NASEM Committee on the Assessment of NIH Research on Women’s Health

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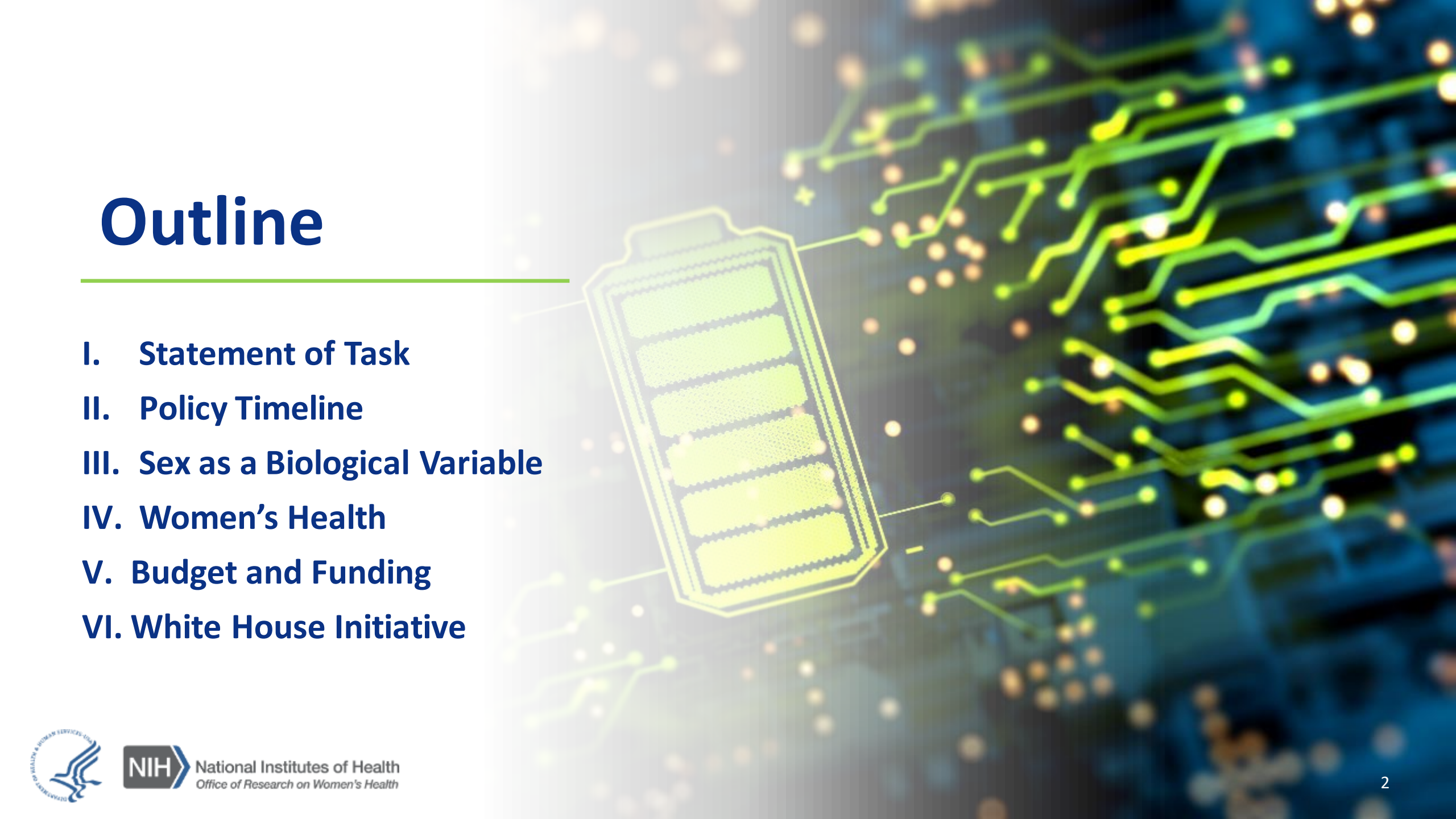
Director, Office of Research on Women's Health
National Institutes of Health

December 14, 2023

Outline

I. Statement of Task
II. Policy Timeline
III. Sex as a Biological Variable
IV. Women's Health
V. Budget and Funding
VI. White House Initiative



Statement of Task (1)

- The National Academies of Sciences, Engineering, and Medicine (NASEM) will convene a consensus committee with specific scientific, ethical, regulatory, and policy expertise to develop a framework for addressing the persistent gaps that remain in the knowledge of women's health across all NIH Institute and Centers (ICs).
- Specifically, the study should be designed to analyze the proportion of research that the NIH funds on conditions that are female-specific and/or more common amongst women or that differently impact women (e.g., different pathophysiology or course of disease), establish how these conditions are defined and ensure that it captures conditions across the lifespan, evaluates sex differences and racial and ethnic health disparities.
- The committee should define women's health for the purpose of the report, taking into account today's social and cultural climate.
- Ultimately, the study should determine the appropriate level of funding that is needed to address gaps in women's health research at NIH.

P.L. 117-328 Consolidated Appropriations Act of 2023

Division H--Departments of Labor, Health and Human Services, and Education, and Related Agencies Appropriations Act, 2023

Statement of Task (2)

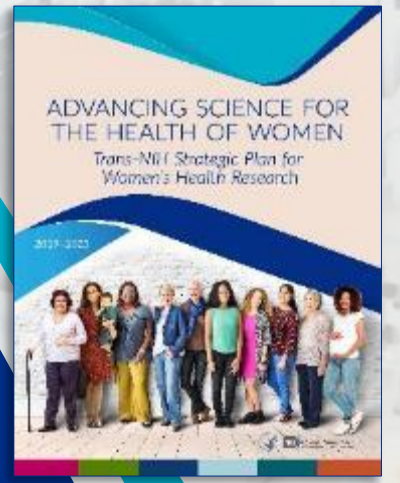
- The NASEM consensus committee, as a first step, will conduct an analysis and develop a matrix of identified NIH research on conditions that are female-specific, more common amongst women or that differently impact women, investigating sex differences, and centered on the unique health needs of women.
- The NASEM consensus committee will make recommendations for the following:
  - Research priorities for NIH-supported research on women's health,
  - NIH training and education efforts to build, support, and maintain a robust women's health research workforce,
  - NIH structure (extra- and intra-mural), systems, and review processes to optimize women's health research,
  - NIH-wide workforce to effectively solicit, review, and support women's health research,
  - Allocation of funding needed to address gaps in women's health research at NIH.
- The committee will identify metrics to ensure that research is tracked to meet the continuing health needs of women.

P.L. 117-328 Consolidated Appropriations Act of 2023

Division H--Departments of Labor, Health and Human Services, and Education, and Related Agencies Appropriations Act, 2023

ORWH Mission

- Enhance and expand women's health research
- Include women and minority groups in clinical research
- Promote career advancement for women in biomedical careers



NIH Vision

- Sex and gender integrated into biomedical research
- Every woman receives evidence-based care
- Women in science careers reach their full potential

Timeline of NIH Inclusion Policies

1986 — NIH encourages inclusion of women

1994 — NIH requires inclusion of women and members of racial and ethnic minority groups

1998 — NIH requires inclusion of children

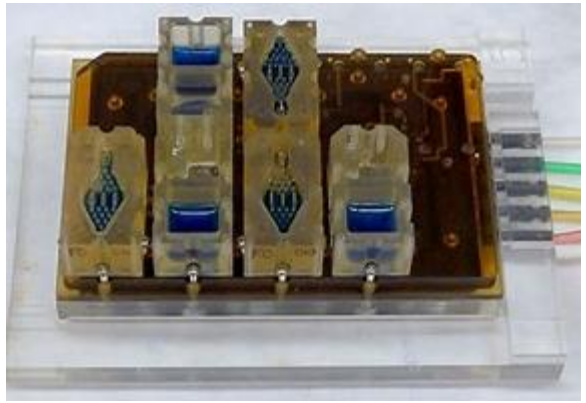
2017 — New phase 3 reporting requirements

2019 — NIH requires inclusion of individuals of all ages

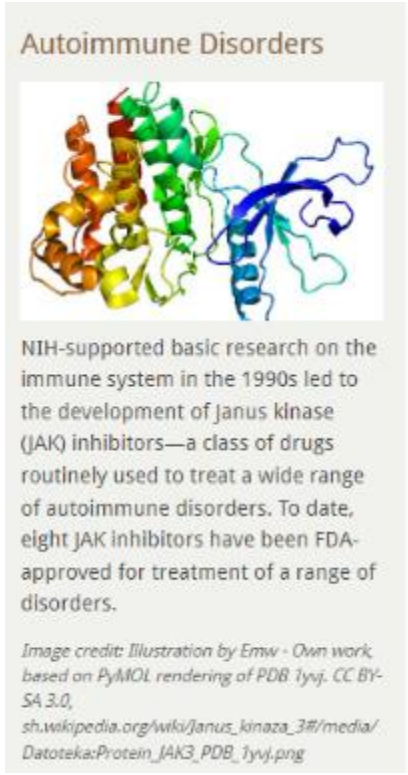
2022 — NIH clarifies phase 3 project outcomes requirements

