HIV risks similar to cisgender women's risks, and to assess differences in PrEP acceptability and adherence. In this supplement to the parent grant studying self-testing and PrEP in transgender women in Uganda, investigators conducted in-depth interviews with transgender men to understand individual, interpersonal, community, and social contextual factors that influence HIV/STI risk. The behavioral HIV risk assessment included sexual practices, alcohol and drug use, partner violence, gender dysphoria, male hormone use, and willingness to take PrEP among transgender men. Understanding correlates of HIV risk and PrEP uptake in this understudied population will provide crucial data to policymakers when considering scale-up of HIV prevention interventions and contribute to HIV epidemic control.

This OAR activity is aligned with Goals 1 ("Advance rigorous research that is relevant to the health of women") and 2 ("Develop methods and leveraging data sources to consider sex and gender influences that enhance research for the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

NIH Workshops: In FY 2019–2020, OAR provided funding to NIAAA to support a workshop "***Advancing Adherence to Pre-exposure Prophylaxis (PrEP) for HIV/AIDS Prevention among Alcohol-Using Populations***," which included a focus on women and HIV. The purpose of this workshop was to provide a forum to exchange ideas related to the design of multilevel (individual, interpersonal, social structural) alcohol-related behavioral research along the translational research continuum that may include the use of innovative methods to ending the HIV epidemic. The role of alcohol use and its impact on women at risk for and living with HIV was one of the workshop's multiple prevention themes and follows from data regarding incidence and prevalence of the HIV epidemic in the U.S.—along with the Ending the HIV Epidemic in the U.S. (EHE) initiative, launched in FY 2020, and the 2021–2025 Trans-NIH Strategic Plan for HIV and HIV-Related Research. The workshop participants also discussed the changing patterns of alcohol use among women and study findings that increases in alcohol consumption increase the risk for exposure to HIV and reduce adherence to medications and complicate HIV treatment.

The following workshop presentations specifically addressed the topic of HIV and women. They are currently under preparation as articles for a special issue of *AIDS and Behavior*:

- Outcomes of Implementing in the Real World a Women's Intervention for Alcohol Reduction and ART Adherence in Cape Town, South Africa
- Randomized Controlled Trial of an Alcohol-related Sexual Risk Reduction Intervention with Adolescents: The Role of Neurocognitive Activation During Risky Decision-Making
- Addressing unhealthy alcohol use and the HIV pre-exposure prophylaxis care continuum in primary care: A scoping review
- Use of alcohol challenge experiments to identify mechanisms of behavior change in HIV prevention interventions

This OAR activity is aligned with Goal 3 ("Enhance dissemination and implementation of evidence to improve the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

HIV-Related BIRCWH Awards: In FY 2019–2020, OAR provided partial funding to support several NICHD K12 awards through the ORWH-led program **Building Interdisciplinary Research Careers in Women's Health** (BIRCWH), a mentored career-development initiative designed to connect junior faculty (BIRCWH Scholars) to senior faculty with shared interest in women's health and sex differences research.

- Emory University BIRCWH program
- UCSF-Kaiser BIRCWH program
- Johns Hopkins University BIRCWH program

This OAR activity is aligned with Goals 1 ("Advance rigorous research that is relevant to the health of women") and 2 ("Develop methods and leveraging data sources to consider sex and gender influences that enhance research for the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

IV. Advancement of Women in Biomedical Careers

Support of Early-Stage Investigators: To stimulate the funding of new applications and to improve the current landscape of NIH-funded HIV early-stage investigators (ESIs), OAR has committed to providing a single year of funding to ICs to support meritorious ESI grant proposals related to HIV/AIDS research that did not meet the ICs' payline. This 1-year funding was used to fund the first year of an R01 grant or to support a R56 Bridge Award. In FY 2020, OAR provided funding to support nine HIV-related projects targeting ESIs, eight of which were to women investigators:

- Enhancing HIV assisted contact tracing in Malawi through blended learning: An Implementation Science Study (R01, NIMH)
- HIV+ Service Delivery and Telemedicine through Effective PROs (R01, NIMH)
- Adherence Connection for Counseling, Education, and Support (ACCESS) (R01, NINR)
- Dyadic management of HIV cardiometabolic comorbidities among couples in Malawi (R01, NHLBI)
- Metabolic impact of FGF-21 in adipose tissue and liver of PLWH (R01, NIDDK)
- Nutrition to Optimize, Understand, and Restore Insulin Sensitivity in HIV for Oklahoma (NOURISH-OK) (R01, NIDDK)
- Targeting the HIV-1 reservoir with a combination of an IDLV-SIVGag therapeutic vaccine and Fc-engineered bnAbs (R56, NIAID)
- Structural Studies of APOBEC-Vif Complexes (R56, NIAID)

This OAR activity is aligned with Goal 4 ("Promote training and careers to develop a well-trained, diverse, and robust workforce to advance science for the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

OAR Advisory Council (OARAC): Over the past several years, this Federal advisory committee has prioritized significant participation and contributions by women leaders in the workforce, as well as women investigators and community members. The 2019–2020 OARAC roster included a woman as the chairperson and 50% women among voting members (OAR, 2020). Women scientists are regularly featured as presenters; the February 2020 OARAC meeting featured three women scientists who presented scientific advances related to the role of novel technologies and HIV simulation modeling to improve care and treatment outcomes among PWH on antiretroviral therapy (ART), facilitate the prioritization of HIV/AIDS research investments, and help address critical disparities in HIV-related health outcomes.

This OAR activity is aligned with Goal 4 ("Promote training and careers to develop a well-trained, diverse, and robust workforce to advance science for the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

V. Inclusion of Women in Clinical Research

HIV Clinical Trials Networks and Other Large Multi-IC HIV Cohorts:

- NIH supports multiple networks that conduct innovative clinical research to accelerate progress against the HIV epidemic and advance four key areas of HIV/AIDS research: prevention, vaccines, adult therapeutics, and maternal, adolescent, and pediatric therapeutics. While all of the HIV Clinical Trials Networks conduct research relevant to women's health, the **International Maternal Pediatric Adolescent AIDS Clinical Trials** (IMPAACT) is specifically focused on developing and evaluating new treatments and cure strategies for HIV and HIV-related complications and coinfections in girls, pregnant women, and postpartum women.
- The **International Epidemiology Databases to Evaluate AIDS** (IeDEA) Consortium collaborates to define key variables, harmonize data, and implement methodology to effectively pool

globally diverse data as a cost-effective means of generating large datasets. The IeDEA Mother and Infant working group aims to promote healthy outcomes for pregnant women and mothers living with HIV and serves as a hub to provide infrastructure for enhanced data collection, analysis, and dissemination to advance research related to pregnancy, breastfeeding, and the HIV care continuum.

» The **Women's Interagency HIV Study** (WIHS) is a long-standing multicenter prospective observational cohort study of women in the United States who are either living with HIV or at risk for HIV acquisition. In 2019, WIHS was consolidated with the Multicenter AIDS Clinical Study (MACS), a study of gay and bisexual men, into the **MACS-WIHS Combined Cohort Study**, to focus on chronic conditions that occur in people living and aging with HIV. The study, with over 5,000 active participants, aims to promote new scientific discoveries in basic and clinical HIV science by sharing data and biospecimens from these research groups and to study sex/gender differences related to HIV-related health outcomes. The study is recruiting underrepresented participants, including Black and Hispanic women from the U.S. South, to achieve a more diverse cohort that reflects the populations living with HIV in the United States.

HIV Clinical Practice Guidelines: Five OARAC-supported working group panels develop and maintain federally approved guidelines for HIV care providers with regard to ART and care management in adults, adolescents, and pediatric populations. There is equal representation by women on all five panels; women serve as panel chairs, co-chairs, executive secretaries, and/or section lead authors/co-authors.

- The Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission evaluates ARV drugs that are available for adults and assesses the risks and benefits of using these drugs in pregnant women.
- The panel's recommendations are based on data from several sources, including direct pharmacokinetic (PK) studies in pregnant women, safety and efficacy studies performed in nonpregnant adults, preclinical animal studies, analyses of reports to the Antiretroviral Pregnancy Registry, and post-marketing surveillance data.
- During FY 2019–2020, 49 guideline updates/revisions (HIV.gov, 2020) were made on various perinatal HIV treatment sections, and two new sections were added (PrEP in pregnancy and Fostemsavir therapy).

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Office of Behavioral and Social Sciences Research

I. Executive Summary

Situated within the Office of the Director's Division of Program Coordinating, Planning, and Strategic Initiatives, the NIH Office of Behavioral and Social Sciences Research (OBSSR) furthers the mission of NIH by emphasizing the critical role that behavioral and social factors play in health, health care, and well-being. As a coordinating office, OBSSR serves as the focal point for coordination and development of policies, goals, and objectives in the behavioral and social sciences at NIH. Although OBSSR does not hold or administer any research grant awards, the office does offer co-funding support to the 27 NIH Institutes and Centers. In fiscal years (FY) 2019 and 2020, OBSSR co-funded many grants and initiatives with a focus on the health of women, particularly related to the behavioral and social sciences aspects of sex and health and disease, health disparities, inclusion of women in clinical research, and women in biomedical science careers and will continue to in the future.

II. Scientific Advances

Although OBSSR does not have any direct research to report for FY 2019–2020 in women's health, recent trans-NIH initiatives led by OBSSR have great promise in resulting in scientific advances for the health of women; this research aligns with Objective 1.3 of the Trans-NIH Strategic Plan for Women's Health Research ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes").

For example, with OppNet, OBSSR is supporting research on biopsychosocial factors of social connectedness and isolation on health, well-being, illness, and recovery. These funding opportunity announcements (FOAs) invite research projects that seek to explain the underlying mechanisms, processes, and trajectories of social relationships and how these factors affect outcomes in health, illness, recovery, and overall well-being. OBSSR expects that results from many projects will be essential for understanding the health of women, especially in the context of the COVID-19 pandemic and social isolation.

In FY 2020, as part of NIH's Helping to End Addiction Long-term (HEAL) Initiative, OBSSR crafted a notice for support of supplements to current HEAL awards to address the challenges for people affected by the opioid crisis from stigma, discrimination, and prejudice related to chronic pain management in the context of opioid use and/or opioid use disorder and its treatment. The notice, NOT-OD-20-101, intends to support strategies to reduce stigma in pain management and opioid use disorder treatment. Stigma can be a challenge for people with pain and/or substance use disorders, their families, caregivers, and clinicians, and as chronic pain affects a higher proportion of women than men around the world, supporting research into strategies to address stigma in these contexts is of particular importance for the health of women.

Reducing barriers to care that exist because of stigma is crucial to caring for people and for treatment effectiveness for both chronic pain management and/or opioid use disorder (OUD) and is important to understanding the stigmas women may experience and how they contribute to OUD.

In FY 2020, for the first time since 2013, OBSSR issued FOAs specifically looking for projects that explore firearm injury and mortality prevention research. To support this important research, including specifically the violence and injury women and girls experience (as noted in the background sections of the FOA and notice of special interest), NIH issued PAR-20-143 and NOT-OD-20-089 and awarded an administrative supplement exploring the firearm violence prevention and State-level policies on maternal mortality. Because the projects are currently in their second (and final) year, OBSSR has not yet seen the results of the research, including whether any projects chose to explore specific sex differences or effects of intimate partner violence.

III. Promotion of Women's Health Research

In FY 2019–2020, OBSSR promoted research on the health of women and recent research results and training initiatives through communications channels—such as social media, webinars, and newsletters—often cross-promoting requests for information (RFIs), announcements, and opportunities from the Office of Research on Women's Health (ORWH).

OBSSR hosted several blog posts on research developments regarding behavioral and social health and the role gender and sex as a biological factor play in research and health outcomes. For example, the NIH Matilda White Riley Behavioral and Social Sciences Honors event often features presentations on the health of women and health disparities. These are early-stage investigators who are honored by OBSSR with an award and featured lecture for their work in health behavior, social sciences, and life course research, and these presentations are aligned with Objectives 4.1 ("Enhance knowledge of sex and gender influences on health and disease among all scientists, clinicians, and other health professionals to accelerate the translation of that knowledge into practice") and 4.2 ("Develop the next generation of researchers to advance science on the health of women") of the Trans-NIH Strategic Plan for Women's Health Research, to enhance knowledge of sex and gender influences on health and disease among all scientists, clinicians, and other health professionals to accelerate the translation of that knowledge into practice and to develop the next generation of researchers to advance science on the health of women. In 2019, Taylor Hargrove, Ph.D., presented on her work titled "Intersecting Social Inequalities and Body Mass Index Trajectories from Adolescence to Early Adulthood," which described analyses on how intersecting environmental, social, and structural inequalities affect body mass index, particularly emphasizing the many inequities among women, including Black and Hispanic American women. For the same awards in 2020, Jaime C. Slaughter-Acey, Ph.D., M.P.H., presented on her work "Skin Tone and Prenatal Care Outcomes Among African-American Women," which explored the role colorism may play in patient–provider interactions in obstetrics. These researchers were selected for these projects and the impact they could have on understanding social stressors and structural inequities' impact on health status.

IV. Advancement of Women in Biomedical Careers

In addition to participating in ORWH's Building Interdisciplinary Research Careers in Women's Health (BIRCWH) program as mentors, OBSSR is committed to supporting women in biomedical careers and developing the next generation. The next generation of biomedical and behavioral researchers will benefit from training in data science to utilize new and emerging data collection methods and technologies. These are related to Objective 4.4 ("Promote and support policies, mentoring and networks, collaborations, and infrastructure to retain and advance women in their careers") of the Trans-NIH Strategic Plan for Women's Health Research, to promote and support policies, mentoring and networks, collaborations, and infrastructure to retain and advance women in their careers. A group of staff members from across NIH identified the key behavioral and social science training needs in data science and the current support for this training by NIH, and they developed and released a request for applications (RFA) titled Predoctoral Training in Advanced Data Analytics for Behavioral and Social Sciences Research (TADA-BSSR). The vision of the TADA-BSSR T32 initiative is to develop a cohort of specialized predoctoral candidates who possess advanced competencies in data science analytics to apply to an increasingly complex landscape of behavioral and social health–related big data. Though not specifically focused on data regarding the health of women, improved methods and understanding of health behavior and social science data will lend skills to those doing research in women's health. Eight T32s were granted in 2020, and these predoctoral training programs aim to integrate computer science, informatics, mathematics, and statistics into behavioral and social sciences research training. OBSSR does not have demographic data on the trainees.

OBSSR supports many recurring trainings via an RFA titled Short Courses on Innovative Methodologies and Approaches in the Behavioral and Social Sciences (R25). While all of the trainings will focus on training women on biomedical careers, some courses in particular are focused on conditions that affect the health of

women or methodologies for conducting research that are relevant to studying the health of women. In addition, some courses are focused on other topics such as Strengthening Causal Inference in Behavioral Obesity Research, the Summer Training Program in Integrative Methods for Mental and Physical Health, and Optimization of Behavioral and Biobehavioral Interventions: building investigator capacity nationwide.

V. Implementation of the NIH Policy on Sex as a Biological Variable (SABV)

Although OBSSR does not manage or administer individual grants, it does work to enhance the resources available to researchers who are implementing NIH's SABV policy. This includes working to standardize behavioral ontologies among the research community to create a shared language and facilitate shared and reproducible findings. After finding that behavioral ontologies were underrepresented in the Medical Subject Headings (MeSH) thesaurus, OBSSR worked with colleagues at the National Library of Medicine, the National Institute on Aging, and the National Institute of Mental Health to include missing synonyms and terms within MeSH, and eventually add more terms for inclusion. Standardizing behavior-related medical and research terms may be able to improve the quality of research regarding behavioral research of sex differences.

VI. Inclusion of Women in Clinical Research

After the 2016 Policy on the Dissemination of NIH-Funded Clinical Trial Information was launched, some researchers faced challenges in fitting these studies into the data fields for submission in ClinicalTrials.gov. OBSSR, the Office of Extramural Research, and the Office of Science Policy worked together to create an alternative funding mechanism to NIH's definition of a clinical trial, Basic Experimental Studies involving Humans (BESH). Studies are designed in a way that may be difficult to address in a system designed to represent one study per record with at least one pre-specified primary outcome measure and with aggregated summary results information provided in tabular format. Therefore, NIH published a guide notice (NOT-OD-19-126) announcing the extension of delayed enforcement of registering and results reporting of BESH on ClinicalTrials.gov through September 24, 2021. Registering and reporting data from BESH studies is integral to understanding the inclusion of women in clinical research.

Office of Disease Prevention

I. Executive Summary

The NIH Office of Disease Prevention (ODP) assesses, facilitates, and stimulates research in disease prevention, including in the health of women. For example, the ODP monitors NIH investments in prevention research and the progress and results of that research through portfolio analysis related to pregnant women and/or postpartum women and sexual and gender minorities. Using portfolio analysis, the ODP looks at patterns and trends, as well as research areas that may benefit from targeted efforts by NIH Institutes and Centers (ICs). The ODP co-funding program supports research that fosters innovation, expands emerging areas of science, and addresses issues of public health importance that are relevant to women's health. Co-funded projects include several grants and workshops related to maternal mortality, fertility, osteoporosis, heart health, physical activity, cancer, and social determinants of health. The office collaborates with the U.S. Preventive Services Task Force and the Community Preventive Services Task Force in identifying and addressing women's health research gaps. ODP staff members also serve on several working groups that promote women's health research, including the NIH Coordinating Committee on Research on Women's Health, the NIH Maternal Morbidity and Mortality Task Force, and the Healthy People Federal Interagency Workgroup. The ODP promotes the use of the best available methods in prevention research and supports the development of better methods, including those that consider sex and gender influences in research. The office disseminates information about research design, measurement, intervention, data analysis, and other methods through its regular Methods: Mind the Gap webinars.

II. Promotion of Women's Health Research

Goal 1 of the Trans-NIH Strategic Plan for Women's Health Research: Advance rigorous research that is relevant to the health of women.

» Through co-funding, the ODP supports research that fosters innovation, expands emerging areas of science, and addresses issues of public health importance that are relevant to the health of women. Examples of projects co-funded by ODP are listed below.

- Physical Activity, Sedentary Behavior, and Cancer Incidence in Women | 5R01CA227122-02
- Improving Breast Cancer Risk Prediction for African American Women: Consideration of Estrogen Receptor Sub-type Specific Risk Factors | 1R01CA228357-01A1
- Continuation of the nuMoM2b Heart Health Study | 1U01HL145358-01A1
- Social and Economic Determinants of Maternal Morbidity in the United States | 1R03HD100709-01A1
- Towards a Research Agenda to Reduce Maternal Mortality in the United States Conference (Lead IC: the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development [NICHD])
- Pregnancy and Maternal Conditions that Increase the Risk of Morbidity and Mortality Workshop (Lead IC: NICHD)
- U.S. Burden of Health Disparities by Race and Ethnicity, Sex, Socioeconomic Status, Age and Location Project (Lead IC: the National Institute on Minority Health and Health Disparities [NIMHD])

» The ODP has also signed on to FOAs that support research relevant to the health of women.

- Fertility Status as a Marker for Overall Health (R01 Clinical Trial Optional) | PAR-20-281
- Fertility Status as a Marker for Overall Health (R21 Clinical Trial Not Allowed) | PAR-20-282
- Tailoring Interventions to Improve Preventive Health Service Use (R61/R33 Clinical Trial Required) | RFA-AG-20-045

- The ODP convened two Pathways to Prevention workshops related to women's health research.
  - Appropriate Use of Drug Therapies for Osteoporotic Fracture Prevention (Lead ICs: the National Institute of Arthritis and Musculoskeletal and Skin Diseases and the National Institute on Aging)
  - Achieving Health Equity in Preventive Services (Lead ICs: NIMHD; the National Cancer Institute; the National Heart, Lung, and Blood Institute; and the National Institute of Diabetes and Digestive and Kidney Diseases)
- The ODP supports the work of the U.S. Preventive Services Task Force and the Community Preventive Services Task Force in identifying research gaps related to the health of women.
- The ODP serves on the Healthy People Federal Interagency Workgroup, the principal advisory body for the development of the Healthy People initiative. Healthy People provides science-based, 10-year national objectives for improving the health of Americans; many of these objectives promote health and well-being for women.
- The ODP also has representation on the NIH Coordinating Committee on Research on Women's Health and the NIH Maternal Morbidity and Mortality Task Force.

Goal 2 of the Trans-NIH Strategic Plan for Women's Health Research: Develop methods and leverage data sources to consider sex and gender influences that enhance research for the health of women.

- The ODP promotes the use of the best available methods in prevention research and supports the development of better methods, which enhance research for the health of women.
- The ODP's Methods: Mind the Gap webinars explore research design, measurement, intervention, data analysis, and other methods of interest in prevention science. A recent webinar was titled "Risk Prediction Models for Breast Cancer in Black Women: The Importance of Considering Molecular Subtypes."

Goal 5 of the Trans-NIH Strategic Plan for Women's Health Research: Improve evaluation of research that is relevant to the health of women.

- The ODP systematically monitors NIH investments in prevention research and the progress and results of that research. The ODP's portfolio analysis assesses NIH prevention research related to:
  - Pregnant women and/or postpartum women
  - Sexual and gender minorities

The ODP looks at patterns and trends, as well as research areas that may benefit from targeted efforts by the ICs.

Office of Research Infrastructure Programs

I. Executive Summary

Established in December 2011, the NIH Office of Research Infrastructure Programs (ORIP) is located within the NIH Office of the Director's Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI). ORIP brings together research activities managed by the Division of Comparative Medicine and the Division of Construction and Instruments. ORIP's mission is to provide research infrastructure and support research-related resource programs. ORIP's infrastructure and resource programs are trans-NIH in nature and align with DPCPSI's mission to ensure that NIH effectively and efficiently addresses and coordinates important areas of emerging scientific opportunities to improve human health.

ORIP advances research on women's health, minority health, and health disparities by supporting infrastructure and shared resources critical to this research through the development and provision of animal models for human disease; access to cutting-edge technologies and instruments that enable biomedical research and clinical investigations of a multitude of health issues; exploration of strategies for consideration of sex differences in animals and cell lines used in NIH-funded studies as a means of enhancing experimental design and increasing reproducibility in preclinical research; and support of educational training programs to engage veterinarian-scientists and diverse early-stage investigators in becoming valuable partners in an integrated, multidisciplinary approach to biomedical/translational research. ORIP also strives to increase the diversity of entrepreneurs in the research resource and infrastructure enterprise by supporting and funding Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) applications from businesses owned by women, minorities, and socially disadvantaged people. The SBIR and STTR programs are highly competitive programs that encourage domestic small businesses to engage in Federal Research/Research and Development (R/R&D) with the potential for commercialization. ORIP's programs have always included—and will continue to include—research projects that focus on sex differences in health and disease, women's health, minority health, and health disparities across the lifespan.

II. Scientific Advances

Advanced Age Affects Physiologic Adaptations to Pregnancy in a Nonhuman Primate Model

The rate of advanced maternal age (AMA) pregnancies, defined as pregnancies in women 35 years or older, is rising as more women are choosing to delay childbirth and motherhood. AMA is one of several factors underlying the high rates of maternal morbidity and mortality in the U.S. While AMA is known to contribute to pregnancy-related pathologies, such as preeclampsia and gestational diabetes mellitus, the molecular and cellular underpinnings of these relationships remain poorly understood. This gap in knowledge is caused in part by the lack of an appropriate preclinical model for AMA. With funding from ORIP, the National Center for Advancing Translational Sciences, and the National Heart, Lung, and Blood Institute, researchers measured third-trimester blood pressure (BP), complete blood counts, iron, and hormone levels in age-diverse pregnant vervet monkeys (also known as African green monkeys) maintained in the Vervet Research Colony at Wake Forest University School of Medicine (Plant et al., 2020). Vervets and other nonhuman primates exhibit many similarities to humans in reproductive biology and pregnancy. The researchers found that AMA vervet mothers had higher diastolic BP and exhibited higher white cell counts with enhanced circulating neutrophils compared with the younger mothers. The AMA mothers also had lower levels of three hormones—estradiol, progesterone, and cortisol. By following the body weight of offspring over the first year of life, the researchers discovered a pattern of postnatal growth retardation in the offspring born to AMA mothers. This investigation expands basic research on female reproductive health issues and develops new approaches to study these issues The results support the future use of vervets as a valuable preclinical model for uncovering the physiologic mediators of negative maternal outcomes of pregnancies at older ages.

This relates to Objectives 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic

health") and 2.1 ("Expand and develop advanced and innovative approaches for study design, data collection, and analysis to optimize data quality and the ability to detect the influences of sex and gender on health and disease") of the Trans-NIH Strategic Plan for Women's Health Research.

A Human Tissue and Organ Resource Facilitates Research on the Health of Women

The use of human biospecimens plays a critical role in accelerating discoveries relevant to diseases specific to or more common in women, as well as diseases with fundamental differences between the sexes. The Human Tissue and Organ Research Resource (HTORR) procures donated human tissues and distributes them to researchers as experimental models. HTORR is funded by ORIP and its IC partners (the National Eye Institute; the National Heart, Lung, and Blood Institute; the National Institute on Aging; the National Institute of Allergy and Infectious Diseases; the National Institute of Arthritis and Musculoskeletal and Skin Diseases; the National Institute of Diabetes and Digestive and Kidney Diseases; the National Institute of Mental Health; and the National Institute of Neurological Disorders and Stroke). The invaluable resources provided by HTORR enabled a wealth of research relevant to the health of women in FY 2019 and FY 2020. For example, lymphangioleiomyomatosis (LAM) is a rare lung disease that occurs primarily in women and results in relentless decline in pulmonary function and, ultimately, respiratory failure. The HTORR program recently distributed 168 biospecimens from 28 LAM donors to 7 investigators, who completed cutting-edge studies of this disease (Guo et al., 2020; Obraztsova et al., 2020). HTORR also supported research on breast cancer with tumor samples recovered following surgery, facilitating the advancement of breast cancer imaging technology (Bowman et al., 2019) and the identification of genes and protein interactions contributing to initiation of tumorigenesis (Chen et al., 2019). In addition, HTORR recently distributed 106 cervical samples to 6 investigators in support of research on vaginal transmission of HIV (Ñahui Palomino et al., 2019) and *Neisseria gonorrhoeae* infection (Yu et al., 2019). HTORR supports research on the discovery and investigation of sex differences, research on the effects of various exposures on disease outcomes, and research on female-specific conditions and diseases, including reproductive diseases. HTORR also advances innovative approaches for data collection by optimization of tissue procurement protocols to enhance reproducibility. Lastly, HTORR leverages partnerships to facilitate the procurement of donated tissues and their use by researchers working to advance the health of women.

