53rd Meeting of the NIH Advisory Committee on Research on Women’s Health

Janine Austin Clayton, M.D., FARVO
NIH Associate Director for Research on Women’s Health
Director, Office of Research on Women's Health
National Institutes of Health
April 14, 2021 – Director’s Report
New in Sex and Gender
Growing attention to SABV in popular and scientific media

**CONSUMER**

- Blood pressure may need to be monitored differently, according to a new study | CNN.com
- Women report worse side effects after a COVID vaccine | NYT
- Biomedical research must consider how sex and gender influence health | Morning Consult
- Progress in considering sex as a biological variable | NPR’s Science Friday [with ORWH’s Dr. Chyren Hunter]

**SCIENTIFIC**

- Considering sex as a biological variable will require a global shift in science culture | Nature Neuroscience and Drug Monkey Blog
- Endocrine Society issues scientific statement on sex differences in research | Endocrine News
- Sex differences in immune responses to viral infection | The Scientist
- Defining valid chronic stress models for depression with female rodents | Biology Psychiatry
- Sex-specific genetic architecture in response to American and ketogenic diets | Nature
- How sex differences play a role in neurological diseases | Neuroscience News

Society for Women’s Health Research and Endocrine Society
Congressional Briefing
March 2, 2021
“I have worked with vascular cells for 20 years and, up until maybe about five years ago, if you asked if the sex of my cells mattered at all, I would have said no,” Clyne said. Then, she worked on a difficult study in which **data appeared “all over the place.”**

“We separated the cell data by sex, and **it all made sense. It was an awakening** for me that we should be studying this.”

Dr. Alisa Morss Clyne, *Neuroscience News*, 3/16/21

https://neurosciencenews.com/neurodegeneration-sex-differences-18050/
Shansky and Murphy call for “global shift in science culture”

The Situation

• View that how disease presents in men is “the standard” is pervasive
• Use of male rodents as the default model organism in preclinical neuroscience research has likely contributed to higher rates of misdiagnosis, adverse drug side effects
• Incentive structure in publishing prioritizes extended research of a phenomenon in males
• SABV directives lack mechanisms to hold recipients accountable

What’s needed?

• Cultural shift in what impactful, high-profile, rigorous science looks like
• Hold researchers accountable by
  o Including SABV compliance in annual progress reports
  o Using compliance as contingency for grant renewals
• Scientists hold each other accountable through manuscript peer review
• Journal editors—who “have the greatest power to shape the culture of scientific research practices”—hold authors to standards

“What we consider ‘rigorous’ must be a body of work that includes males and females in all experiments [excepting those that can only be done in one sex].”
ORWH’s e-learning educates biomedical community on sex and gender

- **Bench to Bedside: Integrating Sex & Gender to Improve Human Health**
  - Immunology | CVD | Pulmonary Disease | Neurology | Endocrinology | Mental Health
  - 900 users (Jan.-Feb. 2021); 784 have begun a module to date

- **Sex as a Biological Variable Primer**
  - With support from NIH and NIH Office of the Director
  - 826 users (Jan.-Feb. 2021)

- **Introduction to the Scientific Basis of Sex- and Gender-Related Differences** | Including facilitator’s guide

Total of 2,323 visitors in Jan./Feb. 2021 | 1171 dashboard registrants to date

[bit.ly/ORWH_eLearning]
New in COVID-19 and Women’s Health
New study finds Black women dying at much higher rates than White men, Asian men

*Demonstrates power of disaggregating data & influence of sex/gender, race, ethnicity*

Black women have COVID-19 mortality rates **almost 4 times higher** than that of White men
- 3 times higher than Asian men
- Higher than Asian and White women

Disparities in mortality **replicate existing racial and gender health inequities.**
- E.g. Black men in GA have highest rates of CVD; Black women and White men have similar rates; White women, the lowest