NIH Supported Research Plays a Critical Role in the Health of Women

Women's Health Initiative

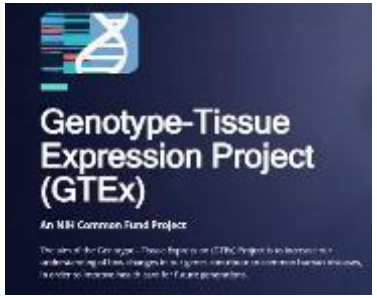


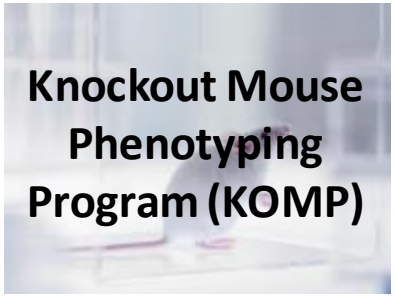
EVATAR™ Modeling the Female Reproductive Tract in 3-D



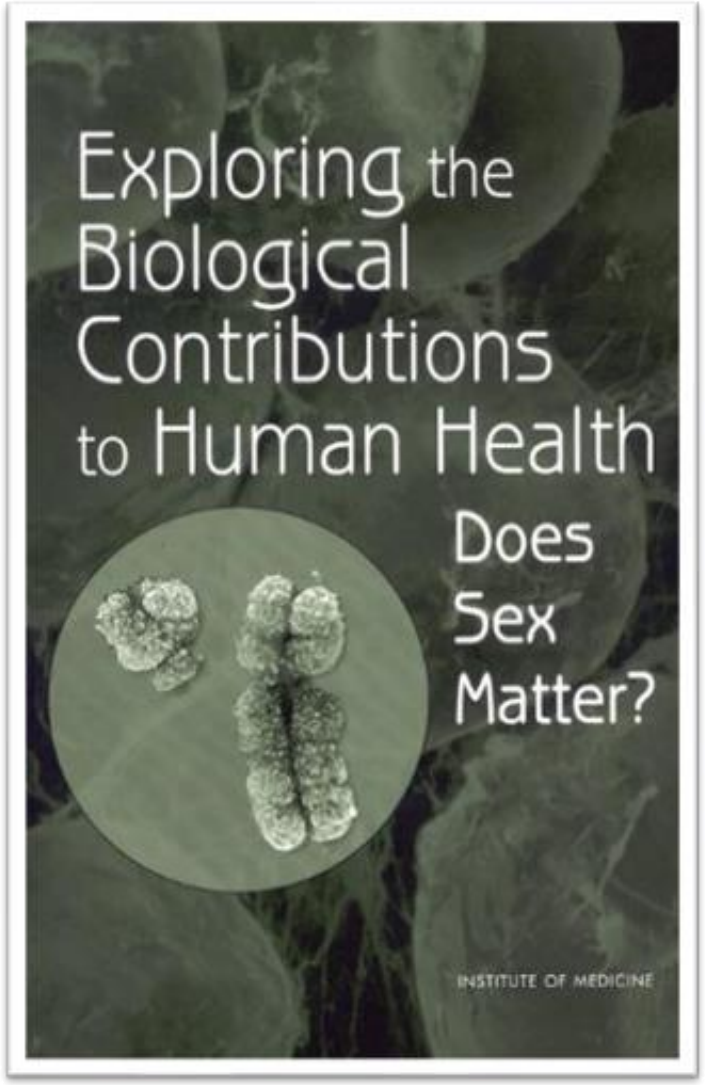
NIH-supported basic science led to JAK inhibitor development

Study of Women's Health Across the Nation





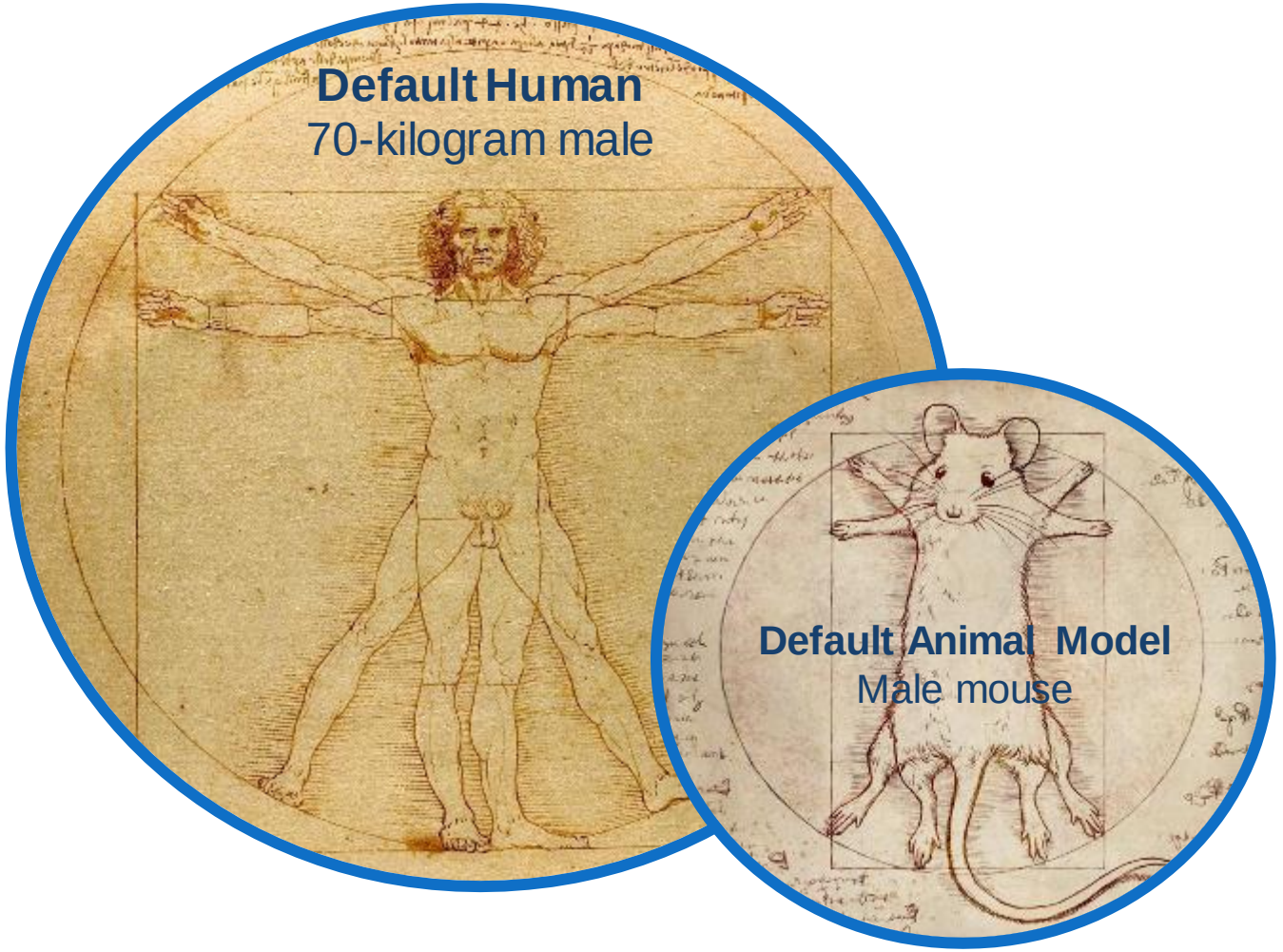
Does Sex Matter? A 2001 NASEM Report



"A common, recurring message emerged … This message is that sex—that is, being male or female—is an important basic human variable that should be considered when designing and analyzing the results of studies in all areas and at all levels of biomedical and health related research."

Institute of Medicine, 2001

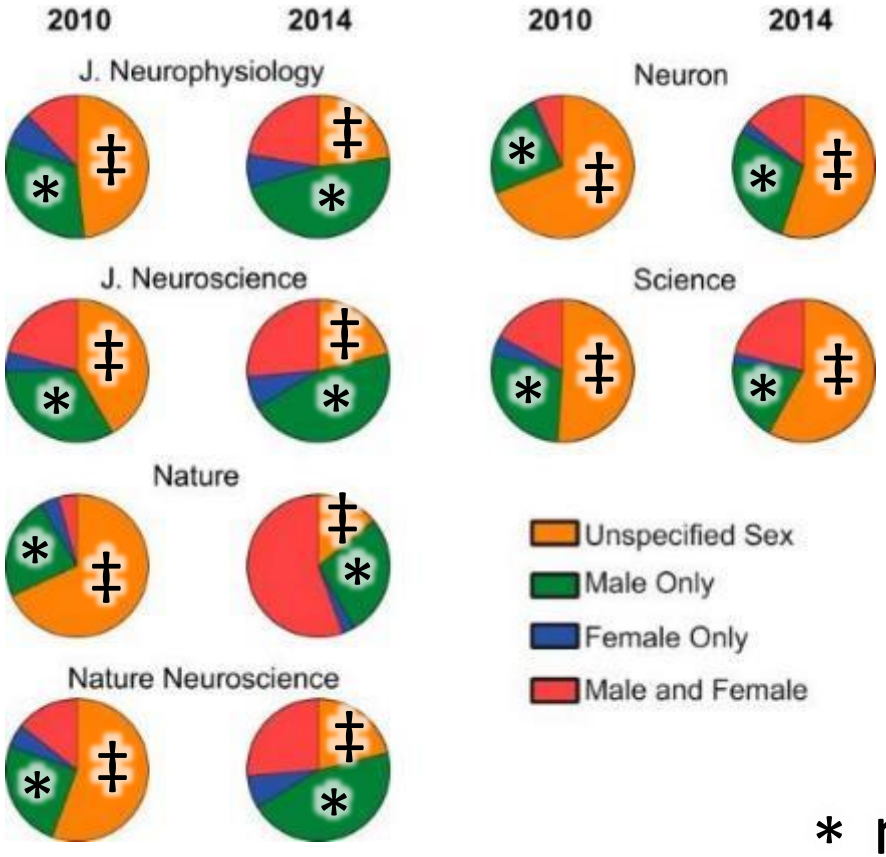
Assumptions about Sex in Biomedical Research