This relates to Objectives 1.1 ("Discover basic biological differences between females and males"), 1.2 ("Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes"), 1.3 ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes"), 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health"), 2.1 ("Expand and develop advanced and innovative approaches for study design, data collection, and analysis to optimize data quality and the ability to detect the influences of sex and gender on health and disease"), and 3.2 ("Identify collaborative opportunities and leverage partnerships to disseminate research that improves the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

Potential Treatment for Metastases of Breast Cancer and Other Cancers

Breast cancer is the second-most common cause of female cancer mortality in the U.S. Approximately 90% of breast cancer deaths result from metastasis, the spread of cancer cells to other parts of the body. Once distant metastases of breast cancer are present, the response rate to chemotherapy is less than 50%, significantly lower than the 90% or higher response rate for primary localized breast cancer. Inflammatory monocytes (IMs) play a key role in the metastasis of breast cancer and other cancers by promoting the migration of circulating tumor cells through the walls of blood vessels and subsequent cancer cell proliferation. IMs are preferentially recruited to metastatic sites, such as the lung and liver, via the monocyte chemoattractant cytokine CCL2. Disruption of this signaling is a promising target for the treatment of metastatic cancers. Recently, researchers used mouse tumor models and human monocyte cultures to investigate the effects of losartan, a type I angiotensin II receptor (AT1R) antagonist, on CCL2-mediated monocyte recruitment and the function of the CCL2 receptor, CCR2 (Regan et al., 2019). The researchers found that losartan and its metabolite

inhibited CCL2–CCR2-mediated IM recruitment. They also revealed details of the molecular mechanism underlying this inhibition. Other studies have shown that losartan reduces the metastatic cancer burden in mice. Collectively, these findings suggest that losartan—and potentially other AT1R blocker drugs—could be repurposed for immunotherapeutic use in treatments for metastatic breast cancer and other metastatic cancers. This basic research study was supported by training and research career development awards from ORIP and research project grants from the National Institute of Allergy and Infectious Diseases; the National Institute of General Medical Sciences; the National Heart, Lung, and Blood Institute; and the National Institute of Neurological Disorders and Stroke. The work contributes to the expansion of research on female-specific conditions and diseases, as well as the development of the next generation of women's health researchers.

This relates to Objectives 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health") and 4.2 ("Develop the next generation of researchers to advance science on the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

Protection Against Intravaginal HIV Infection

Women account for slightly more than 50% of adults living with HIV worldwide, and most HIV infections in women occur through heterosexual transmission. Researchers at the Yerkes National Primate Research Center (YNPRC) are working toward developing vaccines to prevent HIV infection and effective immunotherapies to control HIV in infected individuals. Their approach combines the synergistic effects of multiple arms of the immune system. Recently, YNPRC researchers showed that sequentially immunizing female rhesus monkeys with three heterologous viral vectors (HVV) expressing the major structural protein of HIV and a nanoparticle adjuvanted HIV envelope protein (Env) vaccine induced strong tissue-resident cytotoxic T-cell and antibody responses. The immunized female monkeys also showed enhanced protection against intravaginal challenge with HIV (Petitdemange et al., 2019). Female monkeys immunized following this approach exhibited 66.7% protection after 10 weekly vaginal challenges beginning 1 month after the final immunization. Some animals continued to show this level of protection a year and a half after the last HVV immunization and 8 months after the last Env immunization (Arunachalam et al., 2020). In addition, researchers at the Tulane National Primate Research Center (TNPRC) are also using the rhesus monkey model to advance HIV prevention in women. TNPRC investigators have distinguished vaginal mucins that trap HIV particles and prevent infection from those that transport HIV to susceptible target cells (Schneider et al., 2020). Moreover, they have found that certain antiretroviral compounds approved for oral use may not be safe when applied vaginally or subcutaneously (Su et al., 2020). This body of translational research was funded primarily by multiple grants from ORIP and the National Institute of Allergy and Infectious Diseases. The work contributes to the development of HIV prevention strategies specifically for women.

This relates to Objectives 1.3 ("Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes") and 1.5 ("Expand research on female-specific conditions and diseases, including reproductive stages, and maternal and gynecologic health") of the Trans-NIH Strategic Plan for Women's Health Research.

Estrogen, the Aging Brain, and Female Vulnerability to Alzheimer's Disease

Women account for nearly two-thirds of current Alzheimer's disease (AD) cases. Some studies have linked women's AD vulnerability to estrogen's protective effects on the brain and its decline with menopause. The economic and quality-of-life costs of AD are enormous, and there are currently no interventions that slow disease progression, let alone cure AD. Drugs developed based on rodent models have failed in clinical trials, resulting in a translational gap in AD research. The California National Primate Research Center (CNPRC) has been investigating the role of estrogen in sustaining synaptic and cognitive health in aged female monkeys for 20 years. Recently, CNPRC researchers have extended these studies to the development of a rhesus monkey model of AD, which is based on the demonstrated toxic effects of amyloid beta (Aβ) peptide and targets the earliest phase of AD when brain synapses are lost. CNPRC researchers showed that soluble Aβ oligomers, aggregations of a small number

of Aβ peptides, lead to extensive brain inflammation and synapse loss in the monkeys (Beckman et al., 2019). These effects mimic early AD before overt clinical symptoms appear in patients. The model now can be used to test interventions that may slow or prevent the earliest manifestations of AD. Funded by ORIP and the National Institute on Aging, this basic research study investigated female monkeys because of the higher prevalence of AD in women and the historical bias toward male animals in AD research. The work identifies a hormonal impact on health outcomes in females (Objective 1.3). The work also provides innovative approaches and valid measures to study women's health, as this new monkey model of early AD promises to be a powerful tool in therapeutic development and bridging the gap from other animal models to effective AD treatments.

This relates to Objectives 2.1 ("Expand and develop advanced and innovative approaches for study design, data collection, and analysis to optimize data quality and the ability to detect the influences of sex and gender on health and disease") and 2.2 ("Develop and adapt reliable and valid measures relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

III. Promotion of Women's Health Research

The National Primate Research Centers (NPRCs)

Nonhuman primates (NHPs) are closest to humans in physiology, behavior, and genetics, and their environment and diet can be controlled rigorously, thus eliminating variables that often confound clinical research in humans. NHPs provide critical models for understanding human health, including topics specific to women and girls. The NPRCs were established over 60 years ago, as it is not cost-effective or feasible to duplicate NHP facilities at every institution. As national resources, the seven NPRCs accommodate the needs of researchers throughout the U.S. and facilitate more than 1,000 projects each year, which are funded by several NIH Institutes and Centers, scientific foundations, and other research entities. The program advances research on women's health and elucidates sex differences. NPRC research includes studies to:

- Prevent HIV infection via vaginal and mother-to-child transmission routes and understand the impact of hormones and contraceptives on HIV infection rates (Li et al., 2019; El-Badry et al., 2020; Shapiro et al., 2020);
- Understand reproductive processes such as puberty, pregnancy, and menopause (Aylwin et al., 2019; Merchenthaler et al., 2020; Zimmerman et al., 2020);
- Address reproductive disorders such as polycystic ovarian syndrome and endometriosis, as well as pregnancy complications, preterm labor, fetal alcohol syndrome, and gestational malnutrition (Carbone et al., 2019; Moses et al., 2020; Wang et al., 2020);
- Address the impact of hormones on stress-related disorders that disproportionally affect women, such as anxiety and depression (Reding, Grayson, et al., 2020; Reding, Styner, et al., 2020);
- Prevent or treat infections during pregnancy that adversely affect the developing fetus, such as listeria and Zika virus (Maness et al., 2019; Robbiani et al., 2019; Schouest et al., 2020);
- Detect and treat ovarian cancer (Kim et al., 2020);
- Understand the effect of hormones on Alzheimer's disease, which disproportionately affects women (Beckman et al., 2019); and
- Evaluate potential sex differences in SARS-CoV-2 infections (work in progress).

Investigators can access the NPRCs through their Research and Capabilities website to obtain comprehensive information regarding the range of available programs, resources, and achievements of the NPRCs. An additional website—which targets educators, students, and the general public—provides information on research accomplishments and their impact on human health.

The program aligns with Goals 1 ("Advance rigorous research that is relevant to the health of women") and 2 ("Develop methods and leveraging data sources to consider sex and gender influences that enhance research for the health of women") of the Trans-NIH Strategic Plan for Women's Health Research.

Workshop on the Current Status and Future Enhancements to Animal Models for AIDS Research

Although HIV/AIDS impacts both sexes, women face specific challenges associated with sexual transmission of HIV through the vaginal mucosa and mother-to-child transmission through birth or breastfeeding. These challenges were addressed during a workshop that evaluated animal models used in HIV/AIDS-related research, which was convened by ORIP and the Office of AIDS Research on September 23–24, 2019. Workshop participants discussed the use of rhesus and pigtail macaques to aid our understanding of vaginal infection processes. This included visualizing the distribution of labeled broadly neutralizing antibodies following intravenous administration in macaques and labeled virus to determine viral entry sites. Researchers use the female macaque model to test vaginal prevention strategies, and findings from this line of research were presented at the workshop, as well. Participants discussed the emphasis on prevention of HIV infection in infants through early vaccination or the use of broadly neutralizing antibody therapies. Research in this area is limited, and expansion of the infant macaque model is needed to address this vulnerable population and support therapies in humans.

This workshop aligns with Goal 1 ("Advance rigorous research that is relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research by advancing research on women's health. The workshop also aligns with Goal 3 ("Enhance dissemination and implementation of evidence to improve the health of women"), as highlights of the workshop were disseminated in a report that is available on the ORIP website.

Development of Approaches to Discover Sex-biased Factors that Protect from Disease

Comparing the sexes yields information about inherent biological factors that protect one sex from disease more than the other, which can lead to new therapies that enhance these protective factors and alleviate diseases in both sexes. A major challenge is to recognize protective factors emanating from the sex chromosomes, which make male and female cells different but are difficult to disentangle from the effects of sex hormones produced by the reproductive glands (or gonads). Through its targeted research project grants and programs to support development of animal model and related resources, ORIP continues to make a broad investment in tools, models, and approaches to study sex differences. For example, investigators at the University of California, Los Angeles and the Medical College of Wisconsin supported by an exploratory research project grant from ORIP are working to develop novel transgenic rats that offer new tools to find sex-biased protective factors encoded by the XX and XY sex chromosomes (Prokop et al., 2020). These models enable the comparison of XX and XY rats that are experimentally manipulated such that they develop the same type of gonads, a feat that was achievable previously in laboratory mice but not rats. The new rat lines will be broadly useful to biomedical researchers who seek to discover new protective mechanisms in the many diseases that are more reliably modeled in laboratory rats than mice.

This research contributes to the discovery of basic biological differences between females and males (Objective 1.1 ["Discover basic biological differences between females and males"] of the Trans-NIH Strategic Plan for Women's Health Research), as well as the development of innovative approaches to detect, analyze, and understand sex influences on health and disease (Objective 2.1 [Expand and develop advanced and innovative approaches for study design, data collection, and analysis to optimize data quality and the ability to detect the influences of sex and gender on health and disease]).

IV. Advancement of Women in Biomedical Careers

Training and Career Development Programs for Veterinarian Scientists

ORIP has always and will continue to support training and career development programs, specifically for veterinary students and veterinarians seeking to enter the field of biomedical research. Scientists with veterinary medical expertise contribute to animal, molecular, and genomic studies, as well as translational research that benefits human health. Development awards (K01) assist veterinarians in becoming independent investigators in research related

to comparative medicine. Individual fellowships (F30) provide research training opportunities for veterinary dual-degree students. T32 and T35 training grants offer opportunities for career development, providing long- and short-term support for training veterinarians and veterinary students for research careers in biomedical areas related to comparative medicine, comparative pathology, or other disciplines, to improve and extend healthy lives and prevent illness. The Loan Repayment Program (LRP) recruits and retains health professionals, including veterinarians, into biomedical or biobehavioral research careers through educational debt assistance. For fiscal years 2019 and 2020, women represented approximately 79% of K01 grantees, 71% of F30 fellows, 77% of trainees in the T32 and T35 mentoring/training program, and all LRP awardees supported by ORIP. These programs contribute to efforts to recruit, support, retain, and advance women in the early stages of career development and transition to independence.

This relates to Objective 4.3 ("Enhance and develop programs to recruit, support, retain, and advance women at all stages of their research careers, from early career to leadership positions") of the Trans-NIH Strategic Plan for Women's Health Research.

Increasing Diversity in ORIP's Small Business Programs

To ensure that information about ORIP's small business programs is available to applicants from diverse backgrounds, ORIP added applicant resources to its website in FY 2019 and FY 2020. Success stories from entrepreneur scientists describe the challenges and rewards of preparing small business grant applications. These narratives provide new applicants, especially those from women-owned and socially and economically disadvantaged small businesses, with more insight about what it takes to apply. ORIP's website also includes a Small Business Toolbox to introduce applicants to the program and the process of applying for small business grants. Two animated videos offer tips for creating a small business and an overview of small business grant support from NIH. A fact sheet provides more detail about the grant application process, a Spanish-language version of which was recently developed. ORIP provides a step-by-step guide with wizard functions to walk potential applicants through the selection process and ensure that ORIP is the right fit for their ideas. Finally, ORIP has a flyer with links to many unique resources for small businesses, which have been gathered from several NIH Institutes and Centers that support small business grants. By offering resources in one place, ORIP makes it easy for people from different backgrounds to apply for grants to small business ventures. ORIP's goal is to support their diverse and creative ideas and propel them into development of new technologies that benefit biomedical research. Lastly, ORIP participates in the trans-NIH Entrepreneurial Workforce Diversity Working Group. In FY 2020, this working group began to develop concepts for increasing participation of women and other underrepresented groups in NIH's Small Business Innovation Research and Small Business Technology Transfer programs. These resources and activities offer interventions to improve retention and advancement of women and diverse individuals in research careers.

This relates to Objective 4.5 ("Promote and disseminate research on barriers to the retention and advancement of women in biomedical careers and on interventions to improve their retention and advancement") of the Trans-NIH Strategic Plan for Women's Health Research.

V. Implementation of the NIH Policy on Sex as a Biological Variable (SABV)

At the time of funding, ORIP identifies projects belonging to its women's health portfolio and tracks those projects throughout their duration. These awards fall into four categories: (1) research projects on women's health, (2) centers providing animal and research infrastructure resources used in part for women's health topics, (3) instrumentation supporting women's health and other research, and (4) training and career development grants involving research on women's health. ORIP also has dedicated training programs for veterinary scientists, in which women constitute approximately 70% or more of the trainees. The effectiveness of implementation of NIH's policy to consider SABV in each of these categories is tracked through increases in specific metrics.

For research projects identified as part of ORIP's women's health portfolio, the number of publications that are related to women's health or report sex

differences is tracked. For center and instrumentation awards classified within ORIP's women's health portfolio, the number of projects related to women's health supported by those resources is tracked. For training and career development grants, ORIP tracks publications related to women's health and the successful transition of women trainees to faculty-equivalent and principal investigator positions.

In addition to Research Performance Progress Reports (RPPRs) and searches using NIH software tools, ORIP has developed tracking tools for its own strategic plan (SP) that include a data-driven dashboard for monitoring progress at the program level to capture selected data from RPPRs for specific research center and resource activities. ORIP program staff members record notable accomplishments monthly in a spreadsheet maintained on a shared drive, collect SP highlights monthly from the division directors, and post selected SP highlights on its website.

Lastly, ORIP implements NIH's SABV policy by emphasizing SABV as a critical review criterion in all administrative supplement applications reviewed by program staff. ORIP does this by including SABV in its guidelines for program review, as well as the forms and checklists that program staff members complete when preparing written evaluations. Discussion of how well each applicant addressed SABV is part of ORIP's overall discussions of administrative supplement applications being considered for funding. When an omission of plans to address SABV is found, the relevant ORIP program officer communicates the shortfall to the applicant and requires submission of SABV information before evaluation of the application is completed or any funding recommendations are made.

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Sexual & Gender Minority Research Office

I. Executive Summary

In fiscal years 2019 and 2020, the Sexual & Gender Minority Research Office (SGMRO) spearheaded and participated in a variety of activities to advance women's health. In August 2019, the SGMRO updated the definition of sexual and gender minorities (SGMs) for NIH research to be more expansive and inclusive through NOT-OD-19-139. This increased the ability of investigators to apply for funding opportunities focused on disparity populations, including SGM-identified women. The SGMRO led the development of the fiscal years 2021–2025 NIH Strategic Plan to Advance Research on the Health and Well-being of Sexual & Gender Minorities. The plan, officially released in September 2020, will serve as a framework for SGM health- and research-related endeavors at the NIH for the next 5 years, including those focused on or relevant to SGM women's health and especially those seeking to mitigate existing and emerging health disparities. SGMRO's fiscal year (FY) 2018 SGM Research Portfolio Analysis, released in FY 2019, included for the first time an assessment of specific SGM populations of focus in NIH-funded research—including women who identify as transgender, bisexual, and lesbian—as well as specific special topics of interest in women's health. SGMRO organized the Bisexual Health Research Workshop and its first-ever SGM Health Research Listening Session to enhance our understanding of the health needs and concerns of SGM women, among other populations. SGMRO backed notices of special interest and administrative supplements to support research relevant to women's health. The office also co-funded R21 projects to design and assess research methodologies and measures specifically for the SGM community through RFA-MD-20-005, which could enhance the development and inclusion of SGM projects relevant to women's health. SGMRO held regional workshops, its first SGM Research Symposium, and its second NIH SGM Research Investigator Awards Program, all of which attempted to cultivate an atmosphere of opportunity for women scientists. SGMRO is excited to continue playing a role in advancing SGM women's health research at NIH.

II. Promotion of Women's Health Research

The SGMRO promoted women's health research in a variety of ways in FY 2019–2020, particularly through helping to identify priority areas in SGM women's health (Objective 5.2 ["Identify priority areas for additional study to advance the health of women"] of the Trans-NIH Strategic Plan for Women's Health Research). SGMRO led the development of the FY 2021–2025 NIH Strategic Plan to Advance Research on the Health and Well-being of Sexual and Gender Minorities. The plan, officially released in September 2020, will serve as a framework for SGM health- and research-related endeavors at NIH for the next 5 years, including those focused on or relevant to SGM women's health.

Respectively released in FY 2019 and FY 2020, the FY 2017 and FY 2018 SGM Research Portfolio Analyses described SGM projects in research areas, diseases, and conditions highly relevant to women's health. The FY 2018 analysis included for the first time an assessment of specific SGM populations of focus in NIH-funded research, including women who identify as transgender, bisexual, and lesbian, as well as specific special topics of interest in women's health.

SGMRO hosted events to broaden NIH perspectives in health research relevant to SGM women in FY 2019–2020. The September 2019 Bisexual Health Research Workshop focused on key research gaps and opportunities in the understudied field of bisexual health. The first-ever SGM Health Research Listening Session, which took place in October 2019, convened stakeholders from the health research and advocacy communities to gather comments, concerns, and suggestions about SGM-related research at NIH. Organizations representing priority issues and concerns in SGM women's health were among the invitees. The SGMRO Director, along with a National Institute of Mental Health colleague, presented to the University of Michigan Institute for Research on Women and Gender's Transgender Health Research Group to discuss the SGMRO, grantspersonship, and funding opportunities.

SGMRO, in alignment with Goal 1 ("Advance rigorous research that is relevant to the health of women") of the Trans-NIH Strategic Plan for Women's Health Research to advance rigorous research relevant to women's health, signed on to SGM-relevant notices of special interest (NOSIs) issued by the Office of Research on Women's Health (ORWH) in FY 2020, including one titled Research on the Health of Women of Understudied, Underrepresented and Underreported (U3) Populations and one announcing the availability of administrative supplements for research on sex/gender influences. SGMRO staff members participated in the associated Collaborative Scientific Research Partnerships program review to help develop recommendations on the applications with the highest potential to advance women's health submitted through these NOSIs. SGMRO also provided co-funding for several supplements to studies relevant to women's health through its own SGM Administrative Supplements Program in FY 2019–2020.

III. Advancement of Women in Biomedical Careers

The SGMRO remains committed to promoting and fostering the advancement of women in biomedical careers. The office pursued this goal in part through activities to help develop the next generation of women's health researchers (Objective 4.2 ["Develop the next generation of researchers to advance science on the health of women"] of the Trans-NIH Strategic Plan for Women's Health Research). In FY 2019–2020, SGMRO coordinated three in-person regional workshops—which took place at UCLA, Emory University, and Thomas Jefferson University—and a virtual regional workshop in conjunction with The Ohio State University and the Equitas Health Institute. These workshops were intended to build research and researcher capacity in SGM women's health, among other fields, by increasing understanding of NIH and its granting processes and encouraging the

development of scholarly relationships. SGMRO also held a virtual webinar in June 2020 with the same goals as the regional workshops but with an explicit focus on researchers interested in or actively conducting work in differences in sex development (DSD) and/or intersex populations. SGMRO personnel provided technical assistance to women-identified investigators throughout FY 2019–2020 by providing feedback on SGM-related aspects of their proposals and guiding them to ICs with missions strongly aligned with their specific research aims.

At the first SGM Research Symposium in September 2020, a number of exceptional intramural and extramural investigators at various phases of their careers were invited to give lectures on their research. The symposium featured talks from several women investigators and projects focused on key topics in women's health. All of the awardees of the SGMRO's second NIH SGM Research Investigator Awards Program were women scientists. The program was held in September 2019 to recognize two early-stage investigators and one more established distinguished investigator who have made considerable and outstanding contributions to the field of SGM health research. These activities provide examples of SGMRO's dedication to promoting and advancing women in research at all career stages (all related to Objective 4.3 ["Enhance and develop programs to recruit, support, retain, and advance women at all stages of their research careers, from early career to leadership positions"] of the Trans-NIH Strategic Plan for Women's Health Research).

IV. Implementation of the NIH Policy on Sex as a Biological Variable (SABV)

SGMRO supported the implementation of NIH's SABV policy in several ways in FY 2019 and FY 2020. Development and evaluation of SGM-specific methods and measures and encouraging collection and analysis of data on sexual orientation and gender identity (SOGI) are key scientific and operational goals in the FY 2021–2025 NIH SGM research strategic plan. Robust SOGI-related methods, measures, and data collection help to specify the SGM status of female research participants, allow for stronger design and analysis of research for SGM girls and women, and facilitate more accurate reporting. In FY 2020, SGMRO co-funded several grants on methods and measurement in research with SGM populations through RFA-MD-20-005. SGMRO personnel also developed guidance and criteria for the inclusion of relevant transgender-related projects in the reporting of the NIH women's health budget in FY 2019. These efforts serve to improve the description and quantification of women's health research studies that conduct sex-based analyses and/or report sex-disaggregated results.

Appendix A. NIH Coordinating Committee on Research on Women's Health (CCRWH) Roster

Fiscal Year 2019

	Primary Name	Alternate Name
NIH Institutes and Centers		
CC	Christine Grady, Ph.D., M.S.N.	Ann Berger, M.S.N., M.D.
CSR	Valerie Durrant, Ph.D.	
FIC	Rachel Sturke, Ph.D., M.P.H., M.I.A.	
NCATS	Jane Atkinson, D.D.S.	
NCCIH	Emmeline Edwards, Ph.D.	Della White, Ph.D.
NCI	L. Michelle Bennett, Ph.D.	Diane Palmieri, Ph.D.
NEI	Lisa Neuhold, Ph.D.	
NHGRI	Cristina Kapustij, M.S.	Jennifer Troyer, Ph.D.
NHLBI	Donna Marie DiMichele, M.D.	Xenia Tigno, Ph.D., M.S.
NIA	Kate Nagy, M.A.	Mia Lowden, Ph.D.
NIAAA	Ivana Grakalic, Ph.D.	Deidra Roach, M.D.
NIAID	Johanna Schneider, Ph.D.	Juliane Caviston, Ph.D.
NIAMS	Su-Yau Mao, Ph.D.	Jonelle Drugan, Ph.D.
NIBIB	David George, Ph.D.	Steve Zullo, Ph.D.
NICHD	Lisa Halvorson, M.D., Ph.D.	Candace Tingen, Ph.D.
NIDA	Cora Lee Wetherington, Ph.D. Rita Valentino, Ph.D.	Holly Moore, Ph.D.
NIDCD	Trinh Ly, M.D.	Susan Sullivan, Ph.D.
NIDCR	Lillian Shum, Ph.D.	Dena Fischer, D.D.S., M.S.D., M.S.
NIDDK	Christine Maric-Bilkan, Ph.D.	Eleanor Hoff, Ph.D.
NIEHS	Gwen Collman, Ph.D.	Kelly Chandler, Ph.D.
NIGMS	Judith Greenberg, Ph.D.	
NIMH	Andrea Beckel-Mitchener, Ph.D.	Tamara Lewis Johnson, M.P.H., M.B.A.
NIMHD	Joyce Hunter, Ph.D.	
NINDS	Nina Schor, M.D., Ph.D.	Jim Koenig, Ph.D.
NINR	Yvonne Bryan, Ph.D.	Sung Sug (Sarah) Yoon, Ph.D., RN
NLM	David Landsman, Ph.D.	Rebecca Goodwin, J.D.
NIH Office of the Director		
All of Us	Kelly Gebo, M.D., M.P.H.	
DPCPSI	James Anderson, M.D., Ph.D.	
ECHO	Erin Luetkemeier, Ph.D.	
OAR	Brenda Fredericksen, Ph.D.	
OBSSR	Wendy Smith, Ph.D., M.A., B.C.B.	Katie Morris, M.P.H.
ODP	Elizabeth Neilson, Ph.D., M.P.H., M.S.N.	Kate Winseck, M.S.W.
ODS	Barbara Sorkin, Ph.D.	LaVerne Brown, Ph.D.
OER	Cheryl Kitt, Ph.D.	

	Primary Name	Alternate Name
NIH Office of the Director *(Continued)*		
OLPA	Adrienne Hallett	
ORIP	Stephanie Murphy, V.M.D., Ph.D., DACLAM	
OSP	Carrie Wolinetz, Ph.D.	Ashley Parker, Ph.D.
SGMRO	Christopher Barnhart, Ph.D.	Karen Parker, Ph.D., M.S.W.
CCRWH Executive Secretary FY 2019 Margaret Bevans, RN, Ph.D.		

Fiscal Year 2020

	Primary Name	Alternate Name
NIH Institutes and Centers		
CC	Christine Grady, Ph.D., M.S.N.	Ann Berger, M.S.N., M.D.
CSR	Valerie Durrant, Ph.D.	
FIC	Rachel Sturke, Ph.D., M.P.H., M.I.A.	
NCATS	Jane Atkinson, D.D.S.	
NCCIH	Emmeline Edwards, Ph.D.	Della White, Ph.D.
NCI	L. Michelle Bennett, Ph.D.	Diane Palmieri, Ph.D.
NEI	Lisa Neuhold, Ph.D.	Hongman Song, M.D., Ph.D.
NHGRI	Cristina Kapustij, M.S.	Jennifer Troyer, Ph.D. Tina Gatlin, Ph.D.
NHLBI	Gina Wei, M.D., M.P.H. Donna Marie Dimichele, M.D.	Marrah Lachowicz-Scroggins, Ph.D. Xenia Tigno, Ph.D.
NIA	Kate Nagy, M.A.	Mia Lowden, Ph.D.
NIAAA	Ivana Grakalic, Ph.D.	Deidra Roach, M.D.
NIAID	Johanna Schneider, Ph.D.	Juliane Caviston, Ph.D.
NIAMS	Su-Yau Mao, Ph.D.	Jonelle Drugan, Ph.D.
NIBIB	David George, Ph.D.	Steve Zullo, Ph.D.
NICHD	Lisa Halvorson, M.D., Ph.D.	Candace Tingen, Ph.D.
NIDA	Rita Valentino, Ph.D. Cora Lee Wetherington, Ph.D.	Holly Moore, Ph.D.
NIDCD	Trinh Ly, M.D.	Susan Sullivan, Ph.D.
NIDCR	Lillian Shum, Ph.D.	Dena Fischer, D.D.S., M.S.D., M.S.
NIDDK	Christine Maric-Bilkan, Ph.D.	Eleanor Hoff, Ph.D.
NIEHS	Gwen Collman, Ph.D.	Kelly Chandler, Ph.D.
NIGMS	Dorit Zuk, Ph.D.; Judith Greenberg, Ph.D.	Rochelle Long, Ph.D.; Ann Hagan, Ph.D.
NIMH	Lauren Hill, Ph.D.; Andrea Beckel-Mitchener, Ph.D.	Tamara Lewis Johnson, M.P.H., M.B.A.
NIMHD	Joyce Hunter, Ph.D.	
NINDS	Nina Schor, M.D., Ph.D.	Jim Koenig, Ph.D.
NINR	Yvonne Bryan, Ph.D.	Sung Sug (Sarah) Yoon, Ph.D., RN
NLM	David Landsman, Ph.D.	Rebecca Goodwin, J.D.
NIH Office of the Director		
All of Us	Sheri Schully, Ph.D. Kelly Gebo, M.D., M.P.H.	
DPCPSI	James Anderson, M.D., Ph.D.	
ECHO	Erin Luetkemeier, Ph.D.	
OAR	Brenda Fredericksen, Ph.D.	
OBSSR	Wendy Smith, Ph.D., M.A., B.C.B.	Katie Morris, M.P.H.