Understanding the extremely high death rates of Blacks (M & W) **requires consideration of how social factors interact** with gender and race to shape disparities

While men have higher COVID-19 death rates than women, this sex disparity does not hold across racial groups. In reality, health risks are structured in complex ways that reflect systemic and broader societal inequities.
Two studies show prevalence, severity, sex effects

Ambidirectional cohort study* of patients at Wuhan hospital 1/7/20- 5/29/20

- Most common comorbidities: hypertension (29%), diabetes (12%), CVD (7%)
- Men were two-thirds of the most seriously ill patients (scale 5–6)
- Of the over 75% who reported symptom/s 6 months after onset, most were women
- Most common “Long” symptoms:
  - Fatigue or muscle weakness (63%)
  - Sleep difficulties (26%)
  - Anxiety or depression (23%) – more common in women
- Most seriously ill patients (scale 5–6) as compared to less seriously ill (scale 3)
  - Showed Odds Ratio (OR) of 4·60 for diffusion impairment
  - OR 1·77 for anxiety or depression
  - OR 2·69 for fatigue or muscle weakness
- Women patients in comparison to men
  - OR 2·22 for diffusion impairment
  - OR 1·80 for anxiety or depression
  - OR 1·33 for fatigue or muscle weakness

*48% of participants were women | Huang, C., et al. Lancet. 2021. DOI: 10.1016/S0140-6736(20)32656-8
Lancet article highlights sex/gender-related psych effects

“[B]eing a woman and severity of illness were risk factors for persistent psychological symptoms. Female SARS survivors had higher stress levels and higher levels of depression and anxiety. ... The underlying mechanism of the psychiatric consequences of COVID-19 is likely to be multifactorial and might include the direct effects of viral infection, the immunological response, corticosteroid therapy, ICU stay, social isolation, and stigma.”

Pandemic disproportionately affects women, parents

Comparison of Pre-Pandemic and Pandemic

**Work Hours** | Faculty with small children (0–5 years) reported significantly fewer work hours compared to all other faculty

<table>
<thead>
<tr>
<th>Parents With</th>
<th>Children ages 0-5-years-old</th>
<th>33.7 hours</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Children 6-11; 12-17; none</td>
<td>48.3; 49.5; 49.2*</td>
</tr>
</tbody>
</table>

**Publishing** | Women's first/corresponding author's and coauthor's article submissions decreased significantly

**Other Productivity**

- Faculty with small children completed significantly fewer peer review assignments, attended fewer funding panel meetings, submitted fewer first authors' articles
- Those with older children or no children reported significant increases or stable productivity

*Standard deviation 14.9; 13.9 for all others | **Self-reported
NASEM, NIH studies find COVID impact on scientists

“The National Academies of Sciences • Engineering • Medicine


NIH-supported study documents how pandemic disrupted careers of women in academic STEMM (from March to Nov. 2020)

Found that pandemic negatively affected the well-being of women in academic STEMM fields in these areas:

• Productivity
• Work-life boundary control
• Networking and community building
• Mental well-being

NIH surveys extramural researchers

61% of lab-based researchers (55% overall) said pandemic will negatively affect career trajectory

• Concern greatest among Asian respondents, postdoc fellow/resident
• Among caretakers, concerns greatest among those with children 0-5 years old

42% said mental/physical health negatively affected productivity

• Highest among women, self-identified “other”, early career investigators

78% reported lower productivity

Extramural administrators

83% cited moderate-major impact on research productivity

Most implemented monitoring measures, but 1 in 5 provided or expanded childcare facilities

NIH addresses COVID-19 disruptions with funded and unfunded extensions

Requesting Extensions for Early Career Scientists Whose Career Trajectories Have Been Significantly Impacted by COVID-19 | NOT-OD-21-052

• **No-Cost Extensions** | For most NIH awards, recipients may extend final budget period of the previously approved project period one time, without NIH prior approval