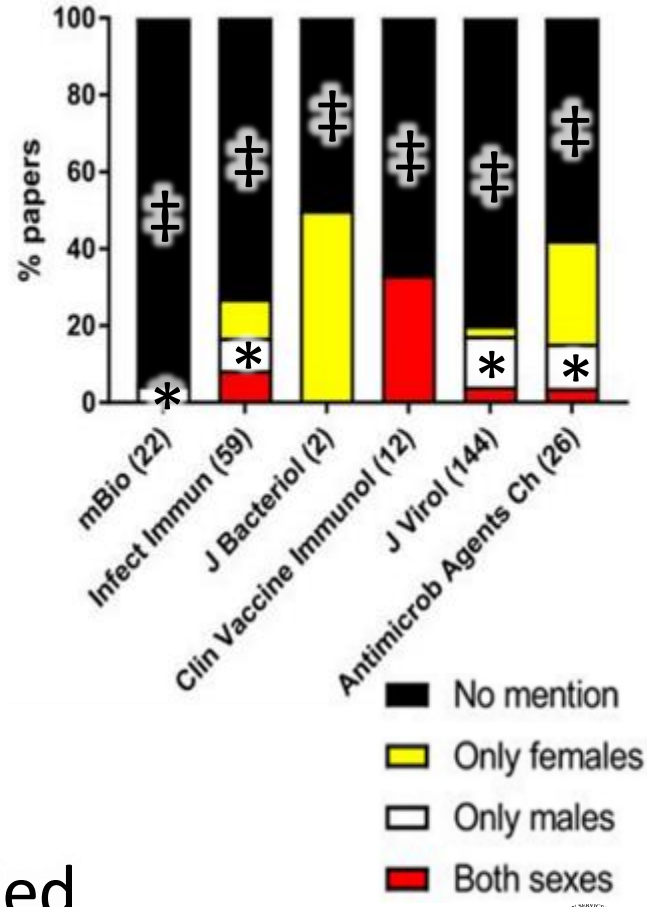
- Fundamental biology assumed to include shared molecular biochemical and physiologic characteristics
- These assumptions have led to evidence gaps

Over-Reliance on Male Models & Lack of Analysis by Sex

Animal Studies in Neuroscience, 2010 & 2014, by Journal



Primary Cell Culture Studies in 2016, by ASM Journal



∗ male only
‡ sex not specified

Will et al. 2017. *eNeuro* **4**: e0278-17.2017.

Potluri et al. 2017. *mBio* **8**: e01868-17.

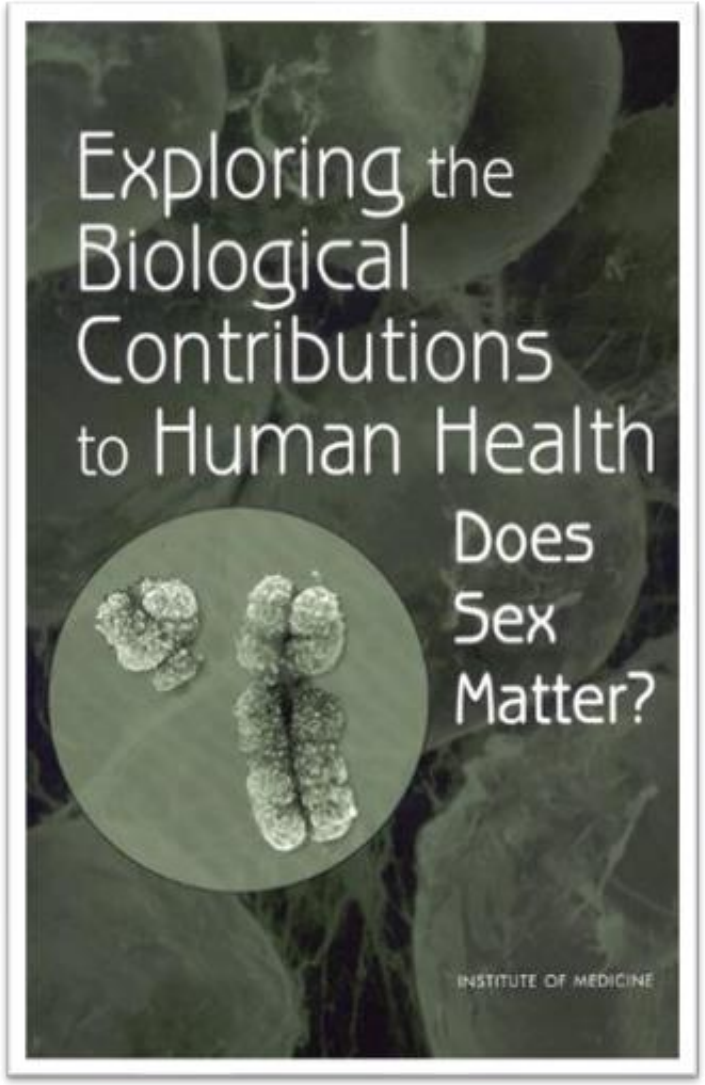
NIH Policy on Sex as a Biological Variable (SABV)

"NIH expects that [SABV] will be factored into research designs, analyses, and reporting in vertebrate animal and human studies.
the scientific literature, preliminary data, or other relevant considerations must be provided for applications proposing to study only one sex."

Effective 01/25/2016

SABV Policy Notice: NOT-OD-15-102

Does Sex Matter? A 2001 NASEM Report

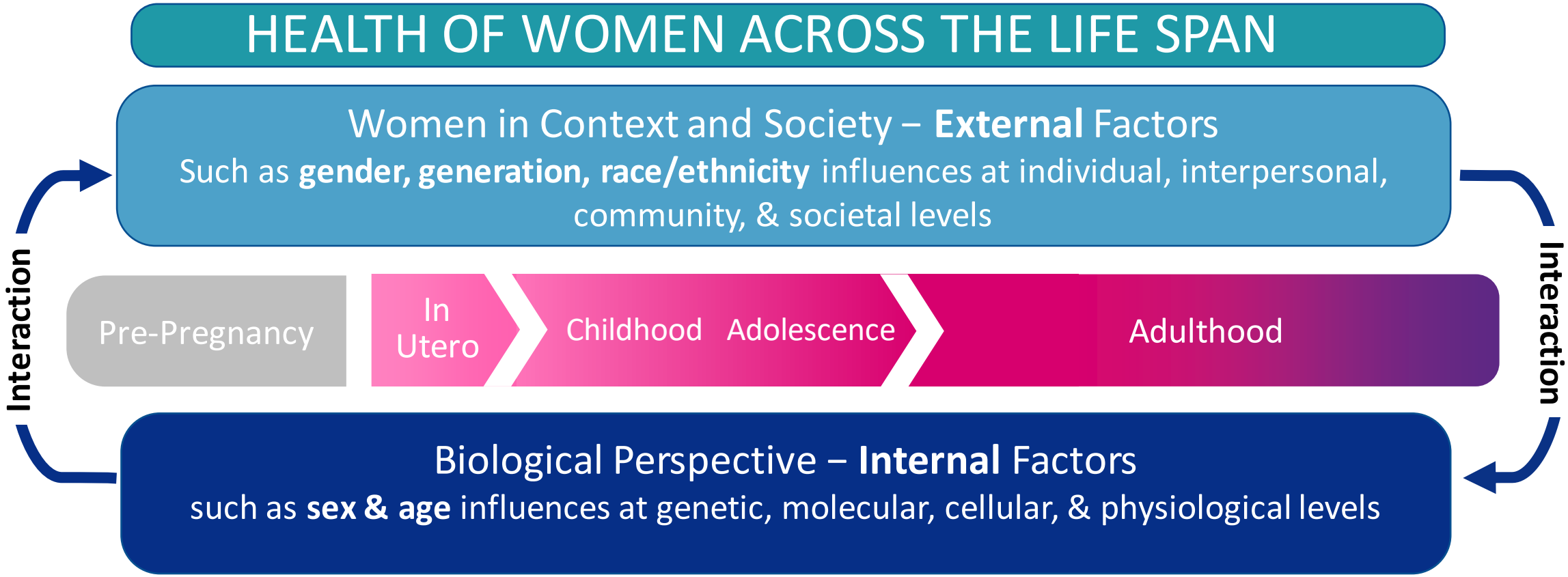


"A common, recurring message emerged … This message is that sex—that is, being male or female—is an important basic human variable that should be considered when designing and analyzing the results of studies in all areas and at all levels of biomedical and health related research.

Differences in health and illness between individuals are influenced not only by individuals' genetic and physiological constitutions but also by environmental and experiential factors, all of which interact."