	Primary Name	Alternate Name
NIH Office of the Director *(Continued)*		
OCPL	Christen Sandoval, M.S.P.H., C.H.E.S.	
ODP	Elizabeth Neilson, Ph.D., M.P.H., M.S.N.	Kate Winseck, M.S.W.
ODS	Barbara Sorkin, Ph.D.	LaVerne Brown, Ph.D.
ODSS	Belinda Seto, Ph.D.	Jessica Mazerik, Ph.D.
OER	Pamela Kearney, M.D.	
OLPA	Adrienne Hallett	
ORIP	Stephanie Murphy, V.M.D., Ph.D., DACLAM	
OSP	Carrie Wolinetz, Ph.D.	Ashley Parker, Ph.D.
SGMRO	Christopher Barnhart, Ph.D.	Karen Parker, Ph.D., M.S.W.
THRO	Maria (Jay) Revilleza, Ph.D.	
CCRWH Executive Secretary FY 2020 Margaret Bevans, RN, Ph.D.		

List of Abbreviations for the NIH Coordinating Committee on Research on Women's Health (CCRWH) Roster

	Primary Name
NIH Institutes and Centers	
CC	NIH Clinical Center
CSR	Center for Scientific Review
FIC	Fogarty International Center
NCATS	National Center for Advancing Translational Sciences
NCCIH	National Center for Complementary and Integrative Health
NCI	National Cancer Institute
NEI	National Eye Institute
NHGRI	National Human Genome Research Institute
NHLBI	National Heart, Lung, and Blood Institute
NIA	National Institute on Aging
NIAAA	National Institute on Alcohol Abuse and Alcoholism
NIAID	National of Allergy and Infectious Diseases
NIAMS	National Institute of Arthritis and Musculoskeletal and Skin Diseases
NIBIB	National Institute of Biomedical Imaging and Bioengineering
NICHD	*Eunice Kennedy Shriver* National Institute of Child Health and Human Development
NIDA	National Institute on Drug Abuse
NIDCD	National Institute on Deafness and Other Communication Disorders
NIDCR	National Institute of Dental and Craniofacial Research
NIDDK	National Institute of Diabetes and Digestive and Kidney Diseases
NIEHS	National Institute of Environmental Health Sciences
NIGMS	National Institute of General Medical Sciences
NIMH	National Institute of Mental Health
NIMHD	National Institute on Minority Health and Health Disparities
NINDS	National Institute of Neurological Disorders and Stroke
NINR	National Institute of Nursing Research
NLM	National Library of Medicine
NIH Office of the Director	
All of Us	*All of Us* Research Program
DPCPSI	Division of Program, Planning, and Strategic Initiatives

	Primary Name
NIH Office of the Director *(Continued)*	
ECHO	Environmental Influences on Child Health Outcomes (ECHO) program
OAR	Office of AIDS Research
OBSSR	Office of Behavioral and Social Sciences Research
OCPL	Office of Communications and Public Liaison
ODP	Office of Disease Prevention
ODS	Office of Dietary Supplements
ODSS	Office of Data Science Strategy
OER	Office of Extramural Research
OLPA	Office of Legislative Policy and Analysis
ORIP	Office of Research Infrastructure Programs
OSP	Office of Science Policy
SGMRO	Sexual and Gender Minority Research Office
THRO	Tribal Health Research Office

Appendix B. Summaries of Research Co-Funded by ORWH

FY	RFA Title	Title	PI Name	Institution	Grant	ORWH Program	Appl Id	RePORTER Project Info
2019	Risk of Adolescence and Injury in HIV Susceptibility (RAIS) (R01)	Developmental Pharmacology of Antiretroviral Metabolism in Mucosal Tissues	Bumpus, Namandje N	Johns Hopkins University	5 R01AI128781-03	SRP	9617203	RePORTER Project Info
2019	Risk of Adolescence and Injury in HIV Susceptibility (RAIS) (R01)	Mucosal Injury from Sexual Practices: Behaviour and Biology of South African Adolescents	Jaspan, Heather Beryl	Seattle Children's Hospital	5 R01AI128792-03	SRP	9618106	RePORTER Project Info
2019	NIH Research Project Grant (Parent R01)	The Impact of the Herpes Zoster Vaccine on Herpes Zoster Ophthalmicus	Acharya, Nisha	University of California, San Francisco	5 R01EY028739-02	SRP	9618871	RePORTER Project Info
2019	Risk of Adolescence and Injury in HIV Susceptibility (RAIS) (R01)	Mucosal Mechanisms of Altered HIV Susceptibility in Adolescents	Klatt, Nichole Rose	University of Miami School of Medicine	5 R01AI128782-04	SRP	9620594	RePORTER Project Info
2019	Maternal Nutrition and Pre-pregnancy Obesity: Effects on Mothers, Infants and Children (R01)	Severe Maternal Morbidity: An Investigation of Racial-Ethnic Disparities, Social Disadvantage & Maternal Weight	Carmichael, Suzan L	Stanford University	5 R01NR017020-02	SRP	9626954	RePORTER Project Info
2019	Risk of Adolescence and Injury in HIV Susceptibility (RAIS) (R01)	Maturation, Infectibility, and Trauma (MIT) Contributes to HIV Susceptibility in Adolescents	Aldrovandi, Grace M	University of California Los Angeles	5 R01AI128796-03	SRP	9635730	RePORTER Project Info
2019	Limited Competition for the Continuation of the Diabetes Prevention Program Outcomes Study (DPPOS) Biostatistics Research Center (Collaborative U01)	22/22 Diabetes Prevention Program Outcomes Study (DPPOS) Phase 3 - Biostatistics Center	Temprosa, Marinella	George Washington University	5 U01DK048489-26	SRP	9637370	RePORTER Project Info
2019	NCI Clinical and Translational Exploratory/ Developmental Studies (R21 Clinical Trial Optional)	Utilizing microRNA-146a to Block Triple-Negative Breast Cancer Cell Colonization	Liu, Runhua	University of Alabama at Birmingham	1 R56CA223077-01A1	R56	9653100	RePORTER Project Info
2019	Molecular Transducers of Physical Activity Consortium Coordinating Center (CCC) (U24)	MoTrPAC Consortium Coordinating Center	Pahor, Marco	University of Florida	5 U24AR071113-03	SRP	9658372	RePORTER Project Info

FY	RFA Title	Title	PI Name	Institution	Grant	ORWH Program	Appl Id	RePORTER Project Info
2019	Mechanisms, Models, Measurement, and Management in Pain Research (R01 Clinical Trial Optional)	An AHEI Dietary Intervention to Reduce Pain in Women with Endometriosis	Harris, Holly Ruth	Fred Hutchinson Cancer Research Center	1 R01NR017951-01A1	SRP	9683808	RePORTER Project Info
2019	NIH Support for Conferences and Scientific Meetings (Parent R13)	Organization for the Study of Sex Differences Annual Meeting	Schwarz, Jaclyn Marie	University of Delaware	5 R13AG056135-03	SRP	9689388	RePORTER Project Info
2019	Adolescent Brain Cognitive Development (ABCD) Study - Research Project Sites (U01)	Adolescent Brain Cognitive Development (ABCD): FIU	Gonzalez, Raul	Florida International University	5 U01DA041156-05	SRP	9691299	RePORTER Project Info
2019	Building Interdisciplinary Research Careers in Women's Health (K12)	Kentucky BIRCWH Program: Training the Next Generation of Womens Health Researchers	Curry, Thomas E	University of Kentucky	5 K12DA035150-08	BIRCWH	9733999	RePORTER Project Info
2019	Human Heredity and Health in Africa (H3Africa): Research Projects (U01)	African Female Breast Cancer Epidemiology (AFBRECANE) Study	Adebamowo, Clement Adebayo	Institute of Human Virology	5 U01HG009784-03	SRP	9735422	RePORTER Project Info
2019	Training Modules to Enhance the Rigor and Reproducibility of Biomedical Research (R25 Clinical Trial Not Allowed)	Addressing Sex as a Biological Variable in Preclinical Pharmacology and Neuroscience Research: Accounting for Neglected Factors and Applying Practical Solutions to Enhance Rigor and Reproducibility	Ferland-Beckham, Chantelle	Cohen Veterans Bioscience, Inc.	1 R25GM133017-01	SRP	9736060	RePORTER Project Info
2019	Mechanisms, Models, Measurement, and Management in Pain Research (R01 Clinical Trial Optional)	The Role of Opioid Adherence Profiles in Cancer Pain Self-Management and Outcomes	Meghani, Salimah H	University of Pennsylvania	1 R01NR017853-01A1	SRP	9738369	RePORTER Project Info
2019	NIH Research Project Grant (Parent R01 Clinical Trial Not Allowed)	Restoration of Homeostasis of Downstream Targets of MeCP2 as a Potential Therapeutic Avenue for Rett Syndrome	MacDonald, Jessica Linn	Syracuse University	1 R01NS106285-01A1	SRP	9738680	RePORTER Project Info
2019	Human Heredity and Health in Africa (H3Africa): COLLABORATIVE CENTERS (U54)	AWI-Gen Phase 2: Genomic and environmental risk factors for cardiometabolic disease in Africans	Ramsay, Michele Michele	Wits Health Consortium (Pty), Ltd.	5 U54HG006938-08	SRP	9739393	RePORTER Project Info
2019	Mentored Research Scientist Development Award (Parent K01 -Independent Clinical Trial Not Allowed)	Insulin-Resistance Genetic and Epigenetic Variants and Their Interactions with Lifestyle Factors in Postmenopausal Breast Cancer	Jung, Su Yon	University of California, Los Angeles	1 K01NR017852-01A1	SRP	9743013	RePORTER Project Info

FY	RFA Title	Title	PI Name	Institution	Grant	ORWH Program	Appl Id	RePORTER Project Info
2019	Pelvic Floor Disorders Network Data Coordinating Center (U24)	Pelvic Floor Disorders Network Data Coordinating Center: (2016-2021)	Gantz, Marie G	Research Triangle Institute	5 U24HD069031-09	SRP	9744741	RePORTER Project Info
2019	Native American Research Centers for Health (NARCH) (S06)	Cherokee Nation Native American Research Center for Health	Khan, Sohail	Cherokee Nation	5 S06GM123546-03	SRP	9751328	RePORTER Project Info
2019	Women's Reproductive Health Research (WRHR) Career Development Program (K12)	OHSU Womens Reproductive Health Research K12 Program	Caughey, Aaron B	Oregon Health & Science University	5 K12HD085809-05	SRP	9751651	RePORTER Project Info
2019	NIH Research Project Grant (Parent R01 Clinical Trial Not Allowed)	Rapid Estrogen Signaling in Brain Circuits that Guide Complex Behavior	Remage-Healey, Luke R	University of Massachusetts Amherst	2 R01NS082179-06	SRP	9755104	RePORTER Project Info
2019	Limited Competition: Research Training for Career Development of Junior Faculty in Medical Education Partnership Initiative (MEPI) Institutions (D43)	NURTURE: Research Training and Mentoring Program for Career Development of Faculty at Makerere University College of Health Sciences	Sewankambo, Nelson K	Makerere University	5 D43TW010132-05	SRP	9756488	RePORTER Project Info
2019	Prevention of Lower Urinary Tract Symptoms in Women: Bladder Health Clinical Centers (PLUS-CCS) (U01)	University of Pennsylvania+ PLUS Clinical Center (PENN+PLUS CC)	Newman, Diane K	University of Pennsylvania	5 U01DK106892-05	SRP	9761519	RePORTER Project Info
2019	Prevention of Lower Urinary Tract Symptoms in Women: Bladder Health Clinical Centers (PLUS-CCS) (U01)	LUTS Prevention in Adolescent Girls and Women Across the Lifespan	Sutcliffe, Siobhan	Washington University	5 U01DK106853-05	SRP	9762915	RePORTER Project Info
2019	Limited Competition: Research Training for Career Development of Junior Faculty in Medical Education Partnership Initiative (MEPI) Institutions (D43)	Partnership for Health Research Training in Kenya (P-HERT)	Wamalwa, Dalton Chekoko	University of Nairobi	5 D43TW010141-05	SRP	9765433	RePORTER Project Info
2019	Limited Competition: Research Training for Career Development of Junior Faculty in Medical Education Partnership Initiative (MEPI) Institutions (D43)	Building Research And Innovation in Nigerias Science - (BRAINS)	Ogunsola, Folasade Tolulope	University of Lagos-College of Medicine	5 D43TW010134-05	SRP	9766426	RePORTER Project Info
2019	Limited Competition: Research Training for Career Development of Junior Faculty in Medical Education Partnership Initiative (MEPI) Institutions (D43)	UZCHS-Promote Excellence in Research and Faculty Enhanced Career Training (PERFECT Program)	Hakim, James Gita	College of Health SCIS University of Zimbabwe	5 D43TW010137-05	SRP	9766429	RePORTER Project Info

FY	RFA Title	Title	PI Name	Institution	Grant	ORWH Program	Appl Id	RePORTER Project Info
2019	Limited Competition: Research Training for Career Development of Junior Faculty in Medical Education Partnership Initiative (MEPI) Institutions (D43)	Strengthening of Research Capacity for Junior Faculty in Tanzania	Mteta, Alfred Kien	Kilimanjaro Christian Medical College	5 D43TW010138-05	SRP	9766430	RePORTER Project Info
2019	Building Interdisciplinary Research Careers in Women's Health (K12)	The Johns Hopkins Clinical Research Scholars in Womens Health (BIRCWH)	Ford, Daniel Ernest	Johns Hopkins University	5 K12HD085845-05	BIRCWH	9768239	RePORTER Project Info
2019	Building Interdisciplinary Research Careers in Women's Health (K12)	UNC BIRCWH	Boggess, Kim A	University of North Carolina at Chapel Hill	5 K12HD001441-20	BIRCWH	9768904	RePORTER Project Info
2019	Building Interdisciplinary Research Careers in Women's Health (K12)	UCSF-Kaiser Building Interdisciplinary Research Careers in Womens Health Program	Brindis, Claire D	University of California, San Francisco	5 K12HD052163-20	BIRCWH	9768905	RePORTER Project Info
2019	Building Interdisciplinary Research Careers in Women's Health (K12)	Emory University BIRCWH Program	Ofotokun, Ighovwerha	Emory University	5 K12HD085850-05	BIRCWH	9768910	RePORTER Project Info
2019	Biodemography of Aging (R01)	Biodemography of Aging in Wild Chimpanzees	Thompson, Melissa Emery	University of New Mexico	5 R01AG049395-05	SRP	9768946	RePORTER Project Info
2019	Building Interdisciplinary Research Careers in Women's Health (K12)	Training in Sex and Gender Differences Research to Improve Womens Health	Oquendo, Maria A	University of Pennsylvania	5 K12HD085848-05	BIRCWH	9769090	RePORTER Project Info
2019	Building Interdisciplinary Research Careers in Women's Health (K12)	Building Interdisciplinary Research Careers in Womens Health at UC Davis	Gold, Ellen B	University of California, Davis	5 K12HD051958-15	BIRCWH	9769534	RePORTER Project Info
2019	Building Interdisciplinary Research Careers in Women's Health (K12)	Mayo Clinic Building Interdisciplinary Research Careers in Womens Health	Miller, Virginia M	Mayo Clinic Rochester	5 K12HD065987-10	BIRCWH	9769537	RePORTER Project Info
2019	Building Interdisciplinary Research Careers in Women's Health (K12)	Oregon BIRCWH: Scholars in Womens Health Research Across the Lifespan	Guise, Jeanne-Marie	Oregon Health & Science University	5 K12HD043488-18	BIRCWH	9769545	RePORTER Project Info
2019	Building Interdisciplinary Research Careers in Women's Health (K12)	Tufts BIRCWH Program	Freund, Karen	Tufts University	5 K12HD092535-03	BIRCWH	9769546	RePORTER Project Info
2019	Building Interdisciplinary Research Careers in Women's Health (K12)	The Colorado Building Interdisciplinary Research Careers in Womens Health Program	Regensteiner, Judith G	University of Colorado Denver	5 K12HD057022-13	BIRCWH	9769809	RePORTER Project Info
2019	Building Interdisciplinary Research Careers in Women's Health (K12)	Building Interdisciplinary Research Careers in Womens Health in Pittsburgh	Sadovsky, Yoel	Magee-Womens Research Institute and Foundation	5 K12HD043441-18	BIRCWH	9771326	RePORTER Project Info

FY	RFA Title	Title	PI Name	Institution	Grant	ORWH Program	Appl Id	RePORTER Project Info
2019	Building Interdisciplinary Research Careers in Women's Health (K12)	Building Interdisciplinary Research in Womens Health	Krousel-Wood, Marie A	Tulane University	5 K12HD043451-18	BIRCWH	9771327	RePORTER Project Info
2019	Building Interdisciplinary Research Careers in Women's Health (K12)	Building Interdisciplinary Research Careers in Womens Health	Andrews, Nancy Catherine	Duke University	5 K12HD043446-18	BIRCWH	9771328	RePORTER Project Info
2019	Building Interdisciplinary Research Careers in Women's Health (K12)	University of MN Building Interdisciplinary Research Carerrs in Womens Health	Berge, Jerica M	University of Minnesota	5 K12HD055887-13	BIRCWH	9771329	RePORTER Project Info
2019	Building Interdisciplinary Research Careers in Women's Health (K12)	Utah Building Interdisciplinary Research Careers in Womens Health Career Development Program	Varner, Michael W	University of Utah	5 K12HD085852-05	BIRCWH	9771330	RePORTER Project Info
2019	Building Interdisciplinary Research Careers in Women's Health (K12)	Building Interdisciplinary Research Careers in Womens Health	Hartmann, Katherine E	Vanderbilt University Medical Center	5 K12HD043483-19	BIRCWH	9772140	RePORTER Project Info
2019	Mentored Clinical Scientist Research Career Development Award (Parent K08)	Sex disparity and estradiol in Fuchs endothelial corneal dystrophy	Patel, Sangita	State University of New York at Buffalo	5 K08EY029007-02	SRP	9772485	RePORTER Project Info
2019	Building Interdisciplinary Research Careers in Women's Health (K12)	UTMB Womens Health Research Scholars Program	Berenson, Abbey B	University of Texas Medical Branch at Galveston	5 K12HD052023-15	BIRCWH	9772522	RePORTER Project Info
2019	Building Interdisciplinary Research Careers in Women's Health (K12)	Building Interdisciplinary Womens Health at MUSC	McGinty, Jacqueline F	Medical University of South Carolina	5 K12HD055885-13	BIRCWH	9772896	RePORTER Project Info
2019	Building Interdisciplinary Research Careers in Women's Health (K12)	Hormones and Genes in Womens Health: Bench to Bedside	Goldstein, Jill M	Brigham and Women's Hospital	5 K12HD051959-15	BIRCWH	9773725	RePORTER Project Info
2019	Limited Competition: Knockout Mouse Production and Phenotyping Project (UM1)	Consortium for large-scale production and phenotyping of knockout mice (UM1)	Dickinson, Mary E	Baylor College of Medicine	5 UM1HG006348-09	SRP	9775199	RePORTER Project Info
2019	Native American Research Centers for Health (NARCH) (S06)	ANTHC NARCH X	Ferucci, Elizabeth D	Alaska Native Tribal Health Consortium	5 S06GM127911-02	SRP	9778885	RePORTER Project Info
2019	Fogarty Global Injury and Trauma Research Training Program (D43)	Biobehavioral Research Approaches to reduce Effects of Trauma on Mental and Physical Health and Cognitive Outcomes in South Africa	Wyatt, Gail E	University of California, Los Angeles	5 D43TW007278-14	SRP	9782747	RePORTER Project Info
2019	Native American Research Centers for Health (NARCH) (S06)	WMAT-JHU NARCH IX Application	Craig, Mariddie J	White Mountain Apache Tribe	5 S06GM123547-03	SRP	9787557	RePORTER Project Info

FY	RFA Title	Title	PI Name	Institution	Grant	ORWH Program	Appl Id	RePORTER Project Info
2019	Specialized Centers of Research Excellence (SCORE) on Sex Differences (U54)	MUSC Specialized Center of Research Excellence on Sex Differences	McRae-Clark, Aimee L	Medical University of South Carolina	5 U54DA016511-17	SCORE	9788372	RePORTER Project Info
2019	Specialized Centers of Research Excellence (SCORE) on Sex Differences (U54)	Sex Differences in the Metabolic Syndrome	Reue, Karen	University of California, Los Angeles	5 U54DK120342-02	SCORE	9788442	RePORTER Project Info
2019	Specialized Centers of Research Excellence (SCORE) on Sex Differences (U54)	Bioenergetic and Metabolic Consequences of the Loss of Gonadal Function	Kohrt, Wendy M	University of Colorado Denver	5 U54AG062319-07	SCORE	9789165	RePORTER Project Info
2019	Specialized Centers of Research Excellence (SCORE) on Sex Differences (U54)	Sex and Age Differences in Immunity to Influenza (SADII)	Klein, Sabra L	Johns Hopkins University	5 U54AG062333-02	SCORE	9789174	RePORTER Project Info
2019	Specialized Centers of Research Excellence (SCORE) on Sex Differences (U54)	Sex-Specific Effects of Endocrine Disruption on Aging and Alzheimers Disease	Mielke, Michelle M	Mayo Clinic Rochester	5 U54AG044170-07	SCORE	9790887	RePORTER Project Info
2019	Specialized Centers of Research Excellence (SCORE) on Sex Differences (U54)	Emory Specialized Center of Research Excellence (SCORE) on Sex Differences	Ofotokun, Ighovwerha	Emory University	5 U54AG062334-02	SCORE	9790907	RePORTER Project Info
2019	Specialized Centers of Research Excellence (SCORE) on Sex Differences (U54)	Sex-Appropriate Treatment Development for Alcohol Use Disorders	McKee, Sherry Ann	Yale University	5 P01AA027473-07	SRP	9794638	RePORTER Project Info
2019	NIH Research Project Grant (Parent R01 Clinical Trial Not Allowed)	Relationship between mental health coverage and outcomes for privately insured women with perinatal mood and anxiety disorders (PMAD)	Zivin, Kara	University of Michigan at Ann Arbor	1 R01MH120124-01	SRP	9799993	RePORTER Project Info
2019	NCI Clinical and Translational Exploratory/ Developmental Studies (R21 Clinical Trial Optional)	Identifying the missing link in inflammatory signaling	Eisenmesser, Elan Z	University of Colorado Denver	1 R56CA230069-01A1	R56	9807309	RePORTER Project Info
2019	NIH Exploratory/ Developmental Research Grant Program (Parent R21 Clinical Trial Not Allowed)	Understanding disparities in the adoption and use of assistive technology by older Hispanics	Orellano-Colon, Elsa M	University of Puerto Rico, Medical Sciences Campus	1 R21NR018039-01A1	SRP	9823724	RePORTER Project Info
2019	Emerging Global Leader Award (K43)	The Role of Sex Steroid Hormones in CD4+ T Cell-mediated Immune Responses to Tuberculosis	Dabitao, Djeneba	University of Sciences, Techniques and Technology of Bamako	1 K43TW011426-01	SRP	9830842	RePORTER Project Info

FY	RFA Title	Title	PI Name	Institution	Grant	ORWH Program	Appl Id	RePORTER Project Info
2019	Emerging Global Leader Award (K43)	Responding to the challenges of Adolescent Perinatal Depression with patient-centered mobile health	Kola, Lola	University of Ibadan, College of Medicine	1 K43TW011046-01A1	SRP	9831112	RePORTER Project Info
2019	Research Supplements to Promote Re-Entry into Biomedical and Behavioral Research Careers (Admin Supp - Clinical Trial Not Allowed)	Live Tumor Culture Core and Tissue Specific Culture (TSC) System for Human Cancers	Ince, Tan A	University of Miami School of Medicine	3 R33CA214310-02S1	SRP	9831339	RePORTER Project Info
2019	NIH Support for Conferences and Scientific Meetings (Parent R13 Clinical Trial Not Allowed)	The Safety of Asthma Medications During Pregnancy and Lactation: Evidence Gaps and How to Fill Them	Chambers, Christina	University of California, San Diego	1 R13HL149440-01	SRP	9837212	RePORTER Project Info
2019	Administrative Supplement for Research on Sex/Gender Influences (Admin Supp Clinical Trial Optional)	Lateralized targeting of hippocampus to model interactions between epilepsy and reproductive endocrine disorders	Christian, Catherine Anne	University of Illinois at Urbana-Champaign	3 R03NS103029-02S1	Sex/ Gender Admin Supp	9852368	RePORTER Project Info
2019	Administrative Supplement for Research on Sex/ Gender Influences (Admin Supp Clinical Trial Optional)	Congenital cytomegalovirus infection, KIR genotypes, and acute lymphoblastic leukemia	Spector, Logan G	University of Minnesota	3 R01CA228478-02S1	Sex/ Gender Admin Supp	9856011	RePORTER Project Info
2019	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	ABCD-USA Consortium: Coordinating Center	Jernigan, Terry L	University of California, San Diego	3 U24DA041147-04S3	SRP	9857102	RePORTER Project Info
2019	Research on the Health of Women of Understudied, Underrepresented and Underreported (U3) Populations An ORWH FY19 Administrative Supplement (Admin Supp Clinical Trial Optional)	Bringing Modern Data Science Tools to Bare on Environmental Mixtures: Administrative Supplement	Miranda, Marie Lynn	Rice University	3 R01ES028819-02S2	U3 Admin Supp	9860530	RePORTER Project Info
2019	Administrative Supplement for Research on Sex/ Gender Influences (Admin Supp Clinical Trial Optional)	Efficacy of Open-Label Placebo, Double-Blind Placebo, and Peppermint Oil in IBS	Lembo, Anthony J	Beth Israel Deaconess Medical Center	3 R01AT008573-05S1	Sex/ Gender Admin Supp	9868563	RePORTER Project Info
2019	Administrative Supplement for Research on Sex/ Gender Influences (Admin Supp Clinical Trial Optional)	Sensory Neuron-Bacteria Interactions in Modulating Pain and the Host Microbiota	Chiu, Isaac Ming-Cheng	Harvard Medical School	3 DP2AT009499-01S1	Sex/ Gender Admin Supp	9869280	RePORTER Project Info