• **Funded Extensions** | May request funded extension for F and K awards -- considered by each IC on case-by-case basis

Other initiatives address barriers to entry and advancement

NIH Challenge Prize to recognize, disseminate transformative institutional approaches [herox.com/NIHGenderDiversityPrize]

- Application deadline: April 16, 2021; awards no later than Sept. 2021

Advancing Gender Inclusive Excellence (AGIE) Coordinating Center

NOITP [grants.nih.gov/grants/guide/notice-files/NOT-OD-21-051.html]

- Collaboration between ORWH and National Institute of Diabetes and Digestive and Kidney Diseases
- Provide organizational framework for management, direction, and coordination of data from activities aimed at removing barriers for women to achieve leadership roles in science

BIRCWH Reissuance

NIH Common Fund’s Faculty Institutional Recruitment for Sustainable Transformation (FIRST) program [commonfund.nih.gov/first]

- To help institutions build self-reinforcing community of scientists, through recruitment of early-career faculty with commitment to inclusive excellences
Childcare costs for Ruth L. Kirschstein National Research Service Award Individual Fellows NOT-OD-21-074

NIH-supported scientific conferences are required to include diversity plan to achieve appropriate representation NOT-OD-21-055

NIH and ORWH Update
Dec.’s ORWH symposium caps 30th anniversary

Keynote speakers
- Pauline M. Maki, Ph.D., explored women’s mental health across the life course
- Research!America president Mary Woolley, M.A., reported on polling showing renewed and heightened belief in science
- Lancet Executive Editor Jocalyn Clark, Ph.D., offered an editor’s perspective on sex differences research | SCORE Meeting keynote speaker

Symposium Attendance
- 264 attendees with another 290 videocast views
- 500 Twitter engagements produced 6.9M impressions
- More than 1000 registrations across all three events, inc. BIRCWH and SCORE meetings

Visit the Virtual Environment
New Administration Update

President Biden and Vice President Harris visit NIH

One of the first federal agencies visited

New health leadership brings science and diversity

**White House**

President’s chief medical advisor – Dr. Anthony Fauci  
President’s science adviser; nominee, Office of Science and Technology Policy director – Dr. Eric Lander  
OSTP – Dr. Tara Schwetz and Dr. Carrie Wolinetz  
COVID-19 Testing Coordinator – Carole Johnson  
Vaccine Chief – Dr. David Kessler  
COVID-19 Equity Task Force Chair – Dr. Marcella Nunez-Smith  
COVID-19 Response Coordinator – Jeff Zients

**HHS**

Secretary – Xavier Becerra  
NIH Director – Dr. Francis S. Collins  
CDC director – Dr. Rochelle P. Walensky  
ASH – Dr. Rachel Levine  
Surgeon General – Dr. Vivek Murthy

“You’re the best America has to offer, NIH.”

Pres. Biden, Feb. 11, 2021
New NIH office, strategic plan to boost nutrition research

Dr. Collins announces NIH-wide Strategic Plan

- First ever
- New ONR to coordinate implementation
- Organized around unifying vision of precision nutrition research
- dpcpsi.nih.gov/onr/strategic-plan
Lindsey A. Criswell, M.D., M.P.H., D.Sc.
Director
National Institute of Arthritis and Musculoskeletal and Skin Diseases

ORWH is participating in NIAMS’s Accelerating Medicines Partnership in Autoimmune and Immune-Mediated Diseases (AMP AIM)

Joni L. Rutter, Ph.D.
Acting Director
National Center for Advancing Translational Sciences

Replacing Christopher P. Austin, M.D., effective April 15, 2021

AMP AIM: Disease Teams for Rheumatoid Arthritis, Lupus, Psoriatic Spectrum Diseases and Sjögren’s Syndrome (RFA-AR-21-015)
AMP AIM: Technology and Analytic Cores and Research Management Unit (UC2) (RFA-AR-21-016)
ORWH leads on COVID-19 sex and gender research