Institute of Medicine, 2001

Extended ORWH Multidimensional Framework that Represents the Intersection of Factors Affecting the Health of Women

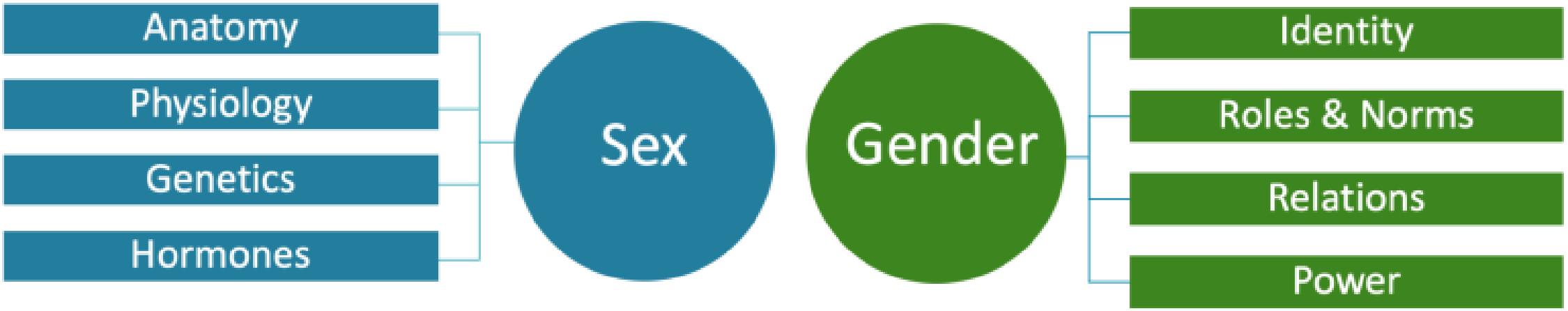


NIH Strategic Plans and Visions

https://report.nih.gov/strategicplans

Sex and Gender Influence Health

Dimensions of Sex (Biological Variable) & Gender (Social and Cultural Variable)



Dimensions of Intersectionality*

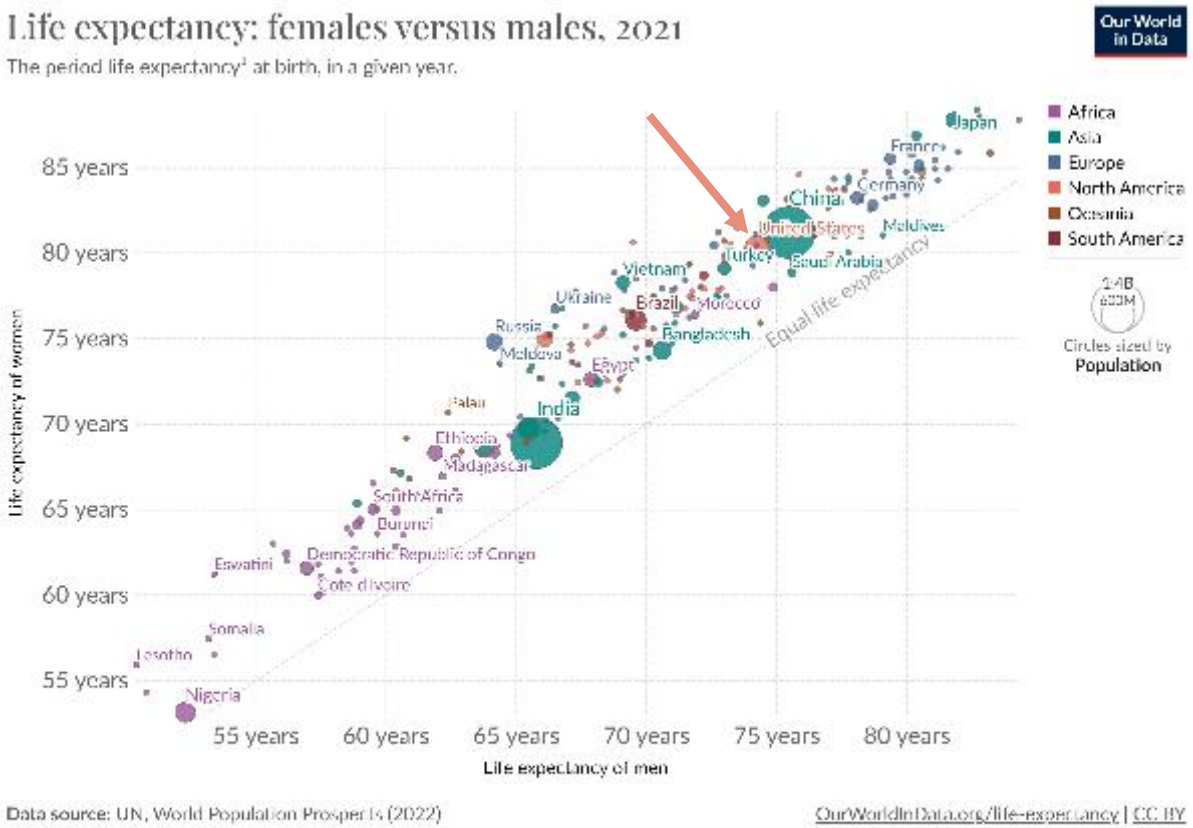
The culmination of a person's multiple domains of identity combined with their lived experience that together influence health status and disease risk (i.e., race, ethnicity, socioeconomic status, generation, caste, sexual orientation).

https://orwh.od.nih.gov/sex-gender/sex-and-gender-in-health-and-disease

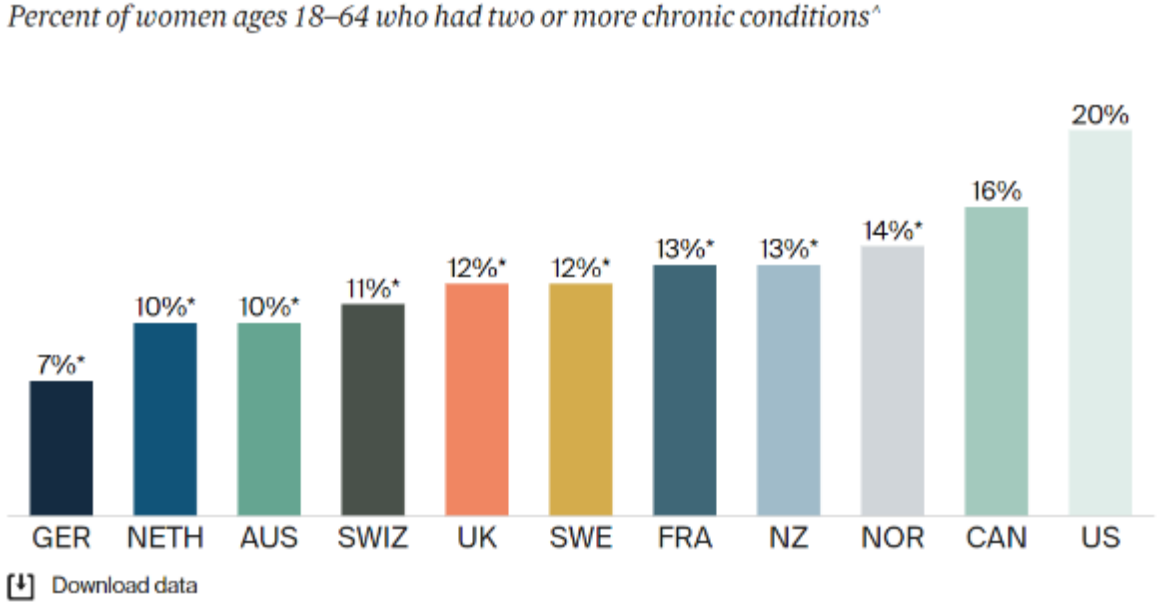
*White & Clayton. 2022. *Med.* DOI: 10.1016/j.medj.2022.04.010

NIH National Institutes of Health
Office of Research on Women's Health

Differences in Health for Women



1. Period life expectancy: Period life expectancy is a metric that summarizes death rates across all age groups in one particular year. For a given year, it represents the average lifespan for a hypothetical group of people, if they experienced the same age-specific death rates throughout their whole lives as the age-specific death rates seen in that particular year. Learn more in our article: "Life expectancy" – What does this actually mean?

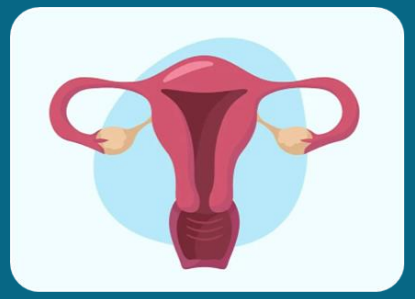


Notes: ^ Having a chronic disease defined as ever being told by a doctor as having two or more of the following: joint pain or arthritis; asthma or chronic lung disease; diabetes; heart disease, including heart attack; or high blood pressure. * Statistically significant difference compared to the United States (p<.05).
Data: The Commonwealth Fund International Health Policy Survey, 2016.