FY	RFA Title	Title	PI Name	Institution	Grant	ORWH Program	Appl Id	RePORTER Project Info
2019	Administrative Supplement for Research on Sex/Gender Influences (Admin Supp Clinical Trial Optional)	Sex and Gender Differences in Response to Behavioral Strategies for Reducing Stress Reactivity	McHugh, Rebecca Kathryn	McLean Hospital	3 R21DA046937-02S1	Sex/ Gender Admin Supp	9870513	RePORTER Project Info
2019	Administrative Supplement for Research on Sex/ Gender Influences (Admin Supp Clinical Trial Optional)	Sex Differences in GBM and Head and Neck Cancers	Gerson, Stanton L	Case Western Reserve University	3 P30CA043703-29S2	Sex/ Gender Admin Supp	9875776	RePORTER Project Info
2019	Administrative Supplement for Research on Sex/ Gender Influences (Admin Supp Clinical Trial Optional)	REBOOT Admin Supplement	Coffin, Phillip O	Public Health Foundation Enterprises	3 R01DA045690-02S1	Sex/ Gender Admin Supp	9877108	RePORTER Project Info
2019	Administrative Supplement for Research on Sex/ Gender Influences (Admin Supp Clinical Trial Optional)	The Impact of Gender Differences on Identification and Treatment of BPSD in Nursing Home Residents with Dementia	Resnick, Barbara	University of Maryland, Baltimore	3 R01NR015982-04S1	Sex/ Gender Admin Supp	9877585	RePORTER Project Info
2019	Administrative Supplement for Research on Sex/ Gender Influences (Admin Supp Clinical Trial Optional)	Peptidergic modulation of thermoregulation and energy expenditure	Tabarean, Iustin Virgil	Scintillon Institute for Photobiology	3 R01NS094800-06S1	Sex/ Gender Admin Supp	9877956	RePORTER Project Info
2019	Administrative Supplement for Research on Sex/ Gender Influences (Admin Supp Clinical Trial Optional)	Understanding working-age adults with mental illness living in nursing homes	Ulbricht, Christine Marie	University of Massachusetts Medical School, Worcester	3 R21MH117262-02S1	Sex/ Gender Admin Supp	9878436	RePORTER Project Info
2019	Administrative Supplement for Research on Sex/ Gender Influences (Admin Supp Clinical Trial Optional)	Aligned Nanofibrillar Scaffolds Enhance Angiogenesis and Viability in Ischemia: Sex Differences Administrative Supplement	Huang, Ngan F	Stanford University	3 R01HL127113-04S1	Sex/ Gender Admin Supp	9878564	RePORTER Project Info
2019	Administrative Supplement for Research on Sex/ Gender Influences (Admin Supp Clinical Trial Optional)	Experimental Model of Depression in Aging: Insomnia, Inflammation, and Affect Mechanisms	Irwin, Michael R	University of California, Los Angeles	3 R01AG051944-04S1	Sex/ Gender Admin Supp	9878591	RePORTER Project Info
2019	ImmuneChip: Engineering Microphysiological Immune Tissue Platforms (U01 Clinical Trial Not Allowed)	Microvascular Permeability, Inflammation, and Lesion Physiology in Endometriosis: A Microphysiological Systems Approach	Griffith, Linda G	Massachusetts Institute of Technology	1 U01EB029132-01	SRP	9882620	RePORTER Project Info

FY	RFA Title	Title	PI Name	Institution	Grant	ORWH Program	Appl Id	RePORTER Project Info
2019	Administrative Supplement for Research on Sex/Gender Influences (Admin Supp Clinical Trial Optional)	Gender difference in miRNA-mediated T cell aging during viral infection	Yao, Zhi Q	East Tennessee State University	3 R01AI114748-05S1	Sex/ Gender Admin Supp	9896225	RePORTER Project Info
2019	Fogarty Global Health Training Program (D43)	University of California Global Health Institute Program for Fellows and Scholars	Cohen, Craig R	University of California, San Francisco	5 D43TW009343-08	SRP	9899815	RePORTER Project Info
2019	Human Genome Reference Center (HGRC) (U41 Clinical Trial Not Allowed)	The WashU-UCSC-EBI Human Genome Reference Center	Wang, Ting	Washington University	1 U41HG010972-01	SRP	9906005	RePORTER Project Info
2019	Research on the Health of Women of Understudied, Underrepresented and Underreported (U3) Populations An ORWH FY19 Administrative Supplement (Admin Supp Clinical Trial Optional)	Urban Revitalization and Long-Term Effects on Diet, Economic, and Health Outcomes	Dubowitz, Tamara	Rand Corporation	3 R01CA149105-08S2	U3 Admin Supp	9906629	RePORTER Project Info
2019	Research on the Health of Women of Understudied, Underrepresented and Underreported (U3) Populations An ORWH FY19 Administrative Supplement (Admin Supp Clinical Trial Optional)	Hypovitaminosis D promotes MED12-associated genomic instability in uterine fibroids	Boyer, Thomas G	University of Texas Health Science Center	3 R01HD094378-02S1	U3 Admin Supp	9907256	RePORTER Project Info
2019	Research on the Health of Women of Understudied, Underrepresented and Underreported (U3) Populations An ORWH FY19 Administrative Supplement (Admin Supp Clinical Trial Optional)	Environmental risk factors for uterine fibroids: a prospective ultrasound study(Supplement)	Wegienka, Ganesa Rebecca	Henry Ford Health System	3 R01ES028235-03S1	U3 Admin Supp	9907405	RePORTER Project Info
2019	Research on the Health of Women of Understudied, Underrepresented and Underreported (U3) Populations An ORWH FY19 Administrative Supplement (Admin Supp Clinical Trial Optional)	Addressing health disparities among understudied women in the deaf and hard of hearing population	Kushalnagar, Poorna	Gallaudet University	3 R01DC014463-05S1	U3 Admin Supp	9909299	RePORTER Project Info

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2019	Research on the Health of Women of Understudied, Underrepresented and Underreported (U3) Populations An ORWH FY19 Administrative Supplement (Admin Supp Clinical Trial Optional)	Inflammation, Vaginal Microbiota, and STI/HIV Risk	Coleman, Jenell S	Johns Hopkins University	3 R01HD092013-03S1	U3 Admin Supp	9910583	RePORTER Project Info
2019	Research on the Health of Women of Understudied, Underrepresented and Underreported (U3) Populations An ORWH FY19 Administrative Supplement (Admin Supp Clinical Trial Optional)	Effects of glucocorticoids on cognition in HIV-infected women-role of the HIV latent reservoir	Rubin, Leah Helane	Johns Hopkins University	3 R01MH113512-03S1	U3 Admin Supp	9911411	RePORTER Project Info
2019	Research on the Health of Women of Understudied, Underrepresented and Underreported (U3) Populations An ORWH FY19 Administrative Supplement (Admin Supp Clinical Trial Optional)	Perception of dysarthric speech: An objective model of dysarthric speech evaluation with actionable outcomes	Liss, Julie M	Arizona State University-Tempe Campus	3 R01DC006859-13S1	U3 Admin Supp	9911475	RePORTER Project Info
2019	Research on the Health of Women of Understudied, Underrepresented and Underreported (U3) Populations An ORWH FY19 Administrative Supplement (Admin Supp Clinical Trial Optional)	Disparities in Patterns of Recurrent Stroke in the Elderly	Lichtman, Judith H	Yale University	3 R01AG056628-02S1	U3 Admin Supp	9911542	RePORTER Project Info
2019	Research on the Health of Women of Understudied, Underrepresented and Underreported (U3) Populations An ORWH FY19 Administrative Supplement (Admin Supp Clinical Trial Optional)	Toward patient-centered medication adherence support for pregnant and postpartum women living with HIV in the age of digital health and Artificial Intelligence.	Momplaisir, Florence M	Drexel University	3 R01MD013558-02S1	U3 Admin Supp	9911543	RePORTER link unavailable at time of report
2019	Research on the Health of Women of Understudied, Underrepresented and Underreported (U3) Populations An ORWH FY19 Administrative Supplement (Admin Supp Clinical Trial Optional)	Administrative Supplement to Placental miRNA profiles associated with maternal insulin resistance and fetal adiposity: maternal-placental crosstalk	O'Tierney-Ginn, Perrie F	Tufts Medical Center	3 R01HD091735-03S1	U3 Admin Supp	9911807	RePORTER Project Info

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2019	NIH Research Project Grant (Parent R01 Clinical Trial Required)	Healthy Beyond Pregnancy: Leveraging Behavior Economics to Improve Postpartum Care	Himes, Katherine P	Magee-Womens Research Institute and Foundation	1 R56NR017933-01A1	R56	9913829	RePORTER Project Info
2019	Research on the Health of Women of Understudied, Underrepresented and Underreported (U3) Populations An ORWH FY19 Administrative Supplement (Admin Supp Clinical Trial Optional)	Optimized tDCS for fibromyalgia: targeting the endogenous pain control system	Fregni, Felipe	Spaulding Rehabilitation Hospital	3 R01AT009491-02S1	U3 Admin Supp	9938026	RePORTER Project Info
2019	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Study of Womens Health Across the Nation (SWAN) V	Finkelstein, Joel S	Massachusetts General Hospital	3 U01AG012531-25S1	SRP	9954806	RePORTER Project Info
2019	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Study of Womens Health Across the Nation (SWAN) V: UC Davis/Kaiser	Gold, Ellen B	University of California, Davis	3 U01AG012554-25S1	SRP	9954953	RePORTER Project Info
2019	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Study of Womens Health Across the Nation (SWAN) V: Pittsburgh	Matthews, Karen	University of Pittsburgh	3 U01AG012546-25S1	SRP	9955920	RePORTER Project Info
2019	Limited Competition for the Continuation of the Hepatitis B Research Network Clinical Centers (U01)	Harvard Hepatitis B Consortium	Lau, Daryl T	Beth Israel Deaconess Medical Center	3 U01DK082919-12S1	SRP	9959674	RePORTER Project Info
2019	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Study of Womens Health Across the Nation (SWAN) V: Chicago site	Kravitz, Howard M	Rush University Medical Center	3 U01AG012505-25S1	SRP	9960906	RePORTER Project Info
2019	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	The Study of Women Across a Lifespan: SWAN	Derby, Carol A	Albert Einstein College of Medicine	3 U01AG012535-26S1	SRP	9964038	RePORTER Project Info

FY	RFA Title	Title	PI Name	Institution	Grant	ORWH Program	Appl Id	RePORTER Project Info
2019	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Study of Womens Health Across the Nation (SWAN) V: Coordinating Center - Administrative Supplement	Brooks, Maria Mori	University of Pittsburgh	3 U01AG012553-24S1	SRP	9967393	RePORTER Project Info
2019	Administrative Supplement for Research on Sex/Gender Influences (Admin Supp Clinical Trial Optional)	Modeling temporomandibular joint disorders pain: role of transient receptor potential ion channels	Chen, Yong	Duke University	3 R01DE027454-02S1	Sex/ Gender Admin Supp	9978236	RePORTER Project Info
2019	NIH-DOD-VA Pain Management Collaboratory - Pragmatic Clinical Trials Demonstration Projects (UG3/UH3)	Chiropractic Care for Veterans: A Pragmatic Randomized Trial Addressing Dose Effects for cLBP	Long, Cynthia R	Palmer College of Chiropractic	4 UH3AT009761-03	SRP	9980003	RePORTER Project Info
2019	Targeted basic behavioral and social science and intervention development for HIV prevention and care (R01 Clinical Trial Optional)	Monitoring Microaggressions and Adversities to Generate Interventions for Change (MMAGIC) for Black Women Living with HIV	Dale, Sannisha K	University of Miami, Coral Gables	1 R56MH121194-01	R56	9980143	RePORTER Project Info
2019	Prevention of Lower Urinary Tract Symptoms in Women: Bladder Health Clinical Centers (PLUS-CCS) (U01)	PLUS Loyola Clinical Center	Mueller, Elizabeth Rose	Loyola University Chicago	3 U01DK106898-05S1	SRP	9981055	RePORTER Project Info
2019	Administrative Supplement for Research on Sex/ Gender Influences (Admin Supp Clinical Trial Optional)	UAB-UCSD OBrien Center for Acute Kidney Injury Research	Agarwal, Anupam	University of Alabama at Birmingham	3 P30DK079337-12S3	Sex/ Gender Admin Supp	9988079	RePORTER Project Info
2019	Administrative Supplement for Research on Sex/ Gender Influences (Admin Supp Clinical Trial Optional)	CaMKK2 Inhibition as a Dual-Action Bone Anabolic and Anti-Catabolic Therapy in Osteoporosis	Sankar, Uma	Indiana University-Purdue University at Indianapolis	3 R01AR068332-05S1	Sex/ Gender Admin Supp	9988822	RePORTER Project Info
2019	Research on the Health of Women of Understudied, Underrepresented and Underreported (U3) Populations An ORWH FY19 Administrative Supplement (Admin Supp Clinical Trial Optional)	Offering women PrEP with education, shared decision-making and trauma-informed care: the OPENS trial	Dehlendorf, Christine E	University of California, San Francisco	3 R01MD013565-02S1	U3 Admin Supp	9990158	RePORTER Project Info

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2019	Research on the Health of Women of Understudied, Underrepresented and Underreported (U3) Populations An ORWH FY19 Administrative Supplement (Admin Supp Clinical Trial Optional)	NYU Center for the Study of Asian American Health (CSAAH)	Trinh-Shevrin, Chau	New York University School of Medicine	3 U54MD000538-17S3	U3 Admin Supp	9990160	RePORTER Project Info
2019	Administrative Supplement for Research on Sex/Gender Influences (Admin Supp Clinical Trial Optional)	San Antonio Nathan Shock Center of Excellence in the Biology of Aging	Strong, Randy	University of Texas Health Science Center	3 P30AG013319-25S3	Sex/ Gender Admin Supp	9992039	RePORTER Project Info
2019	Administrative Supplement for Research on Sex/ Gender Influences (Admin Supp Clinical Trial Optional)	Investigating Novel Modes of Epigenetic Regulation Through the Polycomb Group	Kalantry, Sundeep	University of Michigan at Ann Arbor	3 R01HD095463-02S1	Sex/ Gender Admin Supp	9994568	RePORTER Project Info
2019	Research on the Health of Women of Understudied, Underrepresented and Underreported (U3) Populations An ORWH FY19 Administrative Supplement (Admin Supp Clinical Trial Optional)	Mechanisms of hypertension in women with polycystic ovary syndrome	Stachenfeld, Nina	John B. Pierce Laboratory, Inc.	3 R01HL135089-02S1	U3 Admin Supp	9995708	RePORTER Project Info
2019	NIH Research Project Grant (Parent R01 Clinical Trial Not Allowed)	Vascular Mechanisms of Hypertension-in-Pregnancy	Khalil, Raouf A	Brigham and Women's Hospital	1 R56HL147889-01	R56	9995759	RePORTER Project Info
2019	Administrative Supplement for Research on Sex/ Gender Influences (Admin Supp Clinical Trial Optional)	Ozone, oxysterols, and lung inflammation	Jaspers, Ilona	University of North Carolina at Chapel Hill	3 R01ES028269-02S2	Sex/ Gender Admin Supp	9995903	RePORTER Project Info
2019	Research on the Health of Women of Understudied, Underrepresented and Underreported (U3) Populations An ORWH FY19 Administrative Supplement (Admin Supp Clinical Trial Optional)	Improving SCD Care using Web-based Guidelines, Nurse Care Managers and Peer Mentors in Primary Care and Emergency Departments in Central North Carolina	Tanabe, Paula	Duke University	3 U01HL133964-04S1	U3 Admin Supp	9998131	RePORTER Project Info

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2019	Administrative Supplement for Research on Sex/Gender Influences (Admin Supp Clinical Trial Optional)	Maintenance and Enhancement of the Atlanta African American Maternal-Child Cohort: Exposome Profiling via High-resolution Metabolomics and Integration of Microbiome-Metabolome-Epigenome Data	Dunlop, Anne Lang	Emory University	3 R24ES029490-02S1	Sex/ Gender Admin Supp	9998551	RePORTER Project Info
2019	Research on the Health of Women of Understudied, Underrepresented and Underreported (U3) Populations An ORWH FY19 Administrative Supplement (Admin Supp Clinical Trial Optional)	Clinical, Genetic, and Proteomic Risk Factors for Pulmonary Hypertension in Heart Failure	Brittain, Evan L	Vanderbilt University Medical Center	3 R01HL146588-01S1	U3 Admin Supp	9999074	RePORTER Project Info
2019	Administrative Supplement for Research on Sex/ Gender Influences (Admin Supp Clinical Trial Optional)	Functional Activation and Targeting of Exosomes for Regenerative Medicine	Ravindran, Sriram	University of Illinois Chicago	3 R01DE027404-02S1	Sex/ Gender Admin Supp	9999086	RePORTER Project Info
2019	Research on the Health of Women of Understudied, Underrepresented and Underreported (U3) Populations An ORWH FY19 Administrative Supplement (Admin Supp Clinical Trial Optional)	Georgia Diabetes Translation Research Center	Narayan, Kabayam M Venkat	Emory University	3 P30DK111024-04S2	U3 Admin Supp	9999726	RePORTER Project Info
2019	Research on the Health of Women of Understudied, Underrepresented and Underreported (U3) Populations An ORWH FY19 Administrative Supplement (Admin Supp Clinical Trial Optional)	University of Arizona Cancer Center - Cancer Center Support Grant	Sweasy, Joann B	University of Arizona	3 P30CA023074-39S3	U3 Admin Supp	10000276	RePORTER Project Info
2019	Administrative Supplement for Research on Sex/ Gender Influences (Admin Supp Clinical Trial Optional)	C. albicans invasion and proliferation during oral infection	Filler, Scott G	Los Angeles Biomedical Research Institute/ Harbor-UCLA Medical Center	3 R01DE026600-03S1	Sex/ Gender Admin Supp	10000390	RePORTER Project Info

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2019	Research on the Health of Women of Understudied, Underrepresented and Underreported (U3) Populations An ORWH FY19 Administrative Supplement (Admin Supp Clinical Trial Optional)	UNC MACS/WIHS Combined Cohort Study Clinical Research Site	Adimora, Adaora A	University of North Carolina at Chapel Hill	3 U01HL146194-01S1	U3 Admin Supp	10002587	RePORTER Project Info
2019	Administrative Supplement for Research on Sex/Gender Influences (Admin Supp Clinical Trial Optional)	Antigen-independent suppression of ocular angiogenesis via the Fc receptor	Ambati, Jayakrishna	University of Virginia	3 R01EY028027-02S1	Sex/ Gender Admin Supp	10003425	RePORTER Project Info
2019	Research on the Health of Women of Understudied, Underrepresented and Underreported (U3) Populations An ORWH FY19 Administrative Supplement (Admin Supp Clinical Trial Optional)	Dana-Farber/ Harvard Cancer Center	Glimcher, Laurie Hollis	Dana-Farber Cancer Institute	3 P30CA006516-54S8	U3 Admin Supp	10004838	RePORTER Project Info
2019	Administrative Supplement for Research on Sex/ Gender Influences (Admin Supp Clinical Trial Optional)	Vulnerability of DHCR7+/- mutation carriers to aripiprazole and trazodone treatment	Mirnics, Karoly	University of Nebraska Medical Center	3 R01MH110636-03S1	Sex/ Gender Admin Supp	10015486	RePORTER Project Info
2019	HEAL Initiative: HEALthy Brain and Child Development Study (HEALthy BCD) (Collaborative R34- Clinical Trial Not Allowed)	2/6 Planning for the HEALthy Early Development Study	Coles, Claire D	Emory University	3 R34DA050340-01S1	SRP	10015724	RePORTER Project Info
2019	HEAL Initiative: HEALthy Brain and Child Development Study (HEALthy BCD) (Collaborative R34- Clinical Trial Not Allowed)	3/6 Planning for the HEALthy Early Development Study	Croff, Julie May	OSU Center for Health Sciences	3 R34DA050343-01S1	SRP	10016736	RePORTER Project Info
2019	HEAL Initiative: HEALthy Brain and Child Development Study (HEALthy BCD) (Collaborative R34- Clinical Trial Not Allowed)	1/6 Planning for the HEALthy Early Development Study	Singer, Lynn T	Case Western Reserve University	3 R34DA050342-01S1	SRP	10020579	RePORTER Project Info
2019	HEAL Initiative: HEALthy Brain and Child Development Study (HEALthy BCD) (R34- Clinical Trial Not Allowed)	A feasibility study of novel technologies to minimize motion-induced biases in functional and structural MRI of young, opioid-affected cohorts	Tisdall, Matthew Dylan	University of Pennsylvania	3 R34DA050297-01S1	SRP	10020594	RePORTER Project Info

FY	RFA Title	Title	PI Name	Institution	Grant	ORWH Program	Appl Id	RePORTER Project Info
2019	Administrative Supplement for Research on Sex/Gender Influences (Admin Supp Clinical Trial Optional)	Pathogenesis of Rebound SIV/HIV Viremia after Antiretrovral Therapy	D'Aquila, Richard T	Northwestern University	3 P01AI131346-03S1	Sex/ Gender Admin Supp	10024236	RePORTER Project Info
2019	Administrative Supplement for Research on Sex/ Gender Influences (Admin Supp Clinical Trial Optional)	Role of neuroestradiol in regulation of the GnRH surge	Terasawa-Grilley, Ei	University of Wisconsin–Madison	3 R01HD089495-02S1	Sex/ Gender Admin Supp	10025846	RePORTER Project Info
2020	NIH Research Project Grant (Parent R01)	Peptidoglycan metabolism and fragment release	Dillard, Joseph P	University of Wisconsin–Madison	5 R01AI097157-08	Sex/ Gender Admin Supp	9814086	RePORTER Project Info
2020	NIH Research Project Grant (Parent R01)	Serotonergic antidepressants as liver tumor preventives	Evason, Kimberley Jane	University of Utah	5 R01CA222570-03	Careers	9827489	RePORTER Project Info
2020	Mentored Patient-Oriented Research Career Development Award (Parent K23 - Independent Clinical Trials Not Allowed)	Complement and Dry Eye Disease Associated with Primary Sjogrens Syndrome	Ziemanski, Jillian F	University of Alabama at Birmingham	5 K23EY028629-02	SRP	9851397	RePORTER Project Info
2020	Specialized Centers of Research Excellence (SCORE) on Sex Differences (U54 Clinical Trial Optional)	Sex Differences in Major Depression: Impact of Prenatal Stress-Immune and Autonomic Dysregulation	Goldstein, Jill M	Massachusetts General Hospital	1 U54MH118919-01A1	SCORE	9853480	RePORTER Project Info
2020	Specialized Centers of Research Excellence (SCORE) on Sex Differences (U54 Clinical Trial Optional)	Center for Stress and Neural Regulation of Reproductive Aging Health Outcomes	Joffe, Hadine	Brigham and Women's Hospital	1 U54AG062322-01A1	SCORE	9854034	RePORTER Project Info
2020	Specialized Centers of Research Excellence (SCORE) on Sex Differences (U54 Clinical Trial Optional)	Yale-SCORE on Sex Differences in Alcohol Use Disorder	McKee, Sherry Ann	Yale University	1 U54AA027989-01	SCORE	9854087	RePORTER Project Info
2020	Specialized Centers of Research Excellence (SCORE) on Sex Differences (U54 Clinical Trial Optional)	Sex related differences in Brain Gut Microbiome Interactions in Irritable Bowel Syndrome	Mayer, Emeran A	University of California, Los Angeles	1 U54DK123755-01	SCORE	9854641	RePORTER Project Info
2020	Specialized Centers of Research Excellence (SCORE) on Sex Differences (U54 Clinical Trial Optional)	The Microvascular Aging and Eicosanoids - Womens Evaluation of Systemic Aging Tenacity (MAE-WEST) (You are never too old to become younger!) Specialized Center for Research Excellence (SCORE)	Cheng, Susan	Cedars-Sinai Medical Center	1 U54AG065141-01	SCORE	9854799	RePORTER Project Info

FY	RFA Title	Title	PI Name	Institution	Grant	ORWH Program	Appl Id	RePORTER Project Info
2020	Addressing the Role of Violence on HIV Care and Viral Suppression (R34 Clinical Trial Optional)	LinkPositively: A Technology-Delivered Peer Navigation and Social Networking Intervention to Improve HIV Care Across the Continuum for Black Women Affected by Interpersonal Violence	Stockman, Jamila Kinshasa	University of California, San Diego	1 R34MH122014-01	SRP	9913297	RePORTER Project Info
2020	NHLBI Clinical Ancillary Studies (R01 - Clinical Trial Optional)	Effect of Intensive Medical Treatment on Quantified Coronary Artery Plaque Components with Serial Coronary CTA in Women with Non-Obstructive CAD	Tamarappoo, Balaji K	Cedars-Sinai Medical Center	1 R01HL151266-01	SRP	9924375	RePORTER Project Info
2020	Pragmatic Research in Healthcare Settings to Improve Diabetes and Obesity Prevention and Care (R18 Clinical Trial Required)	Healthy for 2/ Healthy for U: A Pragmatic Randomized Clinical Trial to Limit Gestational Weight Gain and Prevent Obesity in the Prenatal Care Setting	Bennett, Wendy Lynet	Johns Hopkins University	1 R18DK122416-01A1	SRP	9929087	RePORTER Project Info
2020	Social Epigenomics Research Focused on Minority Health and Health Disparities (R01)	Understanding socioeconomic disparities in perinatal risk: The role of epigenetic and transcriptional regulation in the placenta	Miller, Gregory Evan	Northwestern University	5 R01MD011749-04	U3 Admin Supp	9930464	RePORTER Project Info
2020	Building Interdisciplinary Research Careers in Women's Health (BIRCWH); K12 Clinical Trial Optional	Mayo Clinic Building Interdisciplinary Research Careers in Women's Health	Kantarci, Kejal	Mayo Clinic Rochester	2 K12HD065987-11	BIRCWH	9934722	RePORTER Project Info
2020	Specialized Centers of Research Excellence (SCORE) on Sex Differences (U54)	Sex-Specific Effects of Endocrine Disruption on Aging and Alzheimers Disease	Mielke, Michelle M	Mayo Clinic Rochester	5 U54AG044170-08	SCORE	9936096	RePORTER Project Info
2020	Building Interdisciplinary Research Careers in Women's Health (BIRCWH); K12 Clinical Trial Optional	University of Wisconsin Building Interdisciplinary Research Careers in Womens Health (BIRCWH) Scholars Program	Burnside, Elizabeth S	University of Wisconsin–Madison	1 K12HD101368-01	BIRCWH	9936756	RePORTER Project Info
2020	Building Interdisciplinary Research Careers in Women's Health (BIRCWH); K12 Clinical Trial Optional	UTMB Womens Health Research Scholars Program	Berenson, Abbey B	University of Texas Medical Branch at Galveston	2 K12HD052023-16	BIRCWH	9937452	RePORTER Project Info