**Principles and programs provide direction and information**

- NIH Wide Strategic Plan for COVID-19 Research

**FOAs support only NIH sex- & gender-related research on COVID-19**

- Expanded FOAs to add COVID-19 to scope of Sex and Gender Admin Supps, U3 admin supps, and Sex and Gender R01
Improving representation of women and underrepresented minorities in clinical trials and research

• Speaking later – Dawn Corbett, NIH Inclusion Policy Officer, Office of Extramural Research

• CEAL: NIH Community Engagement Alliance Against COVID-19 Disparities

• Participation in March 29 NASEM Overcoming Barriers to Diversifying Clinical Trials workshop

• 21st Century Cures Act expanded inclusion in key ways:
  o to individuals of all ages – and established a path to include pregnant and lactating women
  o Requires NIH-defined applicable phase III clinical trials to report results disaggregated by sex/gender, race, and ethnicity into ClinicalTrials.gov

Sex Differences in Major Depression: Impact of Prenatal Stress-Immune and Autonomic Dysregulation | Jill Goldstein (1 U54 MH118919-01A1)

- “Identify stress-immune pathway abnormalities, beginning in fetal development, that have shared consequences for sex differences in brain circuitry regulating mood and lifelong recurrent MDD and dysregulation of hormone and immune responses to stress, and autonomic and neurovascular dysfunction in early midlife”

Sex Differences in Disorders of the Brain and Heart – A Global Crisis of Multimorbidity and Novel Opportunity JAMA Psychiatry, 2021

- Sex/gender differences in the co-occurrence major depressive disorder, CVD, Alzheimer’s disease
- These interconnected disorders of brain and heart are critical preexisting conditions into which the COVID-19 infectious crisis has interacted
- Proposes adoption by investigators and funders of life span approach to tackling multimorbidity of brain and heart disorders that is targeted toward sex/gender differences from prenatal development through aging and illness causes before disease manifestation
Sex and gender: modifiers of health, disease, and medicine

<table>
<thead>
<tr>
<th>TABLE 1: Sex and gender differences in leading causes of mortality</th>
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<tbody>
<tr>
<td><strong>Sex differences</strong></td>
</tr>
<tr>
<td><strong>Heart disease</strong></td>
</tr>
<tr>
<td><strong>Cancer</strong></td>
</tr>
<tr>
<td><strong>COPD and asthma</strong></td>
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<tr>
<td><strong>Ischaemic stroke</strong></td>
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<tr>
<td><strong>Alzheimer’s disease</strong></td>
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<td><strong>Type 2 diabetes</strong></td>
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<tr>
<td><strong>Influenza</strong></td>
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<tr>
<td><strong>Chronic kidney disease</strong></td>
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<tr>
<td><strong>Chronic liver diseases</strong></td>
</tr>
<tr>
<td><strong>Depression</strong></td>
</tr>
</tbody>
</table>

COPD=chronic obstructive pulmonary disease. NASH=non-alcoholic fatty liver disease. NASH=non-alcoholic steatohepatitis.
LinkPositively: A Technology-Delivered Peer Navigation and Social Networking Intervention to Improve HIV Care Across the Continuum for Black Women Affected by Interpersonal Violence Grant Number: R34MH122014-01

Core components

- Virtual peer navigation – phone and text check-ins; weekly one-on-one video sessions to build coping skills and navigate care
- Social networking platform for peer support
- Educational and self-care database with healthy living/self-care tips
- GPS-enabled resource locator for care & ancillary support service agencies
- ART self-monitoring and reminder system
Implementing a Maternal health and Pregnancy Outcomes Vision for Everyone

NIH-wide program funding interdisciplinary research in foundational biology, behavioral, & sociocultural science

- Gain evidence on causes of maternal mortality & morbidity
- Improve health for women before, during, & after delivery
- Reduce preventable causes of maternal deaths

Promote health equity in the U.S.