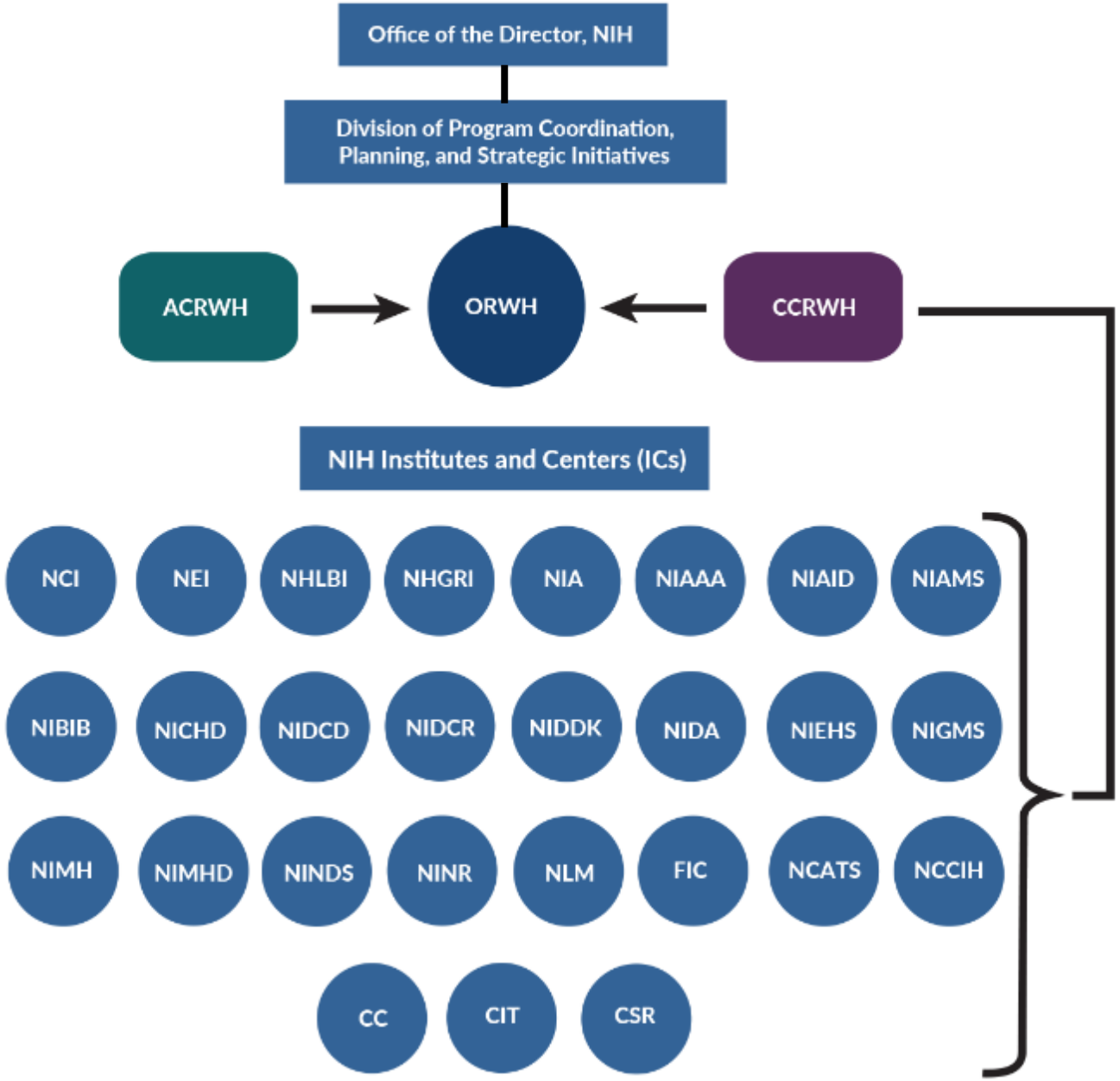
Munira Z. Gunja et al. (Commonwealth Fund, Dec. 2018). https://doi.org/10.26099/wy8a-7w13

Defining Women's Health

Condition Type	Examples
Female specific	• *Endometriosis* • *Cervical Cancer* • *Menopause*
Disproportionately impact women	• *Autoimmune Disease* • *Mental Health* • *Pain Conditions*
Present and progress differently in women	• *Heart Disease* • *Stroke* • *Metabolic Disorders*



Source: NIH Revitalization Act of 1993



What is ORWH's relation to the rest of NIH?

ORWH co-funds & complements ICO research

NIH-wide WHR Biennial Report

https://orwh.od.nih.gov/sites/orwh/files/docs/ORWH_BiennialReport2019_20_508.pdf

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

Collaboration is Key to Women's Health Research at NIH

NIH-Wide Strategic Plan

NIH Institutes and Centers

Partnership

Office of Research on Women's Health

Driving synergistic research priorities

- Workshops
- Priority Setting
- NIH-Wide Workgroups
- Funding Opportunities & Initiatives

NIH Vision

SIGNATURE PROGRAMS

ORWH Advances Study of Sex & Gender and the Health of Women through Collaborations across NIH

BIRCWH

Building Interdisciplinary Research Careers in Women's Health

8 ICOs

Mentored Career Development

SCORE

Specialized Centers of Research Excellence on Sex Differences

6 ICOs

Disease-Agnostic Research Centers

RFA-OD-22-014

Administrative Supplements

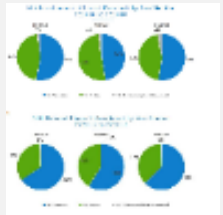
Sex and Gender

22 ICOs

Understudied, Underrepresented, & Underreported (U3)

16 ICOs

Funding Program to Expand Sex & Gender Data



R01

Intersection of sex & gender influences on health & disease

11 ICOs

Sex & Gender Influences on Health & Disease

RFA-OD-22-028

R21 & R01

Understanding Chronic Conditions Understudied Among Women

6 ICOs

A 2021 Women's Health Conference Report

RFA-OD-23-103
RFA-OD-23-014

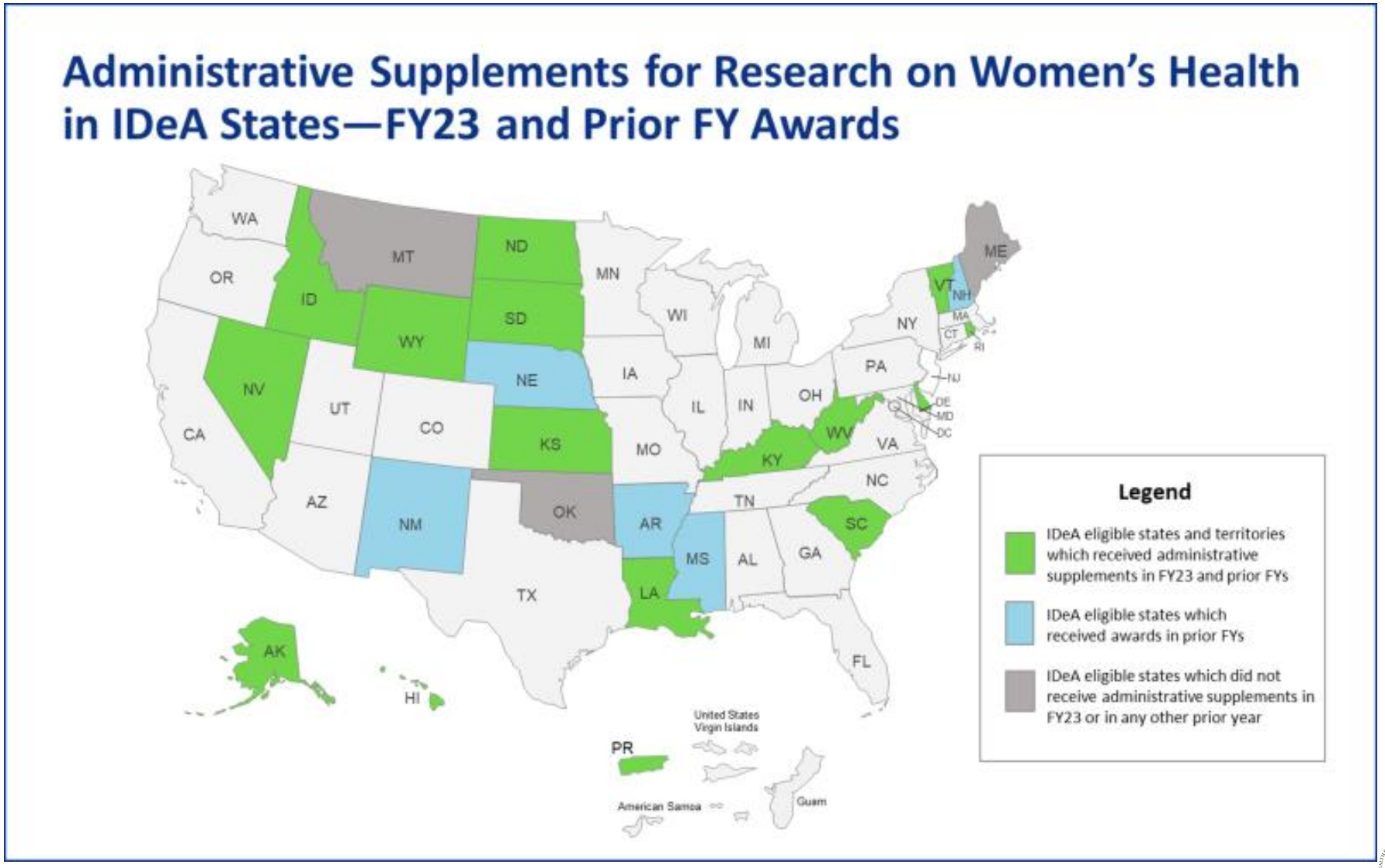
IDeA States

NOSI: Administrative Supplements for Research on Women's Health in the IDeA States – 2023 Update

NOTICE	**NOT-GM-22-005**
DUE DATE	October 17, 2022; October 17, 2023; and October 17, 2024
GOAL	To expand research and research capacity in the IDeA states to address important issues of women's health across the lifespan. Research on maternal and infant morbidity and mortality is of particular interest.
ISSUED BY 16 ICOs	NIGMS with ORWH, NEI, NHLBI, NIA, NIAID, NIBIB, NICHD, NIDCR, NIDA, NIEHS, NINR, NCCIH, NCI, ODP, SGMRO
BUDGET	Up to $200,000 for 1 year in direct costs.
CONTACTS	**Crina Frincu (NIGMS)–** Inquiries related to IDeA program and policy requirements **Regine Douthard (ORWH)** – inquiries related to scientific content of the applications **POs from each ICO are listed to answer IC-specific questions**
FUNDING	**$16.4 million awarded:** 60 grants in 20 IDeA states & Puerto Rico since 2020

https://www.nigms.nih.gov/grants/Pages/Funding.aspx?tab=All

ORWH partners with NIGMS and ICs on Women's Health Research in IDeA States



NIH funded randomized controlled trials reporting outcomes by sex (and race and ethnicity) increased significantly