FY	RFA Title	Title	PI Name	Institution	Grant	ORWH Program	Appl Id	RePORTER Project Info
2020	Building Interdisciplinary Research Careers in Women's Health (BIRCWH); K12 Clinical Trial Optional	Building Interdisciplinary Research Careers in Womens Health at UC Davis	Lane, Nancy E	University of California, Davis	2 K12HD051958-16	BIRCWH	9937485	RePORTER Project Info
2020	Building Interdisciplinary Research Careers in Women's Health (BIRCWH); K12 Clinical Trial Optional	UCSF-Kaiser Department of Research Building Interdisciplinary Research Careers in Women's Health (BIRCWH) Program	Brindis, Claire D	University of California, San Francisco	2 K12HD052163-21	BIRCWH	9937863	RePORTER Project Info
2020	Building Interdisciplinary Research Careers in Women's Health (BIRCWH); K12 Clinical Trial Optional	Emory University BIRCWH Program	Ofotokun, Ighovwerha	Emory University	2 K12HD085850-06	BIRCWH	9937936	RePORTER Project Info
2020	Building Interdisciplinary Research Careers in Women's Health (BIRCWH); K12 Clinical Trial Optional	The Johns Hopkins Clinical Research Scholars in Womens Health (BIRCWH)	Ford, Daniel Ernest	Johns Hopkins University	2 K12HD085845-06	BIRCWH	9938052	RePORTER Project Info
2020	Building Interdisciplinary Research Careers in Women's Health (BIRCWH); K12 Clinical Trial Optional	Hormones and Genes in Womens Health: From Bench to Bedside	Goldstein, Jill M	Brigham and Women's Hospital	2 K12HD051959-16	BIRCWH	9938066	RePORTER Project Info
2020	Building Interdisciplinary Research Careers in Women's Health (BIRCWH); K12 Clinical Trial Optional	UIC Building Interdisciplinary Research Careers in Womens Health Program	Maki, Pauline M	University of Illinois Chicago	1 K12HD101373-01	BIRCWH	9938261	RePORTER Project Info
2020	Specialized Centers of Research Excellence (SCORE) on Sex Differences (U54)	Emory Specialized Center of Research Excellence (SCORE) on Sex Differences	Ofotokun, Ighovwerha	Emory University	5 U54AG062334-03	SCORE	9938394	RePORTER Project Info
2020	Specialized Centers of Research Excellence (SCORE) on Sex Differences (U54)	Sex and Age Differences in Immunity to Influenza (SADII)	Klein, Sabra L	Johns Hopkins University	5 U54AG062333-03	SCORE	9939380	RePORTER Project Info
2020	Mechanistic investigations of psychosocial stress effects on opioid use patterns (R01- Clinical Trial Optional)	Psychosocial and neurobiological stress and opioid use trajectories following pregnancy	Rutherford, Helena Jane Victoria	Yale University	1 R01DA050636-01	SRP	9940213	RePORTER Project Info
2020	NIH Pathway to Independence Award (Parent K99/R00 - Independent Clinical Trial Not Allowed)	Omics of Pain in the Context of Declining Estrogen	Wagner, Monica Ann	University of Pittsburgh	1 K99NR019080-01	SRP	9951374	RePORTER Project Info

FY	RFA Title	Title	PI Name	Institution	Grant	ORWH Program	Appl Id	RePORTER Project Info
2020	Fogarty Global Health Training Program (D43)	University of California Global Health Institute Program for Fellows and Scholars	Cohen, Craig R	University of California, San Francisco	5 D43TW009343-09	SRP	9966058	RePORTER Project Info
2020	Research Project Grant (Parent R01 Clinical Trial Not Allowed)	The role of host-microbial interactions in altering preterm birth risk among black women	Elovitz, Michal A	University of Pennsylvania	2 R01NR014784-06	SRP	9970866	RePORTER Project Info
2020	Small Grants for New Investigators to Promote Diversity in Health-Related Research (R21 Clinical Trial Optional)	The Monthly Cycling of Food Insecurity and Diabetes Risk	Bermudez-Millan, Angela	University of Connecticut School of Medicine/DNT	1 R21DK122312-01A1	SRP	9979399	RePORTER Project Info
2020	Specialized Centers of Research Excellence (SCORE) on Sex Differences (U54)	Bioenergetic and Metabolic Consequences of the Loss of Gonadal Function	Kohrt, Wendy M	University of Colorado Denver	5 U54AG062319-08	SCORE	9984225	RePORTER Project Info
2020	Training Modules to Enhance the Rigor and Reproducibility of Biomedical Research (R25 Clinical Trial Not Allowed)	Addressing Sex as a Biological Variable in Preclinical Pharmacology and Neuroscience Research: Accounting for Neglected Factors and Applying Practical Solutions to Enhance Rigor and Reproducibility	Ferland-Beckham, Chantelle	Cohen Veterans Bioscience, Inc.	5 R25GM133017-02	SRP	9985132	RePORTER Project Info
2020	Building Interdisciplinary Research Careers in Women's Health (K12)	Kentucky BIRCWH Program: Training the Next Generation of Womens Health Researchers	Curry, Thomas E	University of Kentucky	5 K12DA035150-09	BIRCWH	9985767	RePORTER Project Info
2020	NIH Exploratory/ Developmental Research Grant Program (Parent R21 Clinical Trial Not Allowed)	Understanding disparities in the adoption and use of assistive technology by older Hispanics	Orellano-Colon, Elsa M	University of Puerto Rico, Medical Sciences Campus	5 R21NR018039-02	SRP	9986039	RePORTER Project Info
2020	Native American Research Centers for Health (NARCH) (S06)	ANTHC NARCH X	Ferucci, Elizabeth D	Alaska Native Tribal Health Consortium	5 S06GM127911-03	SRP	9988454	RePORTER Project Info
2020	Building Interdisciplinary Research Careers in Women's Health (K12)	Building Interdisciplinary Womens Health at MUSC	McGinty, Jacqueline F	Medical University of South Carolina	5 K12HD055885-14	BIRCWH	9990801	RePORTER Project Info
2020	Specialized Centers of Research Excellence (SCORE) on Sex Differences (U54)	MUSC Specialized Center of Research Excellence on Sex Differences	McRae-Clark, Aimee L	Medical University of South Carolina	5 U54DA016511-18	SCORE	9991809	RePORTER Project Info

FY	RFA Title	Title	PI Name	Institution	Grant	ORWH Program	Appl Id	RePORTER Project Info
2020	Limited Competition: Knockout Mouse Production and Phenotyping Project (UM1)	Consortium for large-scale production and phenotyping of knockout mice (UM1)	Dickinson, Mary E	Baylor College of Medicine	5 UM1HG006348-10	SRP	9993556	RePORTER Project Info
2020	Building Interdisciplinary Research Careers in Women's Health (K12)	University of MN Building Interdisciplinary Research Carerrs in Womens Health	Berge, Jerica M	University of Minnesota	5 K12HD055887-14	BIRCWH	9994319	RePORTER Project Info
2020	Building Interdisciplinary Research Careers in Women's Health (K12)	Oregon BIRCWH: Scholars in Womens Health Research Across the Lifespan	Guise, Jeanne-Marie	Oregon Health & Science University	5 K12HD043488-19	BIRCWH	9995541	RePORTER Project Info
2020	Building Interdisciplinary Research Careers in Women's Health (K12)	Tufts BIRCWH Program	Freund, Karen	Tufts University	5 K12HD092535-04	BIRCWH	9995546	RePORTER Project Info
2020	Building Interdisciplinary Research Careers in Women's Health (K12)	Building Interdisciplinary Research Careers in Womens Health	Hartmann, Katherine E	Vanderbilt University Medical Center	5 K12HD043483-20	BIRCWH	9996348	RePORTER Project Info
2020	Building Interdisciplinary Research Careers in Women's Health (K12)	Building Interdisciplinary Research Careers in Womens Health	Andrews, Nancy Catherine	Duke University	5 K12HD043446-19	BIRCWH	9996351	RePORTER Project Info
2020	Building Interdisciplinary Research Careers in Women's Health (K12)	Building Interdisciplinary Research in Womens Health	Krousel-Wood, Marie	Tulane University	5 K12HD043451-19	BIRCWH	9996741	RePORTER Project Info
2020	Building Interdisciplinary Research Careers in Women's Health (K12)	The Colorado Building Interdisciplinary Research Careers in Womens Health Program	Regensteiner, Judith G	University of Colorado Denver	5 K12HD057022-14	BIRCWH	9997984	RePORTER Project Info
2020	Building Interdisciplinary Research Careers in Women's Health (K12)	Building Interdisciplinary Research Careers in Womens Health in Pittsburgh	Sadovsky, Yoel	Magee-Womens Research Institute and Foundation	5 K12HD043441-19	BIRCWH	10000187	RePORTER Project Info
2020	Human Heredity and Health in Africa (H3Africa): Research Projects (U01)	African Female Breast Cancer Epidemiology (AFBRECANE) Study	Adebamowo, Clement Adebayo	Institute of Human Virology	5 U01HG009784-04	SRP	10000207	RePORTER Project Info
2020	Native American Research Centers for Health (NARCH) (S06)	Cherokee Nation Native American Research Center for Health	Khan, Sohail	Cherokee Nation	5 S06GM123546-04	SRP	10003323	RePORTER Project Info
2020	Specialized Centers of Research Excellence (SCORE) on Sex Differences (U54)	Sex Differences in the Metabolic Syndrome	Reue, Karen	University of California, Los Angeles	5 U54DK120342-03	SCORE	10004046	RePORTER Project Info

FY	RFA Title	Title	PI Name	Institution	Grant	ORWH Program	Appl Id	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Pelvic Floor Disorders Network Data Coordinating Center: (2016-2021)	Gantz, Marie G	Research Triangle Institute	3 U24HD069031-09S1	SRP	10004349	RePORTER Project Info
2020	NIH Pathway to Independence Award (Parent K99/R00 - Independent Clinical Trial Not Allowed)	Is Preeclampsia and Spontaneous Preterm Delivery Associated with Vascular and Cardiac Function?	Minissian, Margo	Cedars-Sinai Medical Center	5 K99NR018679-02	SRP	10005487	RePORTER Project Info
2020	Environmental Influences on Child Health Outcomes (ECHO) Pediatric Cohorts (UG3/UH3)	Environmental Influences on Child Health Outcomes in the Northern Plains Safe Passage Study Cohort	Elliott, Amy J	Avera McKennan	5 UH3OD023279-06	SRP	10011948	RePORTER Project Info
2020	Fogarty Global Injury and Trauma Research Training Program (D43)	Biobehavioral Research Approaches to reduce Effects of Trauma on Mental and Physical Health and Cognitive Outcomes in South Africa	Wyatt, Gail E	University of California, Los Angeles	5 D43TW007278-15	SRP	10013301	RePORTER Project Info
2020	NIH-DOD-VA Pain Management Collaboratory - Pragmatic Clinical Trials Demonstration Projects (UG3/UH3)	Chiropractic Care for Veterans: A Pragmatic Randomized Trial Addressing Dose Effects for cLBP	Long, Cynthia R	Palmer College of Chiropractic	5 UH3AT009761-04	SRP	10017158	RePORTER Project Info
2020	Native American Research Centers for Health (NARCH) (S06)	WMAT-JHU NARCH IX Application	Craig, Mariddie J	White Mountain Apache Tribe	5 S06GM123547-04	SRP	10020999	RePORTER Project Info
2020	Research Supplements to Promote Re-Entry into Biomedical and Behavioral Research Careers (Admin Supp - Clinical Trial Not Allowed)	Environmental Influences on Childhood Outcomes in the Northern Plains Safe Passage Study Cohorts	Elliott, Amy J	Avera McKennan	3 UH3OD023279-05S1	Careers	10051191	RePORTER Project Info
2020	Prevention of Lower Urinary Tract Symptoms (PLUS) Research Consortium Clinical Research Centers (U01 Clinical Trial Optional)	PLUS Loyola Clinical Center	Mueller, Elizabeth Rose	Loyola University Chicago	2 U01DK106898-06	SRP	10053477	RePORTER Project Info
2020	Prevention of Lower Urinary Tract Symptoms (PLUS) Research Consortium Clinical Research Centers (U01 Clinical Trial Optional)	Penn+Plus Clinical Research Center	Newman, Diane K	University of Pennsylvania	2 U01DK106892-06	SRP	10053952	RePORTER Project Info

FY	RFA Title	Title	PI Name	Institution	Grant	ORWH Program	Appl Id	RePORTER Project Info
2020	The Intersection of Sex and Gender Influences on Health and Disease (R01 Clinical Trial Optional)	Gender and sex differences in phthalate-induced toxicity in the reproductive system	Flaws, Jodi A	University of Illinois at Urbana-Champaign	1 R01ES032163-01	Sex/ Gender R01	10055877	RePORTER Project Info
2020	The Intersection of Sex and Gender Influences on Health and Disease (R01 Clinical Trial Optional)	Hormonal control of HIV latency	Bosque, Alberto	George Washington University	1 R01AI154518-01	Sex/ Gender R01	10062324	RePORTER Project Info
2020	The Intersection of Sex and Gender Influences on Health and Disease (R01 Clinical Trial Optional)	Sex, Gender and the Immuno-pathogenesis of HIV	Scully, Eileen Patricia	Johns Hopkins University	1 R01AI154541-01	Sex/ Gender R01	10062569	RePORTER Project Info
2020	The Intersection of Sex and Gender Influences on Health and Disease (R01 Clinical Trial Optional)	Dissection of the mechanisms underlying sex-influenced cardiovascular disease	Shavit, Jordan A	University of Michigan at Ann Arbor	1 R01ES032255-01	Sex/ Gender R01	10062572	RePORTER Project Info
2020	The Intersection of Sex and Gender Influences on Health and Disease (R01 Clinical Trial Optional)	Sex Determines Age-related Changes in the Repertoire and Function of Natural Antibodies Protective against Streptococcus pneumoniae with Increasing Age	Holodick, Nichol Elizabeth	Western Michigan University School of Medicine	1 R01AI154539-01	Sex/ Gender R01	10062693	RePORTER Project Info
2020	The Intersection of Sex and Gender Influences on Health and Disease (R01 Clinical Trial Optional)	The impact of sex and gender on disease progression, from developmental origins	Pisarska, Margareta	Cedars-Sinai Medical Center	1 R01AI154535-01	Sex/ Gender R01	10062754	RePORTER Project Info
2020	The Intersection of Sex and Gender Influences on Health and Disease (R01 Clinical Trial Optional)	Implicit Bias in the Evidence: An Evaluation of Female-Predominant Disease	Simard, Julia F	Stanford University	1 R01AI154533-01	Sex/ Gender R01	10062770	RePORTER Project Info
2020	Womens Reproductive Health Research (WRHR) Career Development Program (K12 Clinical Trial Optional)	OHSU Womens Reproductive Health Research K12 Program	Caughey, Aaron B	Oregon Health & Science University	2 K12HD085809-06	SRP	10063800	RePORTER Project Info
2020	Global Noncommunicable Diseases and Injury Across the Lifespan: Exploratory Research (R21 Clinical Trials Optional)	Pilot of a network-driven, advocacy intervention to promote cervical cancer screening in Uganda	Wanyenze, Rhoda Kitti	Makerere University	1 R21TW011728-01	SRP	10070662	RePORTER Project Info
2020	Research Supplements to Promote Diversity in Health-Related Research (Admin Supp - Clinical Trial Not Allowed)	Fragmented early-life experiences, aberrant circuit maturation, emotional vulnerabilities	Baram, Tallie Z	University of California, Irvine	3 P50MH096889-07S1	Sex/ Gender Admin Supp	10071051	RePORTER Project Info

FY	RFA Title	Title	PI Name	Institution	Grant	ORWH Program	Appl Id	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Novel use of mHealth data to identify states of vulnerability and receptivity to JITAIs	Nahum-Shani, Inbal	University of Michigan at Ann Arbor	3 U01CA229437-03S1	U3 Admin Supp	10090968	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Severe Maternal Morbidity: An Investigation of Racial-Ethnic Disparities, Social Disadvantage & Maternal Weight	Carmichael, Suzan L	Stanford University	3 R01NR017020-03S1	U3 Admin Supp	10091301	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Understanding Ethnic Differences in Cancer: The Multiethnic Cohort Study - DNA Methylation Supplement	Le Marchand, Loïc	University of Hawaii at Manoa	3 U01CA164973-09S1	U3 Admin Supp	10091327	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Elucidating causes of vaginal symptoms using a multi-omics approach - Admin. Supplement	Ravel, Jacques	University of Maryland, Baltimore	3 R01NR015495-05S1	U3 Admin Supp	10091585	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Teen Mothers' Prenatal Cannabis Use and Co-Use with Tobacco	De Genna, Natacha Marie	University of Pittsburgh	3 R01DA046401-02S1	U3 Admin Supp	10091690	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	MMRRC-UC Davis Research on Sex Influences of Genetic Variation Modeling in Female Mice	Lloyd, KC Kent	University of California, Davis	3 U42OD012210-21S2	Sex/ Gender Admin Supp	10092015	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Gender differences in Well-being, Behavior, and Interventions in Hospitalized Persons with Alzheimer disease and Related Dementias (ADRD). In response to PA-18-591	Boltz, Marie	Pennsylvania State University-University Park	3 R01AG054425-04S1	Sex/ Gender Admin Supp	10092371	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Impact of aging on the outcomes of a mouse model of chronic myeloid leukemia	Chen, Wenyong	Beckman Research Institute/City of Hope	3 UH3CA213385-05S1	Sex/ Gender Admin Supp	10092787	RePORTER Project Info

FY	RFA Title	Title	PI Name	Institution	Grant	ORWH Program	Appl Id	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Role of splicing factor SRSF1 in T cell function and autoimmunity	Moulton, Vaishali	Beth Israel Deaconess Medical Center	3 R01AR068974-05S1	Sex/ Gender Admin Supp	10093179	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Sex and Age Differences in Immunity to Influenza (SADII) - Sex/ Gender Influences Supplement	Klein, Sabra L	Johns Hopkins University	3 U54AG062333-03S1	Sex/ Gender Admin Supp	10093232	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Sex Differences in Fetal Brain-Placental Immune Programming in Maternal Obesity	Edlow, Andrea Goldberg	Massachusetts General Hospital	3 R01HD100022-02S1	Sex/ Gender Admin Supp	10093233	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Mechanism of BMP2 regulation of Mandibular Condylar Cartilage Growth	Yadav, Sumit	University of Connecticut School of Medicine/DNT	3 K08DE025914-04S1	Sex/ Gender Admin Supp	10093636	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Mechanisms that Direct Airway Remodeling in Obese Asthma	Ingram, Jennifer L	Duke University	3 R01HL130234-04S1	Sex/ Gender Admin Supp	10093686	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Male/Female differences in psychosis and mood disorders:Dynamic imaging-genomic models for characterizing and predicting psychosis and mood d	Calhoun, Vince D	Georgia State University	3 R01MH118695-03S1	Sex/ Gender Admin Supp	10093861	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Medical Marijuana, Neurocognition, and Subsequent Substance Use	Gilman, Jodi	Massachusetts General Hospital	3 R01DA042043-04S1	Careers	10126259	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Ethical Issues in Fertility Preservation Among Terminal AYA	Vadaparampil, Susan T	H. Lee Moffitt Cancer Center & Research Institute	3 R25CA142519-10S1	SRP	10127252	RePORTER Project Info

FY	RFA Title	Title	PI Name	Institution	Grant	ORWH Program	Appl Id	RePORTER Project Info
2020	Research on biopsychosocial factors of social connectedness and isolation on health, wellbeing, illness, and recovery (R01 Clinical Trials Not Allowed)	Social connections preventing suicide ideation during developmental transitions among young sexual minority women	Taliaferro, Lindsay Adar	University of Central Florida	1 R01MD015896-01	SRP	10127742	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Environmental Influences on Child Health Outcomes in the Northern Plains Safe Passage Study Cohort	Elliott, Amy J	Avera McKennan	3 UH3OD023279-06S1	SRP	10131366	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Maternal Immune Responsiveness As CLinical Target for Preterm Birth Prevention (MIRACL)	Gillespie, Shannon L	Ohio State University	3 K23NR017902-03S1	Careers	10144543	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Availability, accessibility, and structure of opioid use disorder treatment and maternal and child health outcomes	Jarlenski, Marian Patricia	University of Pittsburgh	3 R01DA045675-03S1	SRP	10150397	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Administrative supplement for R01 ES028738	Saha Ramendra N	University of California, Merced	3 R01ES028738-03S1	Careers	10150422	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Leverage Points for Equitable Systemic Change to Reduce Alcohol Exposed Pregnancy	Weimer, Jill M	Sanford Research/ University of South Dakota	3 P20GM121341-04S1	SRP	10151815	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Investigating the maternal microbial metabolite signature in fetal growth abnormalities in a multi-ethnic cohort	Ward, William S	University of Hawaii at Manoa	3 P30GM131944-02S1	SRP	10152438	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Characterizing the Neurobiology of Pathological Dissociation: Mechanisms of Face Perception and Self Referential Processing	Lebois, Lauren Ann McDonough	McLean Hospital	3 K01MH118467-02S1	Careers	10153365	RePORTER Project Info

FY	RFA Title	Title	PI Name	Institution	Grant	ORWH Program	Appl Id	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Wyoming Sensory Biology COBRE	Sun, Qian-Quan	University of Wyoming	3 P20GM121310-04S3	SRP	10154738	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Alaska INBRE 4 One Health	Barnes, Brian M	University of Alaska Fairbanks	3 P20GM103395-20S2	SRP	10155049	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Administrative Supplement to Understanding and Reversing the Effects of Early Life Adversity on Midlife Health: Improving Daily Psychological Stress Responses using an Ecological Momentary Intervention	Mayer, Stephanie Eva	University of California, San Francisco	3 K99AG062778-02S1	Careers	10158791	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	The Role of 27-hydroxy-cholesterol in Breast Cancer: A Population-Based Multiethnic Study	Loo, Lenora WM	University of Hawaii at Manoa	3 R01CA229815-02S1	U3 Admin Supp	10166556	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Admin Supplement - Effects of obesity on the dynamics of Influenza transmission	Schultz-Cherry, Stacey L	St. Jude Children's Research Hospital	3 R01AI140766-02S1	Sex/ Gender Admin Supp	10171538	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Cortical functional connectivity as an early biomarker of recovery in spinal cord injury	Choe, Ann S	Hugo W. Moser Research Institute at Kennedy Krieger, Inc.	3 R21NS104644-02S1	Careers	10174454	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Administrative Supplement: Regulation and Function of RNA Editing in Human Transcriptomes	Lin, Lan	Children's Hospital of Philadelphia	3 R01GM121827-04S1	Careers	10175509	RePORTER Project Info
2020	Addressing Racial Disparities in Maternal Mortality and Morbidity (R01 Clinical Trial Optional)	Minding the gap: a multidisciplinary approach to reducing maternal health disparities in Georgia	Jamieson, Denise Jean	Emory University	1 R01MD016031-01	SRP	10175512	RePORTER Project Info

FY	RFA Title	Title	PI Name	Institution	Grant	ORWH Program	Appl Id	RePORTER Project Info
2020	Exploratory Clinical Trial Grants in Arthritis and Musculoskeletal and Skin Diseases (R21)	TNF-alpha Blockade with Certolizumab to Prevent Pregnancy Complications in High-Risk Patients with APS	Salmon, Jane E	Hospital for Special Surgery	3 R21AR069189-03S1	SRP	10175669	RePORTER Project Info
2020	Urgent Competitive Revision to Existing NIH Grants and Cooperative Agreements (Urgent Supplement - Clinical Trial Optional)	Social stressors and inflammation: A mixed methods approach to preterm birth	Giurgescu, Carmen	University of Central Florida	3 R01MD011575-05S1	SRP	10176636	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Improving Care after cardiac arrest by informing surrogate decision makers	Perman, Sarah M	University of Colorado Denver	3 K23HL138164-04S1	Careers	10176880	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Targeted Treatment of Metastatic Gastro-enteropancreatic Neuroendocrine Tumors	Rose, John B	University of Alabama at Birmingham	3 K08CA234209-02S1	Careers	10179219	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Clinical Evidence Generation from Electronic Health Records for Precision Medicine	Wiley, Laura Katherine	University of Colorado Denver	3 K01LM013088-02S1	Careers	10189099	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Health For All: Advancing Library-Academic Medical Center Partnerships to Navigate Wellness and Scale Preventive Services Access (Admin Supplement)	Simon, Melissa A	Northwestern University	3 G08LM013188-02S1	SRP	10200395	RePORTER Project Info
2020	Change of Grantee Organization (Type 7 Parent Clinical Trial Optional)	Live Tumor Culture Core and Tissue Specific Culture System for Human Cancers	Ince, Tan A	Weill Medical College of Cornell University	7 R33CA214310-03	Careers	10206818	RePORTER Project Info
2020	NIH Research Project Grant (Parent R01 Clinical Trial Not Allowed)	Inter-generational Link of Cardio-Metabolic Risk: Integrate Multi-OMICs with Birth Cohort	Wang, Xiaobin	Johns Hopkins University	3 R01HD098232-02S1	SRP	10214809	RePORTER Project Info
2020	NIH Research Project Grant (Parent R01)	Targeting the estrogen receptor-α to protect functional β-cell mass in women	Mauvais-Jarvis, Franck	Tulane University	3 R01DK074970-11S1	Sex/ Gender Admin Supp	10217788	RePORTER Project Info

FY	RFA Title	Title	PI Name	Institution	Grant	ORWH Program	Appl Id	RePORTER Project Info
2020	Tobacco Regulatory Science (R01 Clinical Trial Optional)	Impact of Flavor on Youth & Young Adults use Intention, Abuse Liability and Perceptions of Cigarillos	Trapl, Erika S	Case Western Reserve University	3 R01DA048529-02S1	U3 Admin Supp	10219379	RePORTER Project Info
2020	NIH Research Project Grant (Parent R01)	Unraveling the pathogenesis of familial dilated cardiomyopathy towards precision medicine	Karakikes, Ioannis	Stanford University	3 R01HL139679-03S2	Sex/ Gender Admin Supp	10221348	RePORTER Project Info
2020	NIH Pathway to Independence Award (Parent K99/R00)	Development of neural processing of sound in infancy	Lau, Bonnie K	University of Washington	3 R00DC016640-03S1	Careers	10225656	RePORTER Project Info
2020	NIDDK Mentored Research Scientist Development Award (K01)	Cancer Survivorship Research and Training in Radiation Cystitis	Zwaans, Bernadette Margaretha Maria	William Beaumont Hospital Research Institute	3 K01DK114334-03S1	Careers	10226404	RePORTER Project Info
2020	Approaches to Identify and Care for Individuals with Inherited Cancer Syndromes (U01 Clinical Trial Required)	Implementing the moon: Getting genomic testing to the public	Bowen, Deborah J	University of Washington	3 U01CA232795-01A1S1	SRP	10228866	RePORTER Project Info
2020	Mentored Patient-Oriented Research Career Development Award (Parent K23)	Avoidable Acute Care Use among Patients with Lupus	Feldman, Candace Hillary	Brigham and Women's Hospital	3 K23AR071500-04S1	Careers	10231465	RePORTER Project Info
2020	Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp - Clinical Trial Optional)	Anti-Candida activity of CCL28 in oropharyngeal candidiasis	Huppler, Anna	Medical College of Wisconsin	3 K08DE026189-04S1	Careers	10231475	RePORTER Project Info
2020	NIDDK Mentored Research Scientist Development Award (K01)	Neural Mechanisms of Overeating Among Children Exposed to Gestational Diabetes Mellitus In Utero	Luo, Shan	University of Southern California	3 K01DK115638-03S1	Careers	10231611	RePORTER Project Info
2020	Building Interdisciplinary Research Careers in Women's Health (K12)	Emory University BIRCWH Program	Ofotokun, Ighovwerha	Emory University	3 K12HD085850-05S1	BIRCWH	10240364	RePORTER Project Info
2020	Specialized Programs of Research Excellence (SPORES) in Human Cancers for Years 2015 and 2016 (P50)	MD Anderson Gynecologic SPORE for Uterine Cancers	Lu, Karen Hsieh	University of Texas MD Anderson Cancer Center	3 P50CA098258-15S1	U3 Admin Supp	10249382	RePORTER Project Info
2020	Emerging Global Leader Award (K43)	Undetectable and Untransmittable: reducing HIV transmission among young women living with HIV, their partners and children in South Africa	Toska, Elona	University of Cape Town	3 K43TW011434-02S1	Careers	10251400	RePORTER Project Info

FY	RFA Title	Title	PI Name	Institution	Grant	ORWH Program	Appl Id	RePORTER Project Info
2020	NIH Research Project Grant (Parent R01)	Natural History of Viral Induced Airway Dysfunction and Asthma in Minority Children	Burchard, Esteban Gonzalez	University of California, San Francisco	3 U01HL138626-03S1	U3 Admin Supp	10252395	RePORTER Project Info
2020	Specialized Programs of Research Excellence (SPORES) in Human Cancers for Years 2015 and 2016 (P50)	MD Anderson Gynecologic SPORE for Uterine Cancers	Lu, Karen Hsieh	University of Texas MD Anderson Cancer Center	3 P50CA098258-15S3	U3 Admin Supp	10265734	RePORTER Project Info

Appendix C. NIH Workforce and Grantees

Part 1: NIH Workforce

This report analyzes data from the NIH Office of Equity, Diversity, and Inclusion's (EDI) Data Analytics Branch. The data were retrieved from nVision based on the HR 44 report, with demographic information as of September 30, 2019, for FY 2019 and September 30, 2020, for FY 2020. The data contain information about individuals' occupational type, the program type within which they worked, the size of the IC where they worked, their self-reported sex, and their self-reported race and ethnicity. All the data in this report are presented as percentages and in aggregate to protect individuals' privacy.