- Evaluate structural & health care system issues in populations with high rates of maternal deaths & complications
- Develop community partnerships to assess vulnerabilities & implement interventions to improve outcomes

36 projects ($7.5M) in Sept. 2020

- 17 ICOs participating; 12 funding projects

nih.gov/research-training/medical-research-initiatives/improve-initiative
REMOTE SUPERVISION FOR IMPLEMENTING COLLABORATIVE CARE FOR PERINATAL DEPRESSION

Photo by manu mangalassery from Pexels

PRENATAL BLOOD PRESSURE PATTERNS TO PREDICT PREGNANCY-RELATED HYPERTENSION & LATER LIFE CVD RISK

Photo by Thirdman from Pexels

ROLE OF HOST-MICROBIAL INTERACTIONS IN ALTERING PRETERM BIRTH RISK AMONG BLACK WOMEN

Photo by Ketut Subiyanto from Pexels
Small Business Initiatives for Innovative Diagnostic Technology for Improving Outcomes for Maternal Health NOT-EB-21-001

• Development of technologies to predict an increased risk for maternal morbidity and mortality (MMM)
• Identification, phenotyping, subtyping, and stratification of patients at greater risk of MMM
• Multi-level interventions to address racial disparities
• Clinical decision-making that considers social and cultural biases
• Wearable, point-of-care, portable, or clinical devices
• Issued by National Institute of Biomedical Imaging and Bioengineering (NIBIB) with:
  o NHLBI, NHGRI, NIAID, NICHD, NIMH, NINDS, NIMHD, NCATS, NIAMS, OD, ORWH

Admin. Supps. and Urgent Competitive Revisions for NIH Grants to Add or Expand Research Focused on Maternal Health, Structural Racism and Discrimination, and COVID-19 NOT-OD-21-071

• Pandemic may amplify psychosocial factors & social determinants of health that contribute to MMM
• Structural racism and discrimination (SRD) could have a profound negative impact
• Understand effects of infection and pandemic on maternal mental health, well-being, functioning and quality of life
• In context of the pandemic:
  o ID psychosocial & behavioral health risk factors that affect mental health
  o Address impact of SRD on maternal health
• Understand how knowledge, attitudes, etc. affect testing & vaccination take-up
• Issued by NIH Office of the Director
ORWH & NIGMS expand WH research in IDeA states

• In partnership with ORWH, popular program expanded scope of research to include WH
• Expands WHR in states with least amount of research funding and of populations disproportionately affected

NOT-GM-21-018

• Research must address at least one goal of the Trans-NIH Strategic Plan for Women’s Health Research
• Maternal morbidity & mortality (MMM)
• Links between MMM and subsequent risks
• FY 2020: $4.8 million/19 selected applications
• Current year: 15 participating ICOs
  • Applications due April 19, 2021
  • Funding in FY 2021

https://www.nigms.nih.gov/News/results/Pages/20201009.aspx
FY20 RESEARCH PROGRAMS FUNDING
ORWH Budget History & FY20 Extramural Award Profile

ORWH FY2020 Extramural Awards by Program (as % of Extramural Budget)

- SCORE (35%)
- BIRCWH (29%)
- Other IC Co-Funds (18%)
- Career Continuity Supp. (4%)
- U3 Admin. Supp. (5%)
- Sex/Gender Admin Supp. (6%)
- Sex/Gender R01 (3%)
- Other IC Co-Funds (18%)
- BIRCWH (29%)
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Note: Award investments do not adjust for inflation.