TABLE 2. INCLUSION AND ANALYSIS BY SEX IN NATIONAL INSTITUTES OF HEALTH-FUNDED CLINICAL TRIALS PUBLISHED IN 2004, 2009, 2015, AND 2021

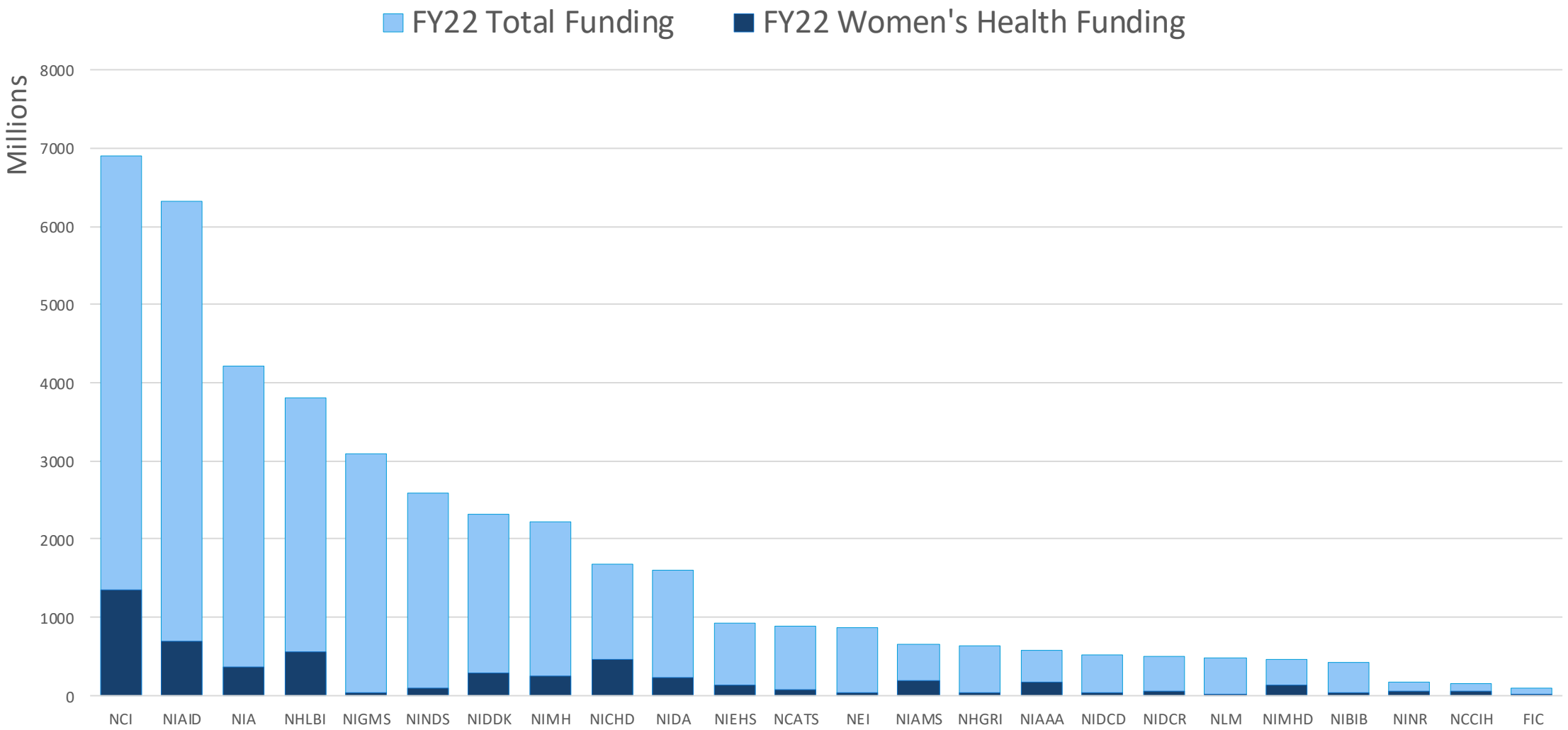
	2004	2009	2015	2021	
Enrollment by sex Median % of women enrolled (interquartile range)	43% (25–61%)	38% (28–54%)	46% (34–56%)	44% (24–56%)	
	n (%)	n (%)	n (%)	n (%)	*Fisher's exact p-value*
Analysis and reporting by sex					
Analysis by sex provided or sex included in statistical analysis	6 (13.0)	14 (25.0)	28 (26.2)	34 (43.0)	<0.01
Did not analyze by sex, but provided explanation	9 (19.6)	6 (10.7)	2 (1.9)	5 (6.3)	
Did not include sex in analysis or provide an explanation	31 (67.4)	36 (64.3)	77 (72.0)	40 (50.6)	
Total	46 (100.0)	56 (100.0)	107 (100.0)	79 (100.0)	

Among studies enrolling male and female participants.

Analysis and reporting by sex, race, and ethnicity significantly increased despite no corresponding increase in enrollment.

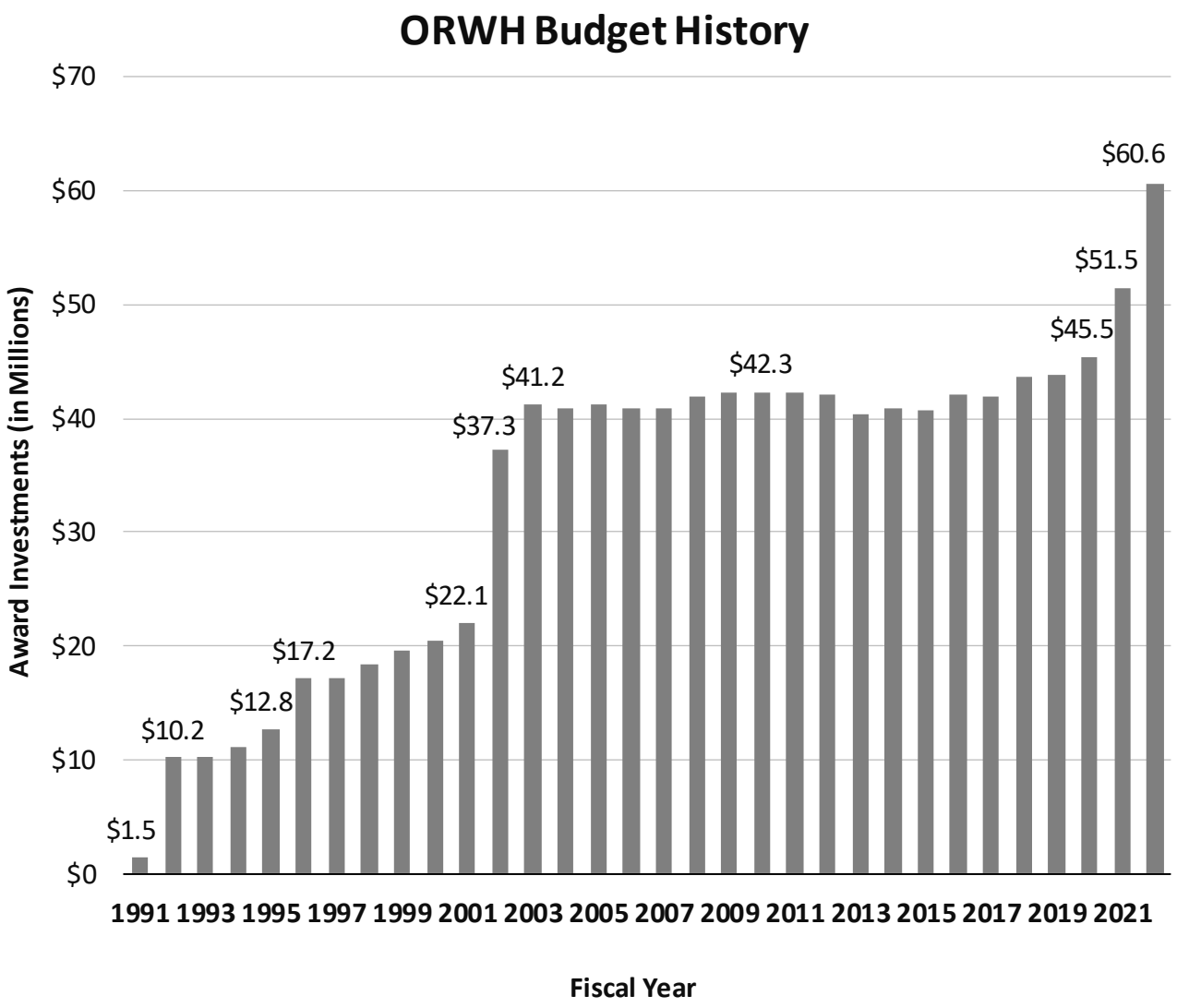
Koch, A. R., Craemer, K. A., Garland, C. E., Fox, W. B., Jones, C. T., Qualls, A. C., Sterr, J. C., & Geller, S. E. (2023). Federally Funded Randomized Controlled Trials Increase Analysis and Reporting of Study Outcomes by Sex, Race, and Ethnicity. Journal of women's health (2002), 10.1089/jwh.2023.0307. Advance online publication. https://doi.org/10.1089/jwh.2023.0307

NIH-Wide Research Investments in Women's Health
($4.6 Billion)