The data were given to ORWH on January 27, 2021. ORWH staff analyzed the data, and the results were provided to Synergy Enterprises, Inc. to prepare for distribution. The data are shown as percentages in each category of interest, broken down by sex and, in some cases, by race and ethnicity. This report is based solely on descriptive statistics, and hypothesis testing was not performed on the data. All differences discussed are thematically meaningful but may not be statistically significant.

The initial data analysis was given to Synergy on February 26, 2021, with subsequent analysis of specific variables performed on March 4 and March 9, 2021. Synergy and ORWH communicated via email and met to discuss draft versions of the charts presented herein. All charts and subsequent discussions were approved by ORWH before publication. Data definitions and limitations follow this discussion.

Data Definitions

Occupational Types

The NIH workforce involves three sectors: Scientific occupations, Infrastructure occupations, and Health and Research occupations. Because of small cell counts, this report does not include many analyses for the Health and Research occupations to protect data confidentiality. Nurses make up a large proportion of the Health and Research occupations. The three sectors are defined as follows:

- Scientific employees directly lead and/or conduct basic or clinical research. They also provide oversight for research, both intramural and extramural. Some examples include, but are not limited to, biologists, health scientist administrators, medical officers, and veterinary staff members. Employees who have a position title containing investigator, scientist, clinician, medical officer, scientific officer, scientific executive, program leader, or policy leader are also classified as Scientific employees.
- Health and Research employees directly support the basic and clinical research conducted at NIH. Many of these occupations are allied health professions. Examples of Health and Research occupations include, but are not limited to, nurses, pharmacists, biological lab technicians, and patient care technicians. To protect data confidentiality, most analyses for this report excluded individuals in the Health and Research occupations.
- Infrastructure employees are those in all occupations that are not classified as Scientific or Health and Research. These occupations support the other occupations and include accountants, budget officers, engineers, and other administrative and maintenance staff members.[32]

Program Types

NIH classifies programs into three categories, based on human resources' organizational codes and determined by the functions and structure of an IC. In general, "Extramural Program" refers to the programs that work with outside researchers; "Intramural Program" refers to the programs that work with NIH's own research staff members; and "Other Program" refers to administrative units. However, individual ICs may vary somewhat in their usage of "Other Program." For example, the National Institute of Allergy and Infectious Diseases' Extramural Administration Branch falls under the institute's Office of the Director; thus, this branch was placed into the "Other" category. On the other hand, the National Institute of Neurological Disorders and Stroke's Intramural Administrative Management Branch

32. NIH Office of Equity, Diversity, and Inclusion's Data Analytics Branch.

is housed under that institute's Division of Intramural Research. Therefore, the work unit is categorized as Intramural. Offices of the Director, including the NIH Office of the Director (OD) and the Office of the Director in every IC, belong to the Other category. This categorization includes all OD program offices, such as the Office of AIDS Research, the Office of Behavioral and Social Sciences Research, and ORWH.

Institute or Center Size

NIH groups ICs by the number of employees. The breakdowns are as follows:

- ICs with 501 employees or more are considered large and include the following: the Clinical Center; the National Cancer Institute; the National Heart, Lung, and Blood Institute; the National Institute of Allergy and Infectious Diseases; the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development; the National Institute of Diabetes and Digestive and Kidney Diseases; the National Institute of Environmental Health Sciences; the National Institute of Mental Health; the National Institute of Neurological Disorders and Stroke; the National Library of Medicine; and the Office of the Director.
- ICs with 201 to 500 employees are considered medium-sized and include the following: the Center for Information Technology, the Center for Scientific Review, the National Eye Institute, the National Human Genome Research Institute, the National Institute on Aging, the National Institute on Alcohol Abuse and Alcoholism, the National Institute of Arthritis and Musculoskeletal and Skin Diseases, the National Institute of Dental and Craniofacial Research, and the National Institute on Drug Abuse.
- ICs with 200 employees or fewer are considered small and include the following: the Fogarty International Center, the National Center for Advancing Translational Sciences, the National Center for Complementary and Integrative Health, the National Institute of Biomedical Imaging and Bioengineering, the National Institute on Deafness and Other Communication Disorders, the National Institute of General Medical Sciences, the National Institute on Minority Health and Health Disparities, and the National Institute of Nursing Research.

Race and Ethnicity

Data on employee race and ethnicity are self-reported. Categories were combined to preserve the privacy of employees. "Race" and "ethnicity" were treated as distinct categories. Thus, if an individual's ethnicity was reported Hispanic, that person was not included in a racial group. The category "Other Races, Including Multiple Races" contains American Indians/Alaska Natives, Native Hawaiians/Pacific Islanders, and individuals of two or more races. These groups were combined to preserve the privacy of the employees.

Leadership

This report breaks leadership into two main categories: senior leadership and individuals with supervisory status. Senior leadership includes the NIH Director, NIH Deputy Directors/Associate Deputy Directors, IC Directors, IC Deputy Directors, Scientific Directors, Clinical Directors, Executive Officers, and Other Executives (SL, ES). Scientific and Clinical Directors serving in acting roles were not counted under senior leadership. This analysis does not include senior leaders in the Commissioned Corps because of the lack of complete demographic data from Commissioned Corps employees. The "Supervisory Status" category includes employees with supervisory status codes of 2, 4, and 5.[33] The sample of supervisory leaders here includes only those with the following pay plans: AD, GS, GP, GM, GR, RS, RF, RG, and RS.[34] This sample of supervisory leaders also excludes those in the senior leadership group defined above.

Promotion

This report defines "promotion" as a change of status, through continuous employment, from one General Schedule (GS) grade to a higher GS grade. Note that promotions in this context did not include tenure-track promotions or conversions from GS to RF. In addition, obtaining a quality step increase was not considered a promotion.

33. Supervisory status is determined by the supervisory status codes of 2 (Supervisor or Manager – GSSG), 4 (Supervisor – CSRA), and 5 (Management Official – CSRA). "Supervisory Status" includes T42 employees. See https://dw.opm.gov/datastandards/referenceData/1578/current?index=S.

34. See the U.S. Office of Personnel Management's Data Standards guide for more information about these pay plans: https://dw.opm.gov/datastandards/referenceData/1497/current?category=&q=pay+plan.

Data Limitations

The NIH data in this report include only full-time-equivalent staff members. Contractors, Commissioned Corps members, and advisory council members were excluded. Additionally, promotion data apply only to GS-track employees and permanent positions. The data do not capture the entire NIH workforce, as key types of employees are excluded, including part-time employees and contractors. The data are presented as percentages only and do not include information on cell-level frequencies to protect individual employees' privacy.

Part 2: Sex and/or Gender Gaps

Methodology

The section of this report titled "NIH Grant Funding and Success Rates: Differences by Sex and/or Gender from Fiscal Years 2016 to 2020," on pages 55–72, examines funding gaps by grant applicants' sex and/or gender, race, ethnicity, and career stage, with an extended discussion on females from underrepresented racial and ethnic groups. For this examination, ORWH acquired relevant data from the Division of Statistical Analysis and Reporting (DSAR) within the NIH Office of Extramural Research's Office of Research Reporting and Analysis. As demographic data included some personal information from grant applicants, all of the analytic results—including data provided to Synergy Enterprises, Inc.—underwent data security clearance by DSAR; the data were not manipulated beyond restructuring for visualization purposes.

NIH has numerous grant mechanisms. This section of the report focuses on research project grants (RPGs) and R01-equivalent grants. An RPG is "an award made to an institution/organization to support discrete, specified, circumscribed projects to be performed by named investigators in areas representing their specific interest and competencies."[35] The R01-equivalent grant family includes DP1, DP2, DP5, R01, R23, R29, R37, R56, RF1, RL1, U01, and R35 from select National Institute of General Medical Sciences (NIGMS) and National Human Genome Research Institute (NHGRI) program announcements (PAs). However, not all of these activities may be in use by NIH every year.

In addition to the application and award counts, this report discusses grant application success rates. According to NIH:

> *Success rates are defined as the percentage of reviewed grant applications that receive funding. They are computed on an FY basis and include applications that are peer-reviewed and either scored or unscored by an Initial Review Group. Success rates are determined by dividing the number of competing applications funded by the sum of the total number of competing applications reviewed and the number of funded carryovers. Applications having one or more submissions for the same project in the same FY are counted only once. Some grants are jointly funded by two or more NIH Institutes and Centers (ICs). Usually, the IC that contributes the most dollars to the grant receives the award count, but the amount contributed by each IC is shown.*

The grant data presented for FY 2020 do not include awards issued through supplemental coronavirus disease 2019 (COVID-19) appropriations and include only those awards made with direct budget authority funds.

Definitions of the NIH RPG

Application Gender

- Female-Only: Application contains only women investigators.
- Male-Only: Application contains only men investigators.
- Mixed-Gender: Multiple–principal investigator (MPI) application contains women and men investigators and/or investigators whose gender is unknown or has been withheld.
- Unknown/Withheld-Only: Application contains only investigators whose gender is unknown or has been withheld.

Application Race and Ethnicity

NIH has adopted the 1997 Office of Management and Budget (OMB) revised minimum standards for

35. This definition of the NIH RPG comes from https://grants.nih.gov/grants/glossary.htm#R. RPGs include these grant activities: R00, R01, R03, R15, R21, R33, R34, R35, R36, R37, R50, R56, R61, RC1, RC2, RC3, RC4, RF1, RL1, RL2, RL9, P01, P42, PM1, PN1, RM1, UA5, UC1, UC2, UC3, UC4, UC7, UF1, UG3, UH2, UH3, UH5, UM1, UM2, U01, U19, U34, DP1, DP2, DP3, DP4, and DP5.

maintaining, collecting, and presenting data on race and ethnicity for all grant applications, contract and intramural proposals, active research grants, cooperative agreements, and contract and intramural projects. The minimum standards are described in the 1997 OMB Statistical Policy Directive No. 15: https://www.govinfo.gov/content/pkg/FR-1997-10-30/pdf/97-28653.pdf.

This directive revised minimum standards to include two ethnic categories ("Hispanic or Latino" and "Not Hispanic or Latino") and five racial categories ("American Indian or Alaska Native," "Asian," "Black or African American," "Native Hawaiian or Other Pacific Islander," and "White"). "Person reporting more than one race" under "race" indicates that an investigator indicated more than one race. "Withheld" under "race" indicates that the investigator chose not to disclose that information. "Unknown" indicates that the item was not completed and was missing in the IMPAC II database. Race and ethnicity are self-reported and subject to change. For this report, the combination of race and ethnicity is applied where Hispanic ethnicity takes priority over race, and the demographics are determined at the application level, where all PIs and MPIs on the same grant need to have the same demographics to be classified in a specific gender/racial/ethnic category. For example, "Other Non-White" includes American Indians/Alaska Natives, those who are more than one race, and Native Hawaiians/Pacific Islanders who are not Hispanic. More specifically:

- American Indian–Only: Application contains only American Indian investigators.
- Asian-Only: Application contains only Asian investigators.
- Black-Only: Application contains only Black investigators.
- Mixed-Race: MPI application contains investigators with different races identified.
- More Than One Race–Only: Application contains only investigators who are more than one race.
- Pacific Islander–Only: Application contains only Pacific Islander investigators.
- Unknown/Withheld-Only: Application contains only investigators whose race is unknown or has been withheld.

» White-Only: Application contains only White investigators.

NIH Institutes and Centers: Beginning in FY 2007, the success rates for the RPG category included grants funded by the National Library of Medicine and the National Cancer Institute's "cancer control" budget category. The National Center for Research Resources was dissolved in FY 2012, so no success rates for this center will be reported for FY 2013 and beyond. The National Center for Advancing Translational Sciences was established in FY 2012, so success rates for this center will be reported for FY 2012 and beyond. Beginning in FY 2012, success rates were reported for two programs moved to the NIH Office of the Director, the Office of Research Infrastructure Programs and the Science Education Partnership Awards.

Excluded from the calculation of success rates are those applications that were withdrawn by applicants prior to review or returned or administratively withdrawn by the Center for Scientific Review or another IC and not peer-reviewed by an Initial Review Group.

a. **Funded carryovers** are those applications that were reviewed and not funded in the review year but were funded in the next year. In the review year, the application is counted only in the success rate denominator (reviewed), but in the next year, when the application is funded, it is included in the success rate numerator (awarded) and denominator (reviewed).

b. **Reasons for returning or withdrawing an application prior to review** include, but are not limited to, the application was late, its budget request exceeded guidelines, and the applicant or the applicant's institution was ineligible.

NIH Success Rate Reporting Categories

Budget mechanism and activity codes: Success rates are shown by specific activity codes (e.g., R01, T32) and budget mechanisms (e.g., RPGs, other research).

Award types: Success rates are shown for all competing grants combined and broken down by new, continuation, and revision (formerly known as competing supplements) grants. New competitive awards (Type 1) comprise projects that have not yet been funded. The continuation category includes competitive renewal awards (Type 2), the subset of extension awards (Type 4) that were competitive, and competitive renewals that had a change of IC or division from one competitive segment (or time period) to the subsequent segment (Type 9). Changes in grantee and institution awards (Type 7) that occurred in the same year as competitive new awards (Type 1) are classified as new grants. Changes in grantee and institution awards (Type 7) that occurred in the same year as competitive renewal awards are classified as continuation grants. The revisions category includes only the subset of Type 3 awards that were competed.

Budget authority: NIH receives the majority of its budget authority through multiple appropriations provided annually under the jurisdiction of the House Appropriations Subcommittee on Labor, Health and Human Services, and Education. NIH also receives resources from the Superfund Research account under the jurisdiction of the House Appropriations Subcommittee on Interior, Environment, and Related Agencies—as well as the mandatory Special Statutory Funding Program for Type 1 Diabetes Research appropriations and reimbursements from other Federal agencies. Beginning in FY 2008, success rates for grants funded from the Superfund Research Program have been reported separately from success rates calculated for grants funded from House Appropriations Subcommittee on Labor, Health and Human Services, and Education appropriations. Prior to FY 2008, the success rates for the "other research" budget mechanism category included grants funded from reimbursable agreements. Since FY 2008, this treatment has not been used. The NIH RPG success rate provided annually to Congress is based on activities funded from House Appropriations Subcommittee on Labor, Health and Human Services, and Education appropriations and the Special Statutory Funding Program for Type 1 Diabetes Research. Success rates for other budget mechanisms and by type of funding source (e.g., direct budget authority from the House Appropriations Subcommittee on Labor, Health and Human Services, and Education and the Special Statutory Funding Program for Type 1 Diabetes Research; the Superfund Research Program; and non–direct budget authority [reimbursables/gift funds/cancer research stamp funds/ Interdepartmental Delegation of Authority funds]) are available in some reports.

Appendix D. Members of the NIH Working Group on Women in Biomedical Careers

Co-Chairs

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

Francis S. Collins, M.D., Ph.D.
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Marie Bernard, M.D.
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Intramural Research

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Chief, Laboratory of Molecular and Cellular Neurobiology, National Institute of Mental Health

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Intramural Research *(Continued)*

Samantha Fede, Ph.D.
Researcher, Clinical Neuroimaging Research Core, National Institute on Alcohol Abuse and Alcoholism (postdoc representative)

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Joan Schwartz, Ph.D.
Special Volunteer, NIH Office of Intramural Research

Kathryn Zoon, Ph.D.
Scientist Emeritus, Cytokine Biology Section, National Institute of Allergy and Infectious Diseases

Appendix E. Aggregate Enrollment Data Tables and Trend Data

Section 1: Metrics Based on Aggregate Enrollment by Sex/Gender

Table 1A: Total Enrollment for All National Institutes of Health (NIH) Clinical Research from FY 2010 to 2020

Fiscal Year	Total Enrollment	Total Females	% Females	Total Males	% Males	Total Unknown	% Unknown	Enrollment in Female-only	% Female-only	Enrollment in Male-only	% Male-only	Females, Excluding Female-only	% Females, Excluding Female-only	Males, Excluding Male-only	% Males, Excluding Male-only
2010	23,363,635	13,102,832	56.1	10,044,444	43.0	216,359	0.9	4,440,402	19.0	1,328,551	5.7	8,662,430	37.1	8,715,893	37.3
2011	15,992,456	9,499,682	59.4	6,287,306	39.3	205,468	1.3	4,562,652	28.5	1,210,876	7.6	4,937,030	30.9	5,076,430	31.7
2012	17,655,238	10,071,897	57.0	7,382,884	41.8	200,457	1.1	3,713,994	21.0	1,096,914	6.2	6,357,903	36.0	6,285,970	35.6
2013	17,580,725	9,961,014	56.7	7,397,295	42.1	222,416	1.3	3,522,251	20.0	1,174,274	6.7	6,438,763	36.6	6,223,021	35.4
2014	28,565,995	16,353,416	57.2	11,038,679	38.6	1,173,900	4.1	3,550,006	12.4	429,440	1.5	12,803,410	44.8	10,609,239	37.1
2015	21,453,866	13,278,481	61.9	7,829,861	36.5	345,524	1.6	3,828,704	17.8	280,567	1.3	9,449,777	44.0	7,549,294	35.2
2016	39,712,265	20,983,081	52.8	17,865,381	45.0	863,803	2.2	2,985,796	7.5	217,876	0.5	17,997,285	45.3	17,647,505	44.4
2017	20,068,789	9,470,264	47.2	10,127,155	50.5	471,370	2.3	1,299,004	6.5	919,239	4.6	8,171,260	40.7	9,207,916	45.9
2018	12,814,162	6,711,564	52.4	5,668,475	44.2	434,123	3.4	1,445,846	11.3	918,805	7.2	5,265,718	41.1	4,749,670	37.1
2019	13,241,413	6,894,390	52.1	5,930,000	44.8	417,023	3.1	1,545,776	11.7	878,398	6.6	5,348,614	40.4	5,051,602	38.2
2020	13,705,659	7,552,684	55.1	5,532,650	40.4	620,325	4.5	1,840,890	13.4	121,670	0.9	5,711,794	41.7	5,410,980	39.5

Table 1B: Total Enrollment for NIH Clinical Research at U.S. Sites from FY 2015 to 2020

Fiscal Year	Total Enrollment	Total Females	% Females	Total Males	% Males	Total Unknown	% Unknown	Enrollment in Female-only	% Female-only	Enrollment in Male-only	% Male-only	Females, Excluding Female-only	% Females, Excluding Female-only	Males, Excluding Male-only	% Males, Excluding Male-only
2015	17,212,103	10,529,683	61.2	6,404,104	37.2	278,316	1.6	3,569,721	20.7	209,567	1.2	6,959,962	40.4	6,194,537	36.0
2016	30,710,848	16,594,940	54.0	13,311,968	43.3	803,940	2.6	2,722,586	8.9	163,430	0.5	13,872,354	45.2	13,148,538	42.8
2017	13,231,166	6,491,639	49.1	6,302,343	47.6	437,184	3.3	1,010,384	7.6	871,532	6.6	5,481,255	41.4	5,430,811	41.0
2018	10,578,286	5,413,405	51.2	4,775,856	45.1	389,025	3.7	1,147,146	10.8	886,491	8.4	4,266,259	40.3	3,889,365	36.8
2019	10,356,075	5,185,006	50.1	4,853,379	46.9	317,690	3.1	1,205,796	11.6	817,553	7.9	3,979,210	38.4	4,035,826	39.0
2020	11,080,871	6,062,190	54.7	4,480,382	40.4	538,299	4.9	1,452,673	13.1	72,788	0.7	4,609,517	41.6	4,407,594	39.8

Table 1C: Total Enrollment for Extramural NIH Clinical Research at U.S. Sites from FY 2015 to 2020

Fiscal Year	Total Enrollment	Total Females	% Females	Total Males	% Males	Total Unknown	% Unknown	Enrollment in Female-only	% Female-only	Enrollment in Male-only	% Male-only	Females, Excluding Female-only	% Females, Excluding Female-only	Males, Excluding Male-only	% Males, Excluding Male-only
2015	14,149,649	8,427,534	59.6	5,525,413	39.0	196,702	1.4	2,277,591	16.1	199,298	1.4	6,149,943	43.5	5,326,115	37.6
2016	27,510,129	14,418,631	52.4	12,415,288	45.1	676,210	2.5	1,377,694	5.0	153,472	0.6	13,040,937	47.4	12,261,816	44.6
2017	10,730,843	5,264,128	49.1	5,136,833	47.9	329,882	3.1	868,102	8.1	861,158	8.0	4,396,026	41.0	4,275,675	39.8
2018	9,074,769	4,650,602	51.2	4,068,126	44.8	356,041	3.9	1,065,792	11.7	876,842	9.7	3,584,810	39.5	3,191,284	35.2
2019	8,617,428	4,294,606	49.8	4,059,871	47.1	262,951	3.1	1,089,780	12.6	807,425	9.4	3,204,826	37.2	3,252,446	37.7
2020	9,365,822	5,184,613	55.4	3,697,229	39.5	483,980	5.2	1,337,059	14.3	61,624	0.7	3,847,554	41.1	3,635,605	38.8

Table 1D: Total Enrollment for Intramural NIH Clinical Research at U.S. Sites from FY 2015 to 2020

Fiscal Year	Total Enrollment	Total Females	% Females	Total Males	% Males	Total Unknown	% Unknown	Enrollment in Female-only	% Female-only	Enrollment in Male-only	% Male-only	Females, Excluding Female-only	% Females, Excluding Female-only	Males, Excluding Male-only	% Males, Excluding Male-only
2015	3,062,454	2,102,149	68.6	878,691	28.7	81,614	2.7	1,292,130	42.2	10,269	0.3	810,019	26.4	868,422	28.4
2016	3,200,719	2,176,309	68.0	896,680	28.0	127,730	4.0	1,344,892	42.0	9,958	0.3	831,417	26.0	886,722	27.7
2017	2,500,323	1,227,511	49.1	1,165,510	46.6	107,302	4.3	142,282	5.7	10,374	0.4	1,085,229	43.4	1,155,136	46.2
2018	1,503,517	762,803	50.7	707,730	47.1	32,984	2.2	81,354	5.4	9,649	0.6	681,449	45.3	698,081	46.4
2019	1,738,647	890,400	51.2	793,508	45.6	54,739	3.1	116,016	6.7	10,128	0.6	774,384	44.5	783,380	45.1
2020	1,715,049	877,577	51.2	783,153	45.7	54,319	3.2	115,614	6.7	11,164	0.7	761,963	44.4	771,989	45.0

Table 1E: Total Enrollment for All NIH-Defined Phase III Clinical Trials from FY 2010 to 2020

Fiscal Year	Total Enrollment	Total Females	% Females	Total Males	% Males	Total Unknown	% Unknown	Enrollment in Female-only	% Female-only	Enrollment in Male-only	% Male-only	Females, Excluding Female-only	% Females, Excluding Female-only	Males, Excluding Male-only	% Males, Excluding Male-only
2010	769,885	408,181	53.0	330,808	43.0	30,896	4.0	119,103	15.5	62,315	8.1	289,078	37.5	268,493	34.9
2011	584,278	333,293	57.0	222,060	38.0	28,925	5.0	82,315	14.1	26,229	4.5	250,978	43.0	195,831	33.5
2012	603,136	374,819	62.1	197,019	32.7	31,298	5.2	58,916	9.8	10,288	1.7	315,903	52.4	186,731	31.0
2013	691,023	506,732	73.3	179,220	25.9	5,071	0.7	217,869	31.5	12,406	1.8	288,863	41.8	166,814	24.1
2014	797,264	478,222	60.0	314,310	39.4	4,732	0.6	32,310	4.1	4,267	0.5	445,912	55.9	309,951	38.9
2015	1,619,508	1,091,910	67.4	507,561	31.3	20,037	1.2	29,368	1.8	4,267	0.3	1,062,542	65.6	503,294	31.1
2016	2,130,389	1,396,503	65.6	710,818	33.4	23,068	1.1	35,463	1.7	7,480	0.4	1,361,040	63.9	703,338	33.0
2017	907,643	535,440	59.0	371,636	40.9	567	0.1	154,733	17.0	10,800	1.2	380,707	41.9	360,836	39.8
2018	417,713	260,652	62.4	155,960	37.3	1,101	0.3	116,019	27.8	10,131	2.4	144,633	34.6	145,829	34.9
2019	329,747	202,483	61.4	119,369	36.2	7,895	2.4	91,232	27.7	374	0.1	111,251	33.7	118,995	36.1
2020	349,651	216,040	61.8	127,864	36.6	5,747	1.6	81,462	23.3	3,914	1.1	134,578	38.5	123,950	35.4

Table 1F: Total Enrollment for All NIH-Defined Phase III Clinical Trials at U.S. Sites from FY 2015 to 2020