Source: NIH IMPAC II FY2020 frozen data.
Note: ORWH total investments = $31,867,666. Funding portfolio excludes Contract R&D and IAA awards.
ORWH FY2020 Extramural Award Investments by IC (including BIRCWH funding)

Source: NIH IMPAC II FY2020 frozen data.
Note: ORWH total investments = $31,867,666. Funding portfolio excludes Contract R&D and IAA awards.
ORWH FY2020 Extramural Award Investments by IC (excluding BIRCWH funding)

Source: NIH IMPAC II FY2020 frozen data.
Note: ORWH total investments = $22,488,025. Funding portfolio excludes BIRCWH program investments, Contract R&D, and IAA awards.
## ORWH Extramural Award Investments by Research Program in FY2020

<table>
<thead>
<tr>
<th>Program</th>
<th>ORWH Investments</th>
<th># of Co-Funding ICs</th>
<th>List of Co-Funding ICs</th>
</tr>
</thead>
<tbody>
<tr>
<td>BIRCWH*</td>
<td>$9,379,641</td>
<td>1</td>
<td>NICHD</td>
</tr>
<tr>
<td>Career Continuity Supp.</td>
<td>$1,217,235</td>
<td>16</td>
<td>FIC; NCI; NHLBI; NIA; NIAID; NIAMS; NIDA; NIDCD; NIDCR; NIDDK; NIEHS; NIGMS; NIMH; NINDS; NINR; NLM</td>
</tr>
<tr>
<td>SCORE</td>
<td>$11,025,174</td>
<td>5</td>
<td>NIA; NIAAA; NIDA; NIDDK; NIMH</td>
</tr>
<tr>
<td>Sex/Gender R01</td>
<td>$1,014,454</td>
<td>2</td>
<td>NIAID; NIEHS</td>
</tr>
<tr>
<td>Sex/Gender Admin Supp.</td>
<td>$2,006,510</td>
<td>10</td>
<td>NCI; NHLBI; NIA; NIAID; NIAMS; NICHD; NIDCR; NIDDK; NIMH; OD-ORIP</td>
</tr>
<tr>
<td>U3 Admin Supp.</td>
<td>$1,635,185</td>
<td>5</td>
<td>NCI; NHLBI; NIDA; NIMHD; NINR</td>
</tr>
<tr>
<td>Other IC Co-Funds</td>
<td>$5,589,467</td>
<td>16</td>
<td>FIC; NCCIH; NCI; NEI; NHGRI; NHLBI; NIAID; NIAMS; NICHD; NIDA; NIMHD; NINR; NLM</td>
</tr>
</tbody>
</table>

* In FY2020, NCI, NIAAA, NIAID, and NIDA also supported the BIRCWH program with additional funds.
Fifth Annual Vivian W. Pinn Symposium
Integrating Sex and Gender Into Biomedical Research as a Path for Better Science and Innovation

Honoring the first full-time director of ORWH, Vivian W. Pinn Symposium is held annually during National Women’s Health Week

May 11-12, 2021 | Virtual Meeting

Illustrate the scientific, societal, and economic opportunities of integrating sex and gender into biomedical research and the power of synergistically working together

- Create bridges and capacity across the scientific enterprise to build a broad-based network of government, non-profit, academic, and business organizations
- Develop strategies to integrate sex and gender considerations into research enterprise
- Apply multidimensional perspective to women’s health to advance the integration of sex and gender considerations via trans-disciplinary approaches and partnerships

For more information: www.nih.gov/women
House and Senate “significant items” request a consensus conference

ORWH will hold a Consensus Conference on October 20-21, 2021, as part of the ACRWH Meeting.

- Must include representatives from ORWH, NICHD, NCI, NHLBI, NIDDK, & other relevant ICOs.

  - Evaluate research and identify priorities to advance the study of women’s health, particularly:
    1. Rising rates of maternal morbidity and mortality;
    2. Rising rates of chronic debilitating conditions in women;
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30TH ANNIVERSARY ISSUES

quarterly newsletter
bit.ly/ORWHInFocus

WOMEN’S HEALTH In Focus AT NIH
A QUARTERLY PUBLICATION OF THE NIH OFFICE OF RESEARCH ON WOMEN’S HEALTH

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