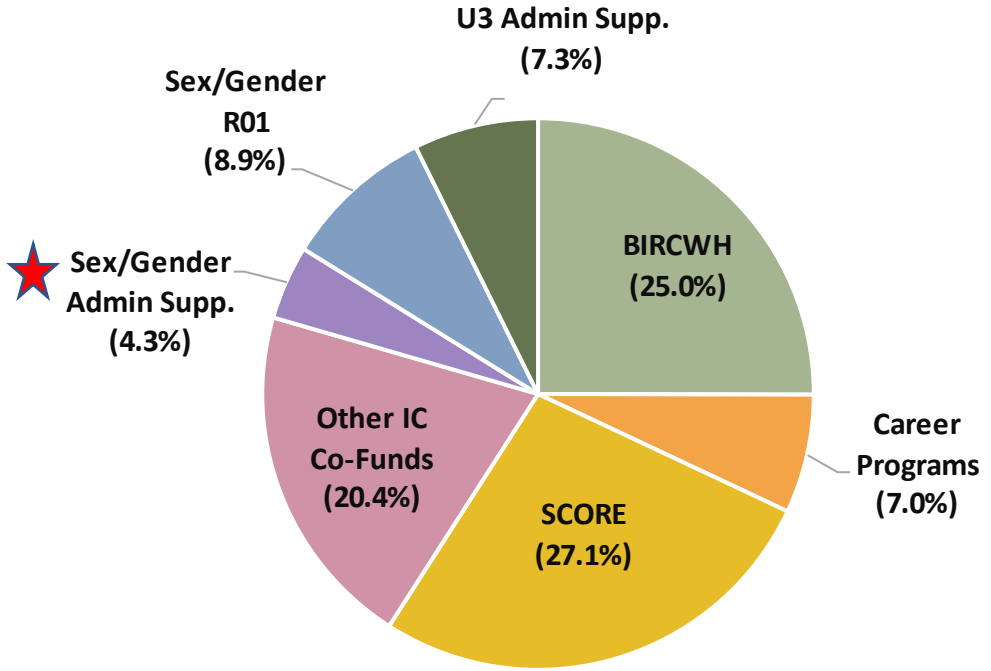


National Institutes of Health
Office of Research on Women's Health

ORWH Budget History & FY2022 Extramural Grant Award Profile



Note: Award investments do not adjust for inflation.



ORWH FY2022 Extramural Grant Awards by Program (as % of Extramural Budget)

Source: NIH IMPAC II FY2022 frozen data.
Note: ORWH total investments = $43,222,779. Funding portfolio excludes R&D contracts, IAA, and Loan Repayment awards.

ORWH Budget History & FY2022 Extramural Grant Award Profile

FY23 Budget Appropriations

$76,480,000 for ORWH

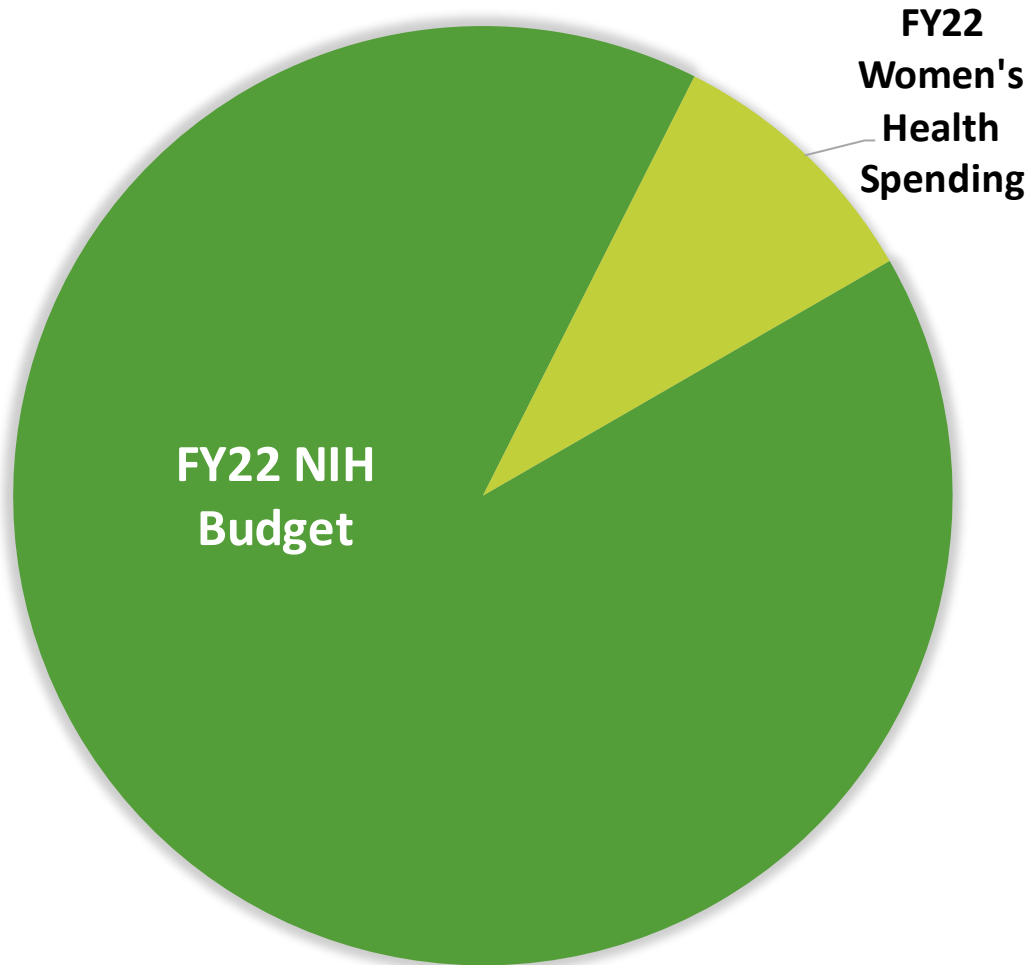
$10,000,000 for OADR-ORWH

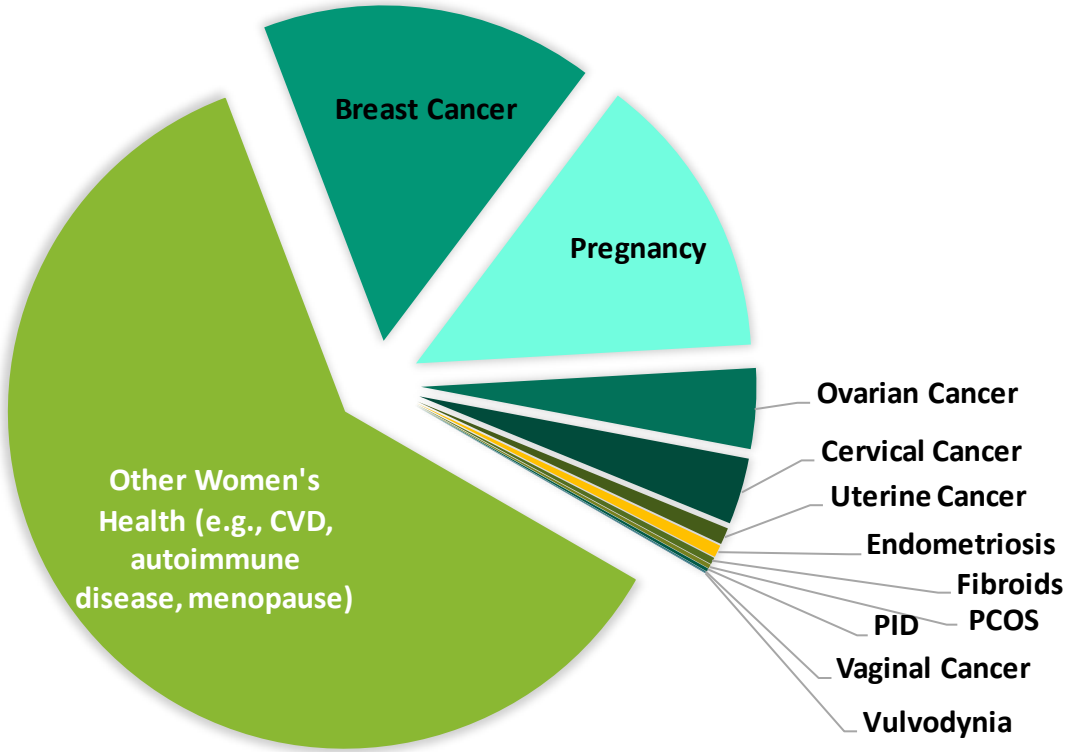
$5,000,000 for BIRCWH

$2,000,000 for NASEM study

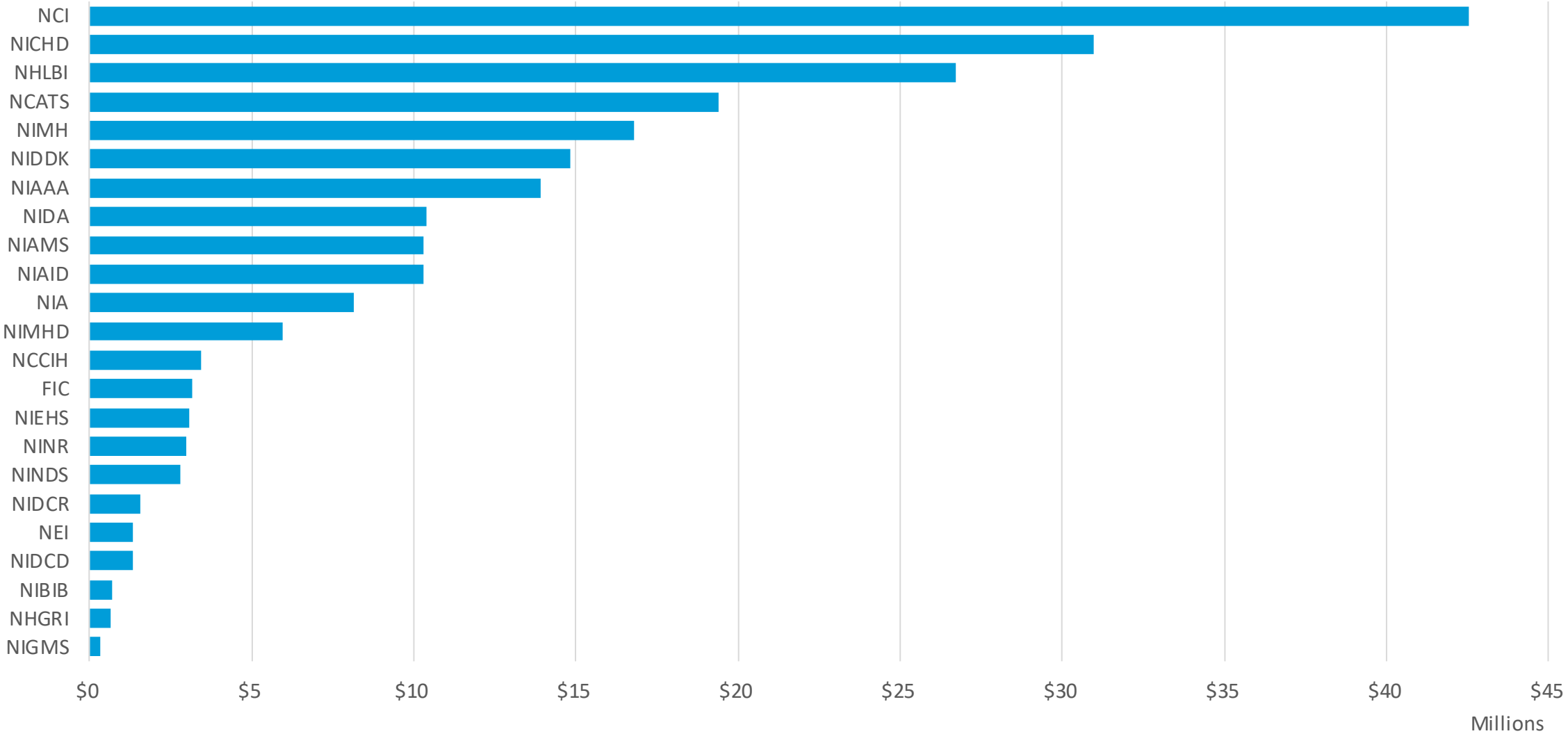
Note: FY23 Appropriations are not separated by category

Women's Health Research Spending By Category





FY22 NIH Funding for Women's Health – Training (T F K awards) ($232 million)



https://reporter.nih.gov/

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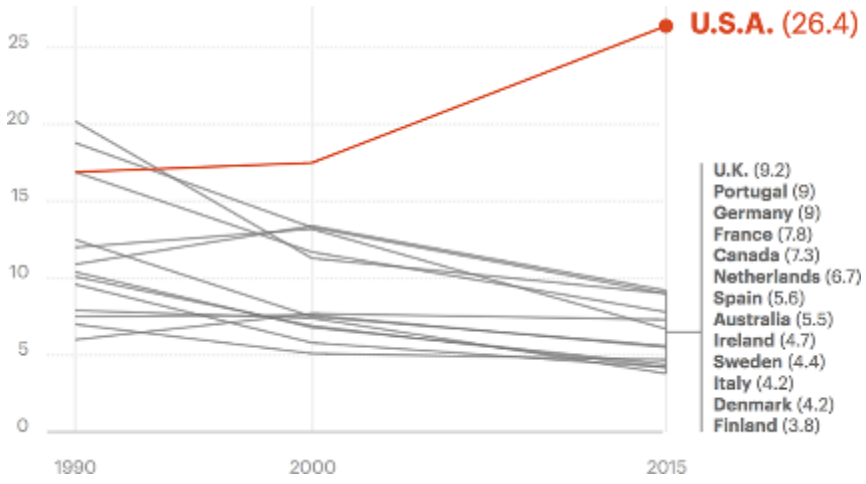
FY21 House and Senate "Significant Items"

The ORWH held the **Advancing NIH Research on the Health of Women: A 2021 Conference** on October 20, 2021, as part of the ACRWH Meeting.

- **Evaluate research** and **identify priorities** to advance the study of women's health
- Coordinated with the CCRWH

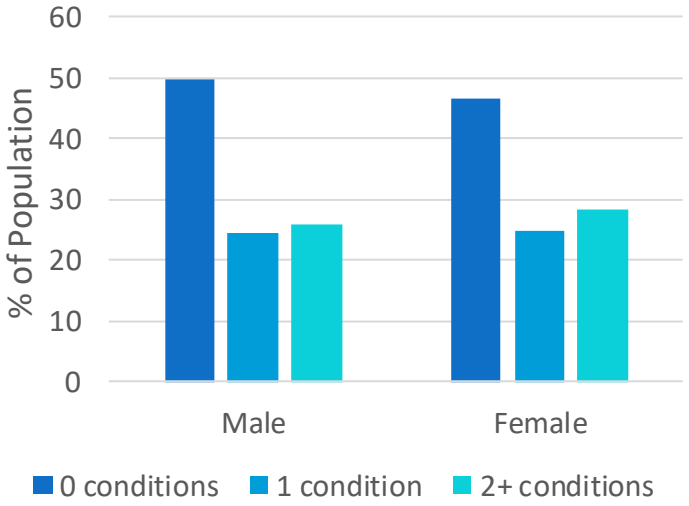
House: https://www.congress.gov/116/crpt/hrpt450/CRPT-116hrpt450.pdf (page 149),
Senate: https://www.appropriations.senate.gov/imo/media/doc/LHHSRept.pdf (page 123)

Rising Rates of Maternal Morbidity and Mortality



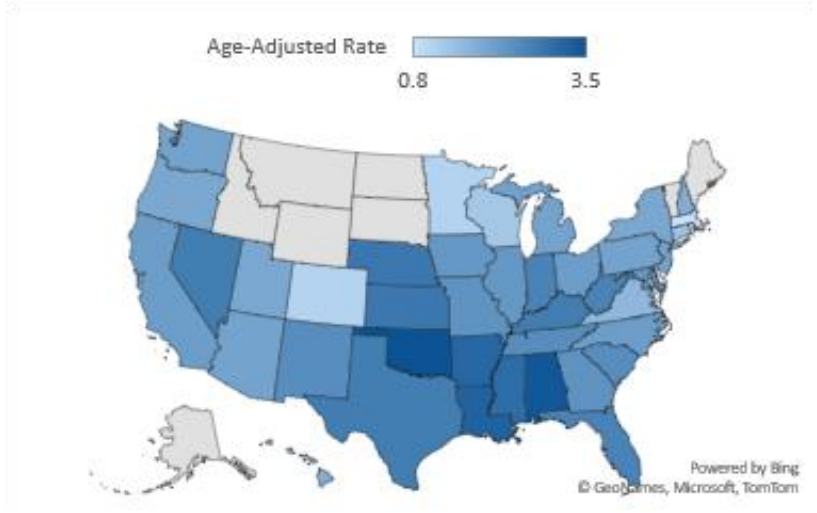
2015, Source: The Lancet. Credit: Rob Weychert/ProPublica

Rising Rates of Chronic Debilitating Conditions in Women



King, DE, etal. JABFM 2018, 31 (4) 503-513.

Stagnant Survival Rates among Cervical Cancer Patients



https://seer.cancer.gov/statfacts/html/cervix.html

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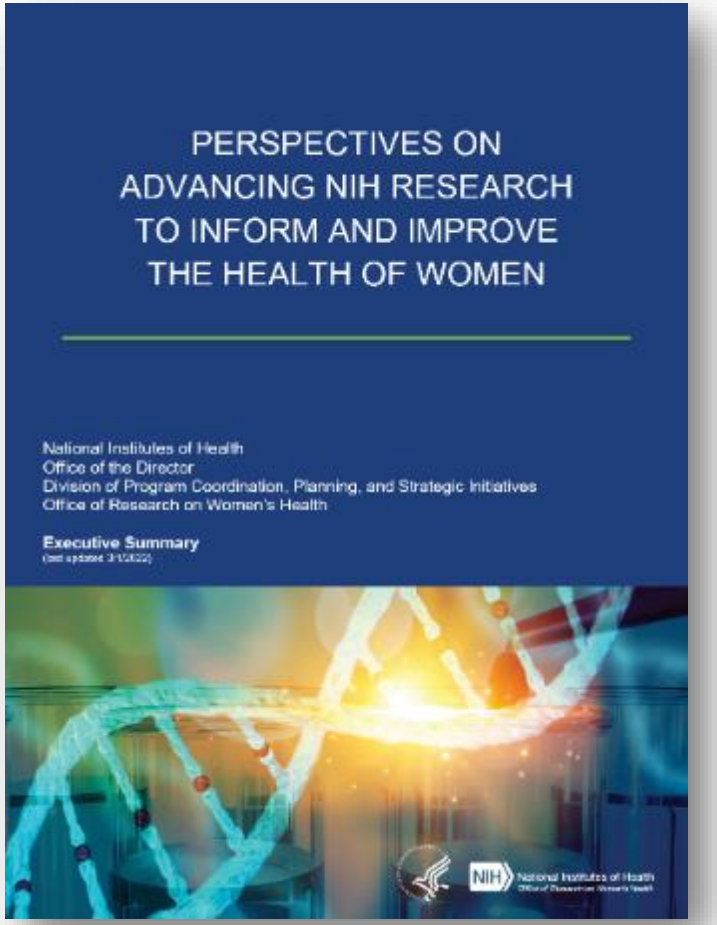