Fiscal Year	Total Enrollment	Total Females	% Females	Total Males	% Males	Total Unknown	% Unknown	Enrollment in Female-only	% Female-only	Enrollment in Male-only	% Male-only	Females, Excluding Female-only	% Females, Excluding Female-only	Males, Excluding Male-only	% Males, Excluding Male-only
2015	173,640	83,932	48.3	89,228	51.4	480	0.3	17,089	9.8	3,361	1.9	66,843	38.5	85,867	49.5
2016	169,893	83,278	49.0	86,425	50.9	190	0.1	22,733	13.4	6,092	3.6	60,545	35.6	80,333	47.3
2017	550,782	330,307	60.0	220,245	40.0	230	0.0	138,934	25.2	8,207	1.5	191,373	34.7	212,038	38.5
2018	335,391	209,985	62.6	124,830	37.2	576	0.2	98,685	29.4	7,468	2.2	111,300	33.2	117,362	35.0
2019	230,040	148,099	64.4	81,012	35.2	929	0.4	78,234	34.0	150	0.1	69,865	30.4	80,862	35.2
2020	189,745	121,041	63.8	66,765	35.2	1,939	1.0	56,547	29.8	3,155	1.7	64,494	34.0	63,610	33.5

Table 1G: Total Enrollment for Extramural NIH-Defined Phase III Clinical Trials at U.S. Sites from FY 2015 to 2020

Fiscal Year	Totals Enrollment	Total Females	% Females	Total Males	% Males	Total Unknown	% Unknown	Enrollment in Female-only	% Female-only	Enrollment in Male-only	% Male-only	Females, Excluding Female-only	% Females, Excluding Female-only	Males, Excluding Male-only	% Males, Excluding Male-only
2015	161,030	74,759	46.4	85,794	53.3	477	0.3	11,067	6.9	3,181	2.0	63,692	39.6	82,613	51.3
2016	158,741	74,969	47.2	83,586	52.7	186	0.1	16,713	10.5	5,911	3.7	58,256	36.7	77,675	48.9
2017	540,640	322,436	59.6	217,976	40.3	228	0.0	132,912	24.6	8,191	1.5	189,524	35.1	209,785	38.8
2018	327,633	206,817	63.1	120,274	36.7	542	0.2	98,429	30.0	7,468	2.3	108,388	33.1	112,806	34.4
2019	218,431	140,865	64.5	76,657	35.1	909	0.4	72,785	33.3	132	0.1	68,080	31.2	76,525	35.0
2020	177,995	113,844	64.0	62,232	35.0	1,919	1.1	51,098	28.7	3,132	1.8	62,746	35.3	59,100	33.2

Table 1H: Total Enrollment for Intramural NIH-Defined Phase III Clinical Trials at U.S. Sites from FY 2015 to 2020

Fiscal Year	Total Enrollment	Total Females	% Females	Total Males	% Males	Total Unknown	% Unknown	Enrollment in Female-only	% Female-only	Enrollment in Male-only	% Male-only	Females, Excluding Female-only	% Females, Excluding Female-only	Males, Excluding Male-only	% Males, Excluding Male-only
2015	12,610	9,173	72.7	3,434	27.2	3	0.0	6,022	47.8	180	1.4	3,151	25.0	3,254	25.8
2016	11,152	8,309	74.5	2,839	25.5	4	0.0	6,020	54.0	181	1.6	2,289	20.5	2,658	23.8
2017	10,142	7,871	77.6	2,269	22.4	2	0.0	6,022	59.4	16	0.2	1,849	18.2	2,253	22.2
2018	7,758	3,168	40.8	4,556	58.7	34	0.4	256	3.3	0	0.0	2,912	37.5	4,556	58.7
2019	11,609	7,234	62.3	4,355	37.5	20	0.2	5,449	46.9	18	0.2	1,785	15.4	4,337	37.4
2020	11,750	7,197	61.3	4,533	38.6	20	0.2	5,449	46.4	23	0.2	1,748	14.9	4,510	38.4

Section 2: Aggregate Enrollment of Race and Ethnicity: Clinical Research

Table 2A: Total Enrollment and Minority Enrollment for all NIH Clinical Research from FY 2010 to 2020

Fiscal Year	Total Enrollees	Minority Enrollees	% Minority Enrollees
2010	23,363,635	7,510,763	32.1
2011	15,992,456	6,488,223	40.6
2012	17,655,238	6,446,175	36.5
2013	17,580,725	6,687,678	38.0
2014	28,565,995	9,582,978	33.5
2015	21,453,866	8,602,086	40.1
2016	39,712,265	14,987,425	37.7
2017	20,068,789	10,075,058	50.2
2018	12,814,162	4,621,528	36.1
2019	13,241,413	5,306,702	40.1
2020	13,705,659	5,422,277	39.6

Table 2B: Total Enrollment and Minority Enrollment for NIH Clinical Research at U.S. Sites from FY 2015 to 2020

Fiscal Year	Total Enrollees	Minority Enrollees	% Minority Enrollees
2015	17,212,103	4,778,010	27.8
2016	30,710,848	11,179,772	36.4
2017	13,231,166	3,742,781	28.3
2018	10,578,286	3,094,979	29.3
2019	10,356,075	3,097,390	29.9
2020	11,080,871	3,559,530	32.1

Table 2C: Total Enrollment and Minority Enrollment for Extramural NIH Clinical Research at U.S. Sites from FY 2015 to 2020

Fiscal Year	Total Enrollees	Minority Enrollees	% Minority Enrollees
2015	14,149,649	4,421,098	31.3
2016	27,510,129	10,770,168	39.1
2017	10,730,843	3,240,677	30.2
2018	9,074,769	2,863,823	31.6
2019	8,617,428	2,781,206	32.3
2020	9,365,822	3,255,607	34.8

Table 2D: Total Enrollment and Minority Enrollment for Intramural NIH Clinical Research at U.S. Sites from FY 2015 to 2020

Fiscal Year	Total Enrollees	Minority Enrollees	% Minority Enrollees
2015	3,062,454	356,912	11.7
2016	3,200,719	409,604	12.8
2017	2,500,323	502,104	20.1
2018	1,503,517	231,156	15.4
2019	1,738,647	316,184	18.2
2020	1,715,049	303,923	17.7

Table 2E: Total Enrollment for All NIH Clinical Research Racial Categories from FY 2015 to 2020

Fiscal Year	Total Enrollment	No. Inclusion Data Record	Minority Enrollment	% Minority Enrollment	American Indian/ Alaska Native	% American Indian/ Alaska Native	Asian	% Asian	Black/ African American	% Black/ African American	Native Hawaiian/ Pacific Islander	% Native Hawaiian/ Pacific Islander	White	% White	More Than One Race	% More Than One Race	Unknown/ Not Reported	% Unknown/ Not Reported
2015	21,453,866	11,082	8,602,086	40.1	488,167	2.3	3,403,915	15.9	2,546,765	11.9	40,321	0.2	10,367,705	48.3	339,308	1.6	4,267,685	19.9
2016	39,712,265	13,069	14,987,425	37.7	618,188	1.6	4,466,346	11.2	4,502,686	11.3	261,649	0.7	19,893,061	50.1	875,399	2.2	9,094,936	22.9
2017	20,068,789	14,580	10,075,058	50.2	130,608	0.7	6,041,535	30.1	2,325,409	11.6	27,863	0.1	9,399,014	46.8	438,059	2.2	1,706,301	8.5
2018	12,814,162	16,209	4,621,528	36.1	124,447	1.0	1,158,703	9.0	2,045,956	16.0	31,054	0.2	7,500,227	58.5	360,906	2.8	1,592,869	12.4
2019	13,241,413	20,976	5,306,702	40.1	332,839	2.5	1,265,006	9.6	2,382,720	18.0	25,109	0.2	7,557,649	57.1	275,442	2.1	1,402,648	10.6
2020	13,705,659	23,856	5,422,277	39.6	125,107	0.9	970,380	7.1	2,686,063	19.6	32,470	0.2	7,583,104	55.3	358,092	2.6	1,950,443	14.2

Table 2F: Total Enrollment for All NIH Clinical Research Ethnic Categories from FY 2015 to 2020

Fiscal Year	Not Hispanic	% Not Hispanic	Hispanic/ Latino	% Hispanic/ Latino	Unknown/ Not Reported	% Unknown/ Not Reported
2015	15,298,198	71.3	2,332,328	10.9	3,823,340	17.8
2016	26,831,115	67.6	4,841,284	12.2	8,039,866	20.2
2017	16,920,869	84.3	1,378,631	6.9	1,769,289	8.8
2018	10,033,964	78.3	1,190,849	9.3	1,589,349	12.4
2019	10,408,121	78.6	1,438,707	10.9	1,394,585	10.5
2020	10,562,148	77.1	1,506,845	11.0	1,636,666	11.9

Table 2G: Total Enrollment for All NIH Clinical Research at U.S. Sites Racial Categories from FY 2015 to 2020

Fiscal Year	Total Enrollment	Minority Enrollment	% Minority Enrollment	American Indian/ Alaska Native	% American Indian/ Alaska Native	Asian	% Asian	Black/ African American	% Black/ African American	Native Hawaiian/ Pacific Islander	% Native Hawaiian/ Pacific Islander	White	% White	More Than One Race	% More Than One Race	Unknown/ Not Reported	% Unknown/ Not Reported
2015	17,212,103	4,778,010	27.8	139,377	0.8	970,862	5.6	1,672,975	9.7	31,675	0.2	9,950,746	57.8	288,773	1.7	4,157,695	24.2
2016	30,710,848	11,179,772	36.4	321,625	1.0	2,395,431	7.8	3,249,188	10.6	252,436	0.8	19,415,746	63.2	829,095	2.7	4,247,327	13.8
2017	13,231,166	3,742,781	28.3	117,270	0.9	422,203	3.2	1,808,949	13.7	27,601	0.2	8,859,771	67.0	390,899	3.0	1,604,473	12.1
2018	10,578,286	3,094,979	29.3	97,257	0.9	423,422	4.0	1,488,023	14.1	30,573	0.3	6,792,076	64.2	297,436	2.8	1,449,499	13.7
2019	10,356,075	3,097,390	29.9	106,917	1.0	330,178	3.2	1,621,811	15.7	23,396	0.2	6,824,704	65.9	218,035	2.1	1,231,034	11.9
2020	11,080,871	3,559,530	32.1	112,525	1.0	440,262	4.0	1,654,856	14.9	28,495	0.3	6,776,754	61.2	295,884	2.7	1,772,095	16.0

Table 2H: Total Enrollment for all NIH Clinical Research at U.S. Sites Ethnic Categories from FY 2015 to 2020

Fiscal Year	Not Hispanic	% Not Hispanic	Hispanic/ Latino	% Hispanic/ Latino	Unknown/ Not Reported	% Unknown/ Not Reported
2015	11,678,565	67.9	1,834,210	10.7	3,699,328	21.5
2016	23,183,045	75.5	4,373,479	14.2	3,154,324	10.3
2017	10,416,536	78.7	1,199,711	9.1	1,614,919	12.2
2018	8,207,889	77.6	983,148	9.3	1,387,249	13.1
2019	8,227,934	79.5	935,848	9.0	1,192,293	11.5
2020	8,385,291	75.7	1,210,907	10.9	1,484,673	13.4

Table 2I: Total Enrollment for Extramural NIH Clinical Research at U.S. Sites Racial Categories from FY 2015 to 2020

Fiscal Year	Total Enrollment	Minority Enrollment	% Minority Enrollment	American Indian/ Alaska Native	% American Indian/ Alaska Native	Asian	% Asian	Black/ African American	% Black/ African American	Native Hawaiian/ Pacific Islander	% Native Hawaiian/ Pacific Islander	White	% White	More Than One Race	% More Than One Race	Unknown/ Not Reported	% Unknown/ Not Reported
2015	14,149,649	4,421,098	31.3	112,119	0.8	931,086	6.6	1,481,082	10.5	26,466	0.2	8,593,188	60.7	278,313	2.0	2,727,395	19.3
2016	27,510,129	10,770,168	39.1	293,887	1.1	2,352,180	8.6	3,028,871	11.0	247,061	0.9	18,012,861	65.5	817,320	3.0	2,757,949	10.0
2017	10,730,843	3,240,677	30.2	86,996	0.8	361,873	3.4	1,543,732	14.4	22,115	0.2	6,997,681	65.2	377,235	3.5	1,341,211	12.5
2018	9,074,769	2,863,823	31.6	70,274	0.8	398,335	4.4	1,363,141	15.0	26,622	0.3	5,611,705	61.8	287,841	3.2	1,316,851	14.5
2019	8,617,428	2,781,206	32.3	77,900	0.9	296,726	3.4	1,462,620	17.0	18,794	0.2	5,509,710	63.9	205,164	2.4	1,046,514	12.1
2020	9,365,822	3,255,607	34.8	83,909	0.9	405,980	4.3	1,502,915	16.0	24,347	0.3	5,479,939	58.5	283,073	3.0	1,585,659	16.9

Table 2J: Total Enrollment for Extramural NIH Clinical Research at U.S. Sites Ethnic Categories from FY 2015 to 2020

Fiscal Year	Not Hispanic	% Not Hispanic	Hispanic/ Latino	% Hispanic/ Latino	Unknown/ Not Reported	% Unknown/ Not Reported
2015	10,250,999	72.5	1,745,814	12.3	2,152,836	15.2
2016	21,757,302	79.1	4,265,923	15.5	1,486,904	5.4
2017	8,519,353	79.4	1,065,979	9.9	1,145,511	10.7
2018	6,866,982	75.7	938,306	10.3	1,269,481	14.0
2019	6,727,443	78.1	851,856	9.9	1,038,129	12.0
2020	6,900,130	73.7	1,132,453	12.1	1,333,239	14.2

Table 2K: Total Enrollment for Intramural NIH Clinical Research at U.S. Sites Racial Categories from FY 2015 to 2020

Fiscal Year	Total Enrollment	Minority Enrollment	% Minority Enrollment	American Indian/ Alaska Native	% American Indian/ Alaska Native	Asian	% Asian	Black/ African American	% Black/ African American	Native Hawaiian/ Pacific Islander	% Native Hawaiian/ Pacific Islander	White	% White	More Than One Race	% More Than One Race	Unknown/ Not Reported	% Unknown/ Not Reported
2015	3,062,454	356,912	11.7	27,258	0.9	39,776	1.3	191,893	6.3	5,209	0.2	1,357,558	44.3	10,460	0.3	1,430,300	46.7
2016	3,200,719	409,604	12.8	27,738	0.9	43,251	1.4	220,317	6.9	5,375	0.2	1,402,885	43.8	11,775	0.4	1,489,378	46.5
2017	2,500,323	502,104	20.1	30,274	1.2	60,330	2.4	265,217	10.6	5,486	0.2	1,862,090	74.5	13,664	0.5	263,262	10.5
2018	1,503,517	231,156	15.4	26,983	1.8	25,087	1.7	124,882	8.3	3,951	0.3	1,180,371	78.5	9,595	0.6	132,648	8.8
2019	1,738,647	316,184	18.2	29,017	1.7	33,452	1.9	159,191	9.2	4,602	0.3	1,314,994	75.6	12,871	0.7	184,520	10.6
2020	1,715,049	303,923	17.7	28,616	1.7	34,282	2.0	151,941	8.9	4,148	0.2	1,296,815	75.6	12,811	0.7	186,436	10.9

Table 2L: Total Enrollment for Intramural NIH Clinical Research at U.S. Sites Ethnic Categories from FY 2015 to 2020

Fiscal Year	Not Hispanic	% Not Hispanic	Hispanic/ Latino	% Hispanic/ Latino	Unknown/ Not Reported	% Unknown/ Not Reported
2015	1,427,566	46.6	88,396	2.9	1,546,492	50.5
2016	1,425,743	44.5	107,556	3.4	1,667,420	52.1
2017	1,897,183	75.9	133,732	5.3	469,408	18.8
2018	1,340,907	89.2	44,842	3.0	117,768	7.8
2019	1,500,491	86.3	83,992	4.8	154,164	8.9
2020	1,485,161	86.6	78,454	4.6	151,434	8.8

Section 3: Aggregate Enrollment of Race and Ethnicity: NIH-Defined Phase III Clinical Trials

Table 3A: Total Enrollment and Minority Enrollment for All NIH-Defined Phase III Clinical Trials from FY 2010 to 2020

Fiscal Year	Total Enrollees	Minority Enrollees	% Minority Enrollees
2010	769,885	447,187	58.1
2011	584,278	347,770	59.5
2012	603,136	396,714	65.8
2013	691,023	526,422	76.2
2014	797,264	627,456	78.7
2015*	1,619,508	1,492,248	92.1
2016*	2,130,389	1,992,237	93.5
2017	907,643	459,046	50.6
2018	417,714	160,615	38.5
2019	329,747	153,529	46.6
2020	349,651	234,614	67.1

**FY2015 and FY2016 includes data from large foreign Phase III trials which tend to have larger numbers of participants than domestic Phase III trials.*

Table 3B: Total Enrollment and Minority Enrollment at U.S. Sites for All NIH-Defined Phase III Clinical Trials from FY 2015 to 2020

Fiscal Year	Total Enrollees	Minority Enrollees	% Minority Enrollees
2015	173,640	70,361	40.5
2016	169,893	72,318	42.6
2017	550,782	123,247	22.4
2018	335,391	104,170	31.1
2019	230,040	70,390	30.6
2020	189,745	84,422	44.5

Table 3C: Total Enrollment and Minority Enrollment at U.S. Sites for Extramural NIH-Defined Phase III Clinical Trials from FY 2015 to 2020

Fiscal Year	Total Enrollees	Minority Enrollees	% Minority Enrollees
2015	161,030	66,176	41.1
2016	158,741	68,176	42.9
2017	540,640	119,772	22.2
2018	327,633	102,285	31.2
2019	218,431	66,730	30.5
2020	177,995	80,594	45.3

Table 3D: Total Enrollment and Minority Enrollment at U.S. Sites for Intramural NIH-Defined Phase III Clinical Trials from FY 2015 to 2020

Fiscal Year	Total Enrollees	Minority Enrollees	% Minority Enrollees
2015	12,610	4,185	33.2
2016	11,152	4,142	37.1
2017	10,142	3,475	34.3
2018	7,758	1,885	24.3
2019	11,609	3,660	31.5
2020	11,750	3,828	32.6

Table 3E: Total Enrollment for All NIH-Defined Phase III Clinical Trials Racial Categories from FY 2015 to 2020

Fiscal Year	Total Enrollment	No. Inclusion Data Record	Minority Enrollment	% Minority Enrollment	American Indian/ Alaska Native	% American Indian/ Alaska Native	Asian	% Asian	Black/ African American	% Black/ African American	Native Hawaiian/ Pacific Islander	% Native Hawaiian/ Pacific Islander	White	% White	More Than One Race	% More Than One Race	Unknown/ Not Reported	% Unknown/ Not Reported
2015	1,619,508	498	1,492,248	92.1	124,444	7.7	976,701	60.3	360,471	22.3	300	0.0	124,641	7.7	2,113	0.1	30,838	1.9
2016	2,130,389	574	1,992,237	93.5	150,019	7.0	1,037,057	48.7	772,419	36.3	320	0.0	139,940	6.6	2,096	0.1	28,538	1.3
2017	907,643	618	459,046	50.6	2,410	0.3	274,218	30.2	133,842	14.7	618	0.1	451,173	49.7	4,341	0.5	41,041	4.5
2018	417,714	717	160,615	38.5	2,390	0.6	18,961	4.5	79,604	19.1	847	0.2	269,943	64.6	15,298	3.7	30,670	7.3
2019	329,747	664	153,529	46.6	2,591	0.8	20,263	6.1	97,737	29.6	377	0.1	178,855	54.2	3,630	1.1	26,294	8.0
2020	349,651	907	234,614	67.1	2,127	0.6	69,041	19.7	105,705	30.2	601	0.2	134,340	38.4	11,724	3.4	26,113	7.5

Table 3F: Total Enrollment for All NIH-Defined Phase III Clinical Trials Ethnic Categories from FY 2015 to 2020

Fiscal Year	Not Hispanic	% Not Hispanic	Hispanic/ Latino	% Hispanic/ Latino	Unknown/ Not Reported	% Unknown/ Not Reported
2015	1,457,366	90.0	154,371	9.5	7,771	0.5
2016	1,941,923	91.2	181,121	8.5	7,345	0.3
2017	790,092	87.0	49,999	5.5	67,552	7.4
2018	354,752	84.9	49,446	11.8	13,515	3.2
2019	284,424	86.3	32,586	9.9	12,737	3.9
2020	285,393	81.6	50,794	14.5	13,464	3.9

Table 3G: Total Enrollment for All NIH-Defined Phase III Clinical Trials at U.S. Sites Racial Categories from FY 2015 to 2020

Fiscal Year	Total Enrollment	Minority Enrollment	% Minority Enrollment	American Indian/ Alaska Native	% American Indian/ Alaska Native	Asian	% Asian	Black/ African American	% Black/ African American	Native Hawaiian/ Pacific Islander	% Native Hawaiian/ Pacific Islander	White	% White	More Than One Race	% More Than One Race	Unknown/ Not Reported	% Unknown/ Not Reported
2015	173,640	70,361	40.5	1,996	1.2	7,632	4.4	41,046	23.6	268	0.2	114,014	65.7	1,742	1.0	6,942	4.0
2016	169,893	72,318	42.6	1,259	0.7	19,470	11.5	29,367	17.3	276	0.2	110,836	65.2	1,973	1.2	6,712	4.0
2017	550,782	123,247	22.4	2,305	0.4	12,042	2.2	71,387	13.0	551	0.1	431,587	78.4	4,223	0.8	28,687	5.2
2018	335,391	104,170	31.1	2,249	0.7	8,992	2.7	49,346	14.7	769	0.2	249,110	74.3	11,905	3.5	13,020	3.9
2019	230,040	70,390	30.6	2,512	1.1	5,543	2.4	41,586	18.1	356	0.2	168,437	73.2	3,124	1.4	8,482	3.7
2020	189,745	84,422	44.5	2,039	1.1	6,130	3.2	36,582	19.3	562	0.3	119,154	62.8	10,582	5.6	14,696	7.7

Table 3H: Total Enrollment for All NIH-Defined Phase III Clinical Trials at U.S. Sites Ethnic Categories from FY 2015 to 2020

Fiscal Year	Not Hispanic	% Not Hispanic	Hispanic/ Latino	% Hispanic/ Latino	Unknown/ Not Reported	% Unknown/ Not Reported
2015	150,486	86.7	20,845	12.0	2,309	1.3
2016	144,849	85.3	21,801	12.8	3,243	1.9
2017	449,879	81.7	38,480	7.0	62,423	11.3
2018	293,131	87.4	35,741	10.7	6,519	1.9
2019	203,326	88.4	20,119	8.7	6,595	2.9
2020	149,155	78.6	32,871	17.3	7,719	4.1

Table 3I: Total Enrollment for Extramural NIH-Defined Phase III Clinical Trials at U.S. Sites Racial Categories from FY 2015 to 2020

Fiscal Year	Total Enrollment	Minority Enrollment	% Minority Enrollment	American Indian/ Alaska Native	% American Indian/ Alaska Native	Asian	% Asian	Black/ African American	% Black/ African American	Native Hawaiian/ Pacific Islander	% Native Hawaiian/ Pacific Islander	White	% White	More Than One Race	% More Than One Race	Unknown/ Not Reported	% Unknown/ Not Reported
2015	161,030	66,176	41.1	1,537	1.0	7,340	4.6	38,110	23.7	261	0.2	105,555	65.6	1,705	1.1	6,522	4.1
2016	158,741	68,176	42.9	859	0.5	19,172	12.1	26,438	16.7	271	0.2	103,776	65.4	1,924	1.2	6,301	4.0
2017	540,640	119,772	22.2	1,842	0.3	11,726	2.2	69,164	12.8	545	0.1	424,758	78.6	4,174	0.8	28,431	5.3
2018	327,633	102,285	31.2	1,975	0.6	8,711	2.7	48,436	14.8	768	0.2	243,227	74.2	11,681	3.6	12,835	3.9
2019	218,431	66,730	30.5	2,009	0.9	5,183	2.4	39,266	18.0	354	0.2	160,313	73.4	3,056	1.4	8,250	3.8
2020	177,995	80,594	45.3	1,393	0.8	5,761	3.2	34,248	19.2	561	0.3	111,061	62.4	10,516	5.9	14,455	8.1

Table 3J: Total Enrollment for Extramural NIH-Defined Phase III Clinical Trials at U.S. Sites Ethnic Categories from FY 2015 to 2020

Fiscal Year	Not Hispanic	% Not Hispanic	Hispanic/ Latino	% Hispanic/ Latino	Unknown/ Not Reported	% Unknown/ Not Reported
2015	138,597	86.1	20,303	12.6	2,130	1.3
2016	134,461	84.7	21,238	13.4	3,042	1.9
2017	440,370	81.5	37,948	7.0	62,322	11.5
2018	285,642	87.2	35,502	10.8	6,489	2.0
2019	192,300	88.0	19,599	9.0	6,532	3.0
2020	137,997	77.5	32,347	18.2	7,651	4.3

Table 3K: Total Enrollment for Intramural NIH-Defined Phase III Clinical Trials at U.S. Sites Racial Categories from FY 2015 to 2020

Fiscal Year	Total Enrollment	Minority Enrollment	% Minority Enrollment	American Indian/ Alaska Native	% American Indian/ Alaska Native	Asian	% Asian	Black/ African American	% Black/ African American	Native Hawaiian/ Pacific Islander	% Native Hawaiian/ Pacific Islander	White	% White	More Than One Race	% More Than One Race	Unknown/ Not Reported	% Unknown/ Not Reported
2015	12,610	4,185	33.2	459	3.6	292	2.3	2,936	23.3	7	0.1	8,459	67.1	37	0.3	420	3.3
2016	11,152	4,142	37.1	400	3.6	298	2.7	2,929	26.3	5	0.0	7,060	63.3	49	0.4	411	3.7
2017	10,142	3,475	34.3	463	4.6	316	3.1	2,223	21.9	6	0.1	6,829	67.3	49	0.5	256	2.5
2018	7,758	1,885	24.3	274	3.5	281	3.6	910	11.7	1	0.0	5,883	75.8	224	2.9	185	2.4
2019	11,609	3,660	31.5	503	4.3	360	3.1	2,320	20.0	2	0.0	8,124	70.0	68	0.6	232	2.0
2020	11,750	3,828	32.6	646	5.5	369	3.1	2,334	19.9	1	0.0	8,093	68.9	66	0.6	241	2.1

Table 3L: Total Enrollment for Intramural NIH-Defined Phase III Clinical Trials at U.S. Sites Ethnic Categories from FY 2015 to 2020

Fiscal Year	Not Hispanic	% Not Hispanic	Hispanic/ Latino	% Hispanic/ Latino	Unknown/ Not Reported	% Unknown/ Not Reported
2015	12,610	94.3	542	4.3	179	1.4
2016	10,388	93.1	563	5.0	201	1.8
2017	9,509	93.8	532	5.2	101	1.0
2018	7,489	96.5	239	3.1	30	0.4
2019	11,026	95.0	520	4.5	63	0.5
2020	11,158	95.0	524	4.5	68	0.6

Section 4: Aggregate Enrollment: Sex/Gender by Race and Ethnicity for NIH Clinical Research

Table 4A: Minority Enrollment by Sex/Gender for All NIH Clinical Research from FY 2015 to 2020

Year	Sex	Total Minority Enrollees	% of Minority Enrollees	Total Enrollees	% Total
2015	Female	5,255,224	39.6	13,278,481	61.9
	Male	3,175,954	23.9	7,829,861	36.5
	Unknown	170,908	1.3	345,524	1.6
2016	Female	8,226,149	39.2	20,983,081	52.8
	Male	6,649,220	37.2	17,865,381	45.0
	Unknown	112,056	13.0	863,803	2.2
2017	Female	4,664,388	49.3	9,470,264	47.2
	Male	5,364,942	53.0	10,127,155	50.5
	Unknown	45,728	9.7	471,370	2.3
2018	Female	2,610,070	38.9	6,711,564	52.4
	Male	1,967,116	34.7	5,668,475	44.2
	Unknown	44,342	10.2	434,123	3.4
2019	Female	3,027,503	43.9	6,894,390	52.1
	Male	2,219,465	37.4	5,930,000	44.8
	Unknown	59,734	14.3	417,023	3.1
2020	Female	3,133,281	41.5	7,552,684	55.1
	Male	2,202,943	39.8	5,532,650	40.4
	Unknown	86,053	13.9	620,325	4.5

Table 4B: Minority Enrollment by Sex/Gender for All NIH Clinical Research at U.S. Sites from FY 2015 to 2020

Year	Sex	Total Minority Enrollees	% of Minority Enrollees	Total Enrollees	% Total
2015	Female	2,737,095	26.0	10,529,683	61.2
	Male	1,921,639	30.0	6,404,104	37.2
	Unknown	119,276	42.9	278,316	1.6
2016	Female	5,855,133	35.3	16,594,940	54.0
	Male	5,256,810	39.5	13,311,968	43.3
	Unknown	67,829	8.4	803,940	2.6
2017	Female	1,962,988	30.2	6,491,639	49.1
	Male	1,751,515	27.8	6,302,343	47.6
	Unknown	28,278	6.5	437,184	3.3
2018	Female	1,715,543	31.7	5,413,405	51.2
	Male	1,360,919	28.5	4,775,856	45.1
	Unknown	18,517	4.8	389,025	3.7
2019	Female	1,680,226	32.4	5,185,006	50.1
	Male	1,406,011	29.0	4,853,379	46.9
	Unknown	11,153	3.5	317,690	3.1
2020	Female	2,075,929	34.2	6,062,190	54.7
	Male	1,459,907	32.6	4,480,382	40.4
	Unknown	23,694	4.4	538,299	4.9

Table 4C: Minority Enrollment by Sex/Gender for Extramural NIH Clinical Research at U.S. Sites from FY 2015 to 2020

Year	Sex	Total Minority Enrollees	% of Minority Enrollees	Total Enrollees	% Total
2015	Female	2,545,119	30.2	8,427,534	59.6
	Male	1,761,708	31.9	5,525,413	39.0
	Unknown	114,271	58.1	196,702	1.4
2016	Female	5,623,816	39.0	14,418,631	52.4
	Male	5,083,588	40.9	12,415,288	45.1
	Unknown	62,764	9.3	676,210	2.5
2017	Female	1,685,598	32.0	5,264,128	49.1
	Male	1,528,194	29.7	5,136,833	47.9
	Unknown	26,885	8.1	329,882	3.1
2018	Female	1,581,696	34.0	4,650,602	51.2
	Male	1,264,241	31.1	4,068,126	44.8
	Unknown	17,886	5.0	356,041	3.9
2019	Female	1,490,090	34.7	4,294,606	49.8
	Male	1,281,235	31.6	4,059,871	47.1
	Unknown	9,881	3.8	262,951	3.1
2020	Female	1,893,445	36.5	5,184,613	55.4
	Male	1,339,392	36.2	3,697,229	39.5
	Unknown	22,770	4.7	483,980	5.2

Table 4D: Minority Enrollment by Sex/Gender for Intramural NIH Clinical Research at U.S. Sites from FY 2015 to 2020

Year	Sex	Total Minority Enrollees	% of Minority Enrollees	Total Enrollees	% Total
2015	Female	191,976	9.1	2,102,149	68.6
	Male	159,931	18.2	878,691	28.7
	Unknown	5,005	6.1	81,614	2.7
2016	Female	231,317	10.6	2,176,309	68.0
	Male	173,222	19.3	896,680	28.0
	Unknown	5,065	4.0	127,730	4.0
2017	Female	277,390	22.6	1,227,511	49.1
	Male	223,321	19.2	1,165,510	46.6
	Unknown	1,393	1.3	107,302	4.3
2018	Female	133,847	17.5	762,803	50.7
	Male	96,678	13.7	707,730	47.1
	Unknown	631	1.9	32,984	2.2
2019	Female	190,136	21.4	890,400	51.2
	Male	124,776	15.7	793,508	45.6
	Unknown	1,272	2.3	54,739	3.1
2020	Female	182,484	20.8	877,577	51.2
	Male	120,515	15.4	783,153	45.7
	Unknown	924	1.7	54,319	3.2

Table 4E: Minority Enrollment by Sex/Gender for All NIH-Defined Phase III Clinical Trials from FY 2015 to 2020

Year	Sex	Total Minority Enrollees	% of Minority Enrollees	Total Enrollees	% Total
2015	Female	1,030,479	94.4	1,091,910	67.4
	Male	442,084	87.1	507,561	31.3
	Unknown	19,685	98.2	20,037	1.2
2016	Female	1,323,770	94.8	1,396,503	65.6
	Male	645,583	90.8	710,818	33.4
	Unknown	22,884	99.2	23,068	1.1
2017	Female	272,200	50.8	535,440	59.0
	Male	186,587	50.2	371,636	40.9
	Unknown	259	45.7	567	0.1
2018	Female	103,639	39.8	260,652	62.4
	Male	56,626	36.3	155,960	37.3
	Unknown	350	31.8	1,101	0.3
2019	Female	95,900	47.4	202,483	61.4
	Male	57,207	47.9	119,369	36.2
	Unknown	422	5.3	7,895	2.4
2020	Female	143,149	66.3	216,040	61.8
	Male	87,244	68.2	127,864	36.6
	Unknown	4,221	73.4	5,747	1.6

Table 4F: Minority Enrollment by Sex/Gender for All NIH-Defined Phase III Clinical Trials at U.S. Sites from FY 2015 to 2020

Year	Sex	Total Minority Enrollees	% of Minority Enrollees	Total Enrollees	% Total
2015	Female	35,848	42.7	83,932	48.3
	Male	34,362	38.5	89,228	51.4
	Unknown	151	31.5	480	0.3
2016	Female	34,156	41.0	83,278	49.0
	Male	38,140	44.1	86,425	50.9
	Unknown	22	11.6	190	0.1
2017	Female	75,081	22.7	330,307	60.0
	Male	48,134	21.9	220,245	40.0
	Unknown	32	13.9	230	0.0
2018	Female	63,253	30.1	209,985	62.6
	Male	40,831	32.7	124,830	37.2
	Unknown	86	14.9	576	0.2
2019	Female	44,424	30.0	148,099	64.4
	Male	25,808	31.9	81,012	35.2
	Unknown	158	17.0	929	0.4
2020	Female	54,453	45.0	121,041	63.8
	Male	29,502	44.2	66,765	35.2
	Unknown	467	24.1	1,939	1.0

Table 4G: Minority Enrollment by Sex/Gender for Extramural NIH-Defined Phase III Clinical Trials at U.S. Sites from FY 2015 to 2020

Year	Sex	Total Minority Enrollees	% of Minority Enrollees	Total Enrollees	% Total
2015	Female	32,534	43.5	74,759	46.4
	Male	33,493	39.0	85,794	53.3
	Unknown	149	31.2	477	0.3
2016	Female	30,878	41.2	74,969	47.2
	Male	37,279	44.6	83,586	52.7
	Unknown	19	10.2	186	0.1
2017	Female	72,140	22.4	322,436	59.6
	Male	47,601	21.8	217,976	40.3
	Unknown	31	13.6	228	0.0
2018	Female	62,460	30.2	206,817	63.1
	Male	39,757	33.1	120,274	36.7
	Unknown	68	12.5	542	0.2
2019	Female	41,801	29.7	140,865	64.5
	Male	24,790	32.3	76,657	35.1
	Unknown	139	15.3	909	0.4
2020	Female	51,716	45.4	113,844	64.0
	Male	28,430	45.7	62,232	35.0
	Unknown	448	23.3	1,919	1.1

Table 4H: Minority Enrollment by Sex/Gender for Intramural NIH-Defined Phase III Clinical Trials at U.S. Sites from FY 2015 to 2020

Year	Sex	Total Minority Enrollees	% of Minority Enrollees	Total Enrollees	% Total
2015	Female	3,314	36.1	9,173	72.7
	Male	869	25.3	3,434	27.2
	Unknown	2	66.7	3	0.0
2016	Female	3,278	39.5	8,309	74.5
	Male	861	30.3	2,839	25.5
	Unknown	3	75.0	4	0.0
2017	Female	2,941	37.4	7,871	77.6
	Male	533	23.5	2,269	22.4
	Unknown	1	50.0	2	0.0
2018	Female	793	25.0	3,168	40.8
	Male	1,074	23.6	4,556	58.7
	Unknown	18	52.9	34	0.4
2019	Female	2,623	36.3	7,234	62.3
	Male	1,018	23.4	4,355	37.5
	Unknown	19	95.0	20	0.2
2020	Female	2,737	38.0	7,197	61.3
	Male	1,072	23.6	4,533	38.6
	Unknown	19	95.0	20	0.2

Table 4I: Enrollment for All NIH-Defined Clinical Research, Sex/Gender by Race and Ethnicity from FY 2019 to 2020

Fiscal Year	Sex Gender	Minority	% Minority	Total Enrollment	% Total	American Indian Alaska Native	% American Indian Alaska Native	Asian	% Asian	Black African American	% Black African American	Native Hawaiian Pacific Islander	% Native Hawaiian Pacific Islander	White	% White	More Than One Race	% More Than One Race	Unknown Not Reported	% Unknown Not Reported
2019	Female	3,027,503	43.9	6,894,390	52.1	221,459	3.2	791,042	11.5	1,269,976	18.4	13,338	0.2	3,895,837	56.5	151,836	2.2	550,902	8.0
	Male	2,219,465	37.4	5,930,000	44.8	109,470	1.8	456,922	7.7	1,101,038	18.6	11,681	0.2	3,641,423	61.4	121,853	2.1	487,613	8.2
	Unknown	59,734	14.3	417,023	3.1	1,910	0.5	17,042	4.1	11,706	2.8	90	0.0	20,389	4.9	1,753	0.4	364,133	87.3
2020	Female	3,133,281	41.5	7,552,684	55.1	69,957	0.9	569,335	7.5	1,535,430	20.3	17,532	0.2	4,273,974	56.6	210,974	2.8	875,482	11.6
	Male	2,202,943	39.8	5,532,650	40.4	54,337	1.0	385,652	7.0	1,134,775	20.5	14,818	0.3	3,281,452	59.3	144,076	2.6	517,540	9.4
	Unknown	86,053	13.9	620,325	4.5	813	0.1	15,393	2.5	15,858	2.6	120	0.0	27,678	4.5	3,042	0.5	557,421	89.9

Fiscal Year	Sex Gender	Not Hispanic	% Not Hispanic	Hispanic Latino	% Hispanic Latino	Unknown Not Reported	% Unknown Not Reported
2019	Female	5,470,825	79.4	844,013	12.2	579,552	8.4
	Male	4,851,599	81.8	565,538	9.5	512,863	8.6
	Unknown	85,697	20.5	29,156	7.0	302,170	72.5
2020	Female	5,933,042	78.6	879,883	11.6	739,759	9.8
	Male	4,532,188	81.9	574,608	10.4	425,854	7.7
	Unknown	96,918	15.6	52,354	8.4	471,053	75.9

Table 4J: U.S. Site Enrollment for All NIH-Defined Clinical Research, Sex/Gender by Race and Ethnicity from FY 2019 to 2020

Fiscal Year	Sex Gender	Minority	% Minority	American Indian Alaska Native	% American Indian Alaska Native	Asian	% Asian	Black African American	% Black African American	Native Hawaiian Pacific Islander	% Native Hawaiian Pacific Islander	White	% White	More Than One Race	% More Than One Race	Unknown Not Reported	% Unknown Not Reported	Not Hispanic	% Not Hispanic	Hispanic Latino	% Hispanic Latino	Unknown Not Reported	% Unknown Not Reported
2019	Female	1,680,226	32.4	58,923	1.1	211,044	4.1	827,878	16.0	12,447	0.2	3,454,691	66.6	121,759	2.3	498,264	9.6	4,210,332	81.2	525,358	10.1	449,316	8.7
	Male	1,406,011	29.0	47,315	1.0	118,096	2.4	790,283	16.3	10,860	0.2	3,356,089	69.1	94,724	2.0	436,012	9.0	3,994,091	82.3	405,474	8.4	453,814	9.4
	Unknown	11,153	3.5	679	0.2	1,038	0.3	3,650	1.1	89	0.0	13,924	4.4	1,552	0.5	296,758	93.4	23,511	7.4	5,016	1.6	289,163	91.0
2020	Female	2,075,929	34.2	63,576	1.0	279,981	4.6	939,289	15.5	15,389	0.3	3,787,400	62.5	178,630	2.9	797,925	13.2	4,719,070	77.8	711,123	11.7	631,997	10.4
	Male	1,459,907	32.6	48,245	1.1	158,738	3.5	711,030	15.9	13,000	0.3	2,966,693	66.2	115,141	2.6	467,535	10.4	3,601,531	80.4	484,246	10.8	394,605	8.8
	Unknown	23,694	4.4	704	0.1	1,543	0.3	4,537	0.8	106	0.0	22,661	4.2	2,113	0.4	506,635	94.1	64,690	12.0	15,538	2.9	458,071	85.1

Table 4K: U.S. Site Enrollment for NIH-Defined Extramural Clinical Research, Sex/Gender by Race and Ethnicity from FY 2019 to 2020

Fiscal Year	Sex Gender	Minority	% Minority	American Indian Alaska Native	% American Indian Alaska Native	Asian	% Asian	Black African American	% Black African American	Native Hawaiian Pacific Islander	% Native Hawaiian Pacific Islander	White	% White	More Than One Race	% More Than One Race	Unknown Not Reported	% Unknown Not Reported	Not Hispanic	% Not Hispanic	Hispanic Latino	% Hispanic Latino	Unknown Not Reported	% Unknown Not Reported
2019	Female	1,490,090	34.7	43,212	1.0	194,364	4.5	729,712	17.0	9,994	0.2	2,788,275	64.9	114,387	2.7	414,662	9.7	3,433,397	79.9	471,600	11.0	389,609	9.1
	Male	1,281,235	31.6	34,048	0.8	101,377	2.5	729,636	18.0	8,720	0.2	2,708,270	66.7	89,250	2.2	388,570	9.6	3,275,007	80.7	376,022	9.3	408,842	10.1
	Unknown	9,881	3.8	640	0.2	985	0.4	3,272	1.2	80	0.0	13,165	5.0	1,527	0.6	243,282	92.5	19,039	7.2	4,234	1.6	239,678	91.1
2020	Female	1,893,445	36.5	48,150	0.9	263,127	5.1	845,431	16.3	13,198	0.3	3,132,765	60.4	171,310	3.3	710,632	13.7	3,949,690	76.2	660,718	12.7	574,205	11.1
	Male	1,339,392	36.2	35,087	0.9	141,362	3.8	653,093	17.7	11,047	0.3	2,325,034	62.9	109,682	3.0	421,924	11.4	2,889,196	78.1	456,873	12.4	351,160	9.5
	Unknown	22,770	4.7	672	0.1	1,491	0.3	4,391	0.9	102	0.0	22,140	4.6	2,081	0.4	453,103	93.6	61,244	12.7	14,862	3.1	407,874	84.3

Table 4L: U.S. Site Enrollment for NIH-Defined Intramural Clinical Research, Sex/Gender by Race from FY 2019 to 2020

Fiscal Year	Sex Gender	Minority	% Minority	American Indian Alaska Native	% American Indian Alaska Native	Asian	% Asian	Black African American	% Black African American	Native Hawaiian Pacific Islander	% Native Hawaiian Pacific Islander	White	% White	More Than One Race	% More Than One Race	Unknown Not Reported	% Unknown Not Reported	Not Hispanic	% Not Hispanic	Hispanic Latino	% Hispanic Latino	Unknown Not Reported	% Unknown Not Reported
2019	Female	190,136	21.4	15,711	1.8	16,680	1.9	98,166	11.0	2,453	0.3	666,416	74.8	7,372	0.8	83,602	9.4	776,935	87.3	53,758	6.0	59,707	6.7
	Male	124,776	15.7	13,267	1.7	16,719	2.1	60,647	7.6	2,140	0.3	647,819	81.6	5,474	0.7	47,442	6.0	719,084	90.6	29,452	3.7	44,972	5.7
	Unknown	1,272	2.3	39	0.1	53	0.1	378	0.7	9	0.0	759	1.4	25	0.0	53,476	97.7	4,472	8.2	782	1.4	49,485	90.4
2020	Female	182,484	20.8	15,426	1.8	16,854	1.9	93,858	10.7	2,191	0.2	654,635	74.6	7,320	0.8	87,293	9.9	769,380	87.7	50,405	5.7	57,792	6.6
	Male	120,515	15.4	13,158	1.7	17,376	2.2	57,937	7.4	1,953	0.2	641,659	81.9	5,459	0.7	45,611	5.8	712,335	91.0	27,373	3.5	43,445	5.5
	Unknown	924	1.7	32	0.1	52	0.1	146	0.3	4	0.0	521	1.0	32	0.1	53,532	98.6	3,446	6.3	676	1.2	50,197	92.4

Table 4M: Enrollment of All NIH-Defined Phase III Trials, Sex/Gender by Race and Ethnicity from FY 2019 to 2020

Fiscal Year	Sex Gender	Minority	% Minority	Total Enrollment	% Total	American Indian Alaska Native	% American Indian Alaska Native	Asian	% Asian	Black African American	% Black African American	Native Hawaiian Pacific Islander	% Native Hawaiian Pacific Islander	White	% White	More Than One Race	% More Than One Race	Unknown Not Reported	% Unknown Not Reported
2019	Female	95,900	47.4	202,483	61.4	1,638	0.8	9,519	4.7	62,300	30.8	210	0.1	114,061	56.3	1,694	0.8	13,061	6.5
	Male	57,207	47.9	119,369	36.2	947	0.8	10,732	9.0	35,155	29.5	167	0.1	64,651	54.2	1,920	1.6	5,797	4.9
	Unknown	422	5.3	7,895	2.4	6	0.1	12	0.2	282	3.6	0	0.0	143	1.8	16	0.2	7,436	94.2
2020	Female	143,149	66.3	216,040	61.8	1,287	0.6	35,682	16.5	65,333	30.2	375	0.2	87,427	40.5	8,221	3.8	17,715	8.2
	Male	87,244	68.2	127,864	36.6	827	0.6	33,345	26.1	36,584	28.6	226	0.2	46,690	36.5	3,480	2.7	6,712	5.2
	Unknown	4,221	73.4	5,747	1.6	13	0.2	14	0.2	3,788	65.9	0	0.0	223	3.9	23	0.4	1,686	29.3

Fiscal Year	Sex Gender	Not Hispanic	% Not Hispanic	Hispanic Latino	% Hispanic Latino	Unknown Not Reported	% Unknown Not Reported
2019	Female	173,815	85.8	22,624	11.2	6,044	3.0
	Male	103,597	86.8	9,835	8.2	5,937	5.0
	Unknown	7,012	88.8	127	1.6	756	9.6
2020	Female	174,070	80.6	35,528	16.4	6,442	3.0
	Male	107,319	83.9	14,868	11.6	5,677	4.4
	Unknown	4,004	69.7	398	6.9	1,345	23.4

Table 4N: U.S. Site Enrollment for NIH-Defined Phase III Trials, Sex/Gender by Race and Ethnicity from FY 2019 and 2020

Fiscal Year	Sex Gender	Minority	% Minority	American Indian Alaska Native	% American Indian Alaska Native	Asian	% Asian	Black African American	% Black African American	Native Hawaiian Pacific Islander	% Native Hawaiian Pacific Islander	White	% White	More Than One Race	% More Than One Race	Unknown Not Reported	% Unknown Not Reported	Not Hispanic	% Not Hispanic	Hispanic Latino	% Hispanic Latino	Unknown Not Reported	% Unknown Not Reported
2019	Female	44,424	30.0	1,612	1.1	3,348	2.3	26,998	18.2	202	0.1	109,784	74.1	1,524	1.0	4,631	3.1	132,527	89.5	12,348	8.3	3,224	2.2
	Male	25,808	31.9	895	1.1	2,191	2.7	14,560	18.0	154	0.2	58,513	72.2	1,584	2.0	3,115	3.8	70,684	87.3	7,649	9.4	2,679	3.3
	Unknown	158	17.0	5	0.5	4	0.4	28	3.0	0	0.0	140	15.1	16	1.7	736	79.2	115	12.4	122	13.1	692	74.5
2020	Female	54,453	45.0	1,252	1.0	3,599	3.0	24,188	20.0	352	0.3	75,903	62.7	7,734	6.4	8,013	6.6	97,125	80.2	20,119	16.6	3,797	3.1
	Male	29,502	44.2	774	1.2	2,524	3.8	12,351	18.5	210	0.3	43,031	64.5	2,826	4.2	5,049	7.6	51,771	77.5	12,358	18.5	2,636	3.9
	Unknown	467	24.1	13	0.7	7	0.4	43	2.2	0	0.0	220	11.3	22	1.1	1,634	84.3	259	13.4	394	20.3	1,286	66.3

Table 4O: U.S. Site Enrollment for NIH-Defined Extramural Phase III Trials, Sex/Gender by Race and Ethnicity from FY 2019 to 2020

Fiscal Year	Sex Gender	Minority	% Minority	American Indian Alaska Native	% American Indian Alaska Native	Asian	% Asian	Black African American	% Black African American	Native Hawaiian Pacific Islander	% Native Hawaiian Pacific Islander	White	% White	More Than One Race	% More Than One Race	Unknown Not Reported	% Unknown Not Reported	Not Hispanic	% Not Hispanic	Hispanic Latino	% Hispanic Latino	Unknown Not Reported	% Unknown Not Reported
2019	Female	41,801	29.7	1,241	0.9	3,137	2.2	25,255	17.9	201	0.1	105,031	74.6	1,492	1.1	4,508	3.2	125,694	89.2	11,995	8.5	3,176	2.3
	Male	24,790	32.3	763	1.0	2,042	2.7	13,983	18.2	153	0.2	55,143	71.9	1,549	2.0	3,024	3.9	66,491	86.7	7,501	9.8	2,665	3.5
	Unknown	139	15.3	5	0.6	4	0.4	28	3.1	0	0.0	139	15.3	15	1.7	718	79.0	115	12.7	103	11.3	691	76.0
2020	Female	51,716	45.4	754	0.7	3,390	3.0	22,454	19.7	352	0.3	71,298	62.6	7,701	6.8	7,895	6.9	90,330	79.3	19,767	17.4	3,747	3.3
	Male	28,430	45.7	626	1.0	2,364	3.8	11,751	18.9	209	0.3	39,544	63.5	2,794	4.5	4,944	7.9	47,408	76.2	12,205	19.6	2,619	4.2
	Unknown	448	23.3	13	0.7	7	0.4	43	2.2	0	0.0	219	11.4	21	1.1	1,616	84.2	259	13.5	375	19.5	1,285	67.0

Table 4P: U.S. Site Enrollment for NIH-Defined Intramural Phase III Trials, Sex/Gender by Race and Ethnicity from FY 2019 to 2020

Fiscal Year	Sex Gender	Minority	% Minority	American Indian Alaska Native	% American Indian Alaska Native	Asian	% Asian	Black African American	% Black African American	Native Hawaiian Pacific Islander	% Native Hawaiian Pacific Islander	White	% White	More Than One Race	% More Than One Race	Unknown Not Reported	% Unknown Not Reported	Not Hispanic	% Not Hispanic	Hispanic Latino	% Hispanic Latino	Unknown Not Reported	% Unknown Not Reported
2019	Female	2,623	36.3	371	5.1	211	2.9	1,743	24.1	1	0.0	4,753	65.7	32	0.4	123	1.7	6,833	94.5	353	4.9	48	0.7
	Male	1,018	23.4	132	3.0	149	3.4	577	13.2	1	0.0	3,370	77.4	35	0.8	91	2.1	4,193	96.3	148	3.4	14	0.3
	Unknown	19	95.0	0	0.0	0	0.0	0	0.0	0	0.0	1	5.0	1	5.0	18	90.0	0	0.0	19	95.0	1	5.0
2020	Female	2,737	38.0	498	6.9	209	2.9	1,734	24.1	0	0.0	4,605	64.0	33	0.5	118	1.6	6,795	94.4	352	4.9	50	0.7
	Male	1,072	23.6	148	3.3	160	3.5	600	13.2	1	0.0	3,487	76.9	32	0.7	105	2.3	4,363	96.2	153	3.4	17	0.4
	Unknown	19	95.0	0	0.0	0	0.0	0	0.0	0	0.0	1	5.0	1	5.0	18	90.0	0	0.0	19	95.0	1	5.0

Section 5: Valid Analysis Requirement for NIH-Funded Phase III Clinical Trials

Table 5: Valid Analysis Requirements for NIH-Defined Phase III Extramural Grants Reported for Fiscal Years 2019 and 2020

Fiscal Year	Total IERs	IERs Requiring Race-Ethnicity Valid Analysis	% IERs Requiring Race-Ethnicity Valid Analysis	IERs Requiring Sex-Gender Valid Analysis	% IERs Requiring Sex-Gender Valid Analysis
2019	664	622	93.7	625	94.1
2020	907	853	94.0	800	88.2

Note: Plans for valid analysis methodologies specified in the project application are reported for all IERs, including IERs that have no reported actual enrollment at the time of reporting.

Appendix F. Inclusion Certification Forms

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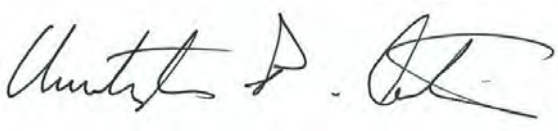

February 14, 2021

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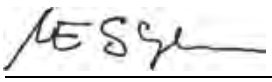

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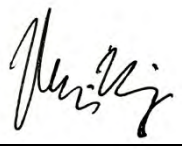

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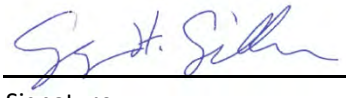

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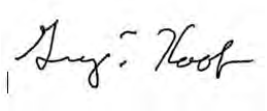

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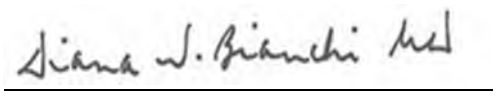

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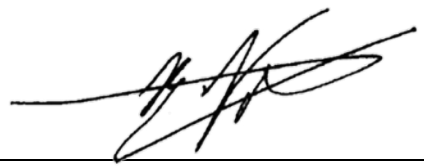

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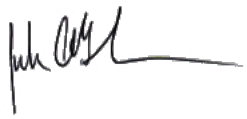

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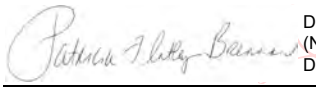

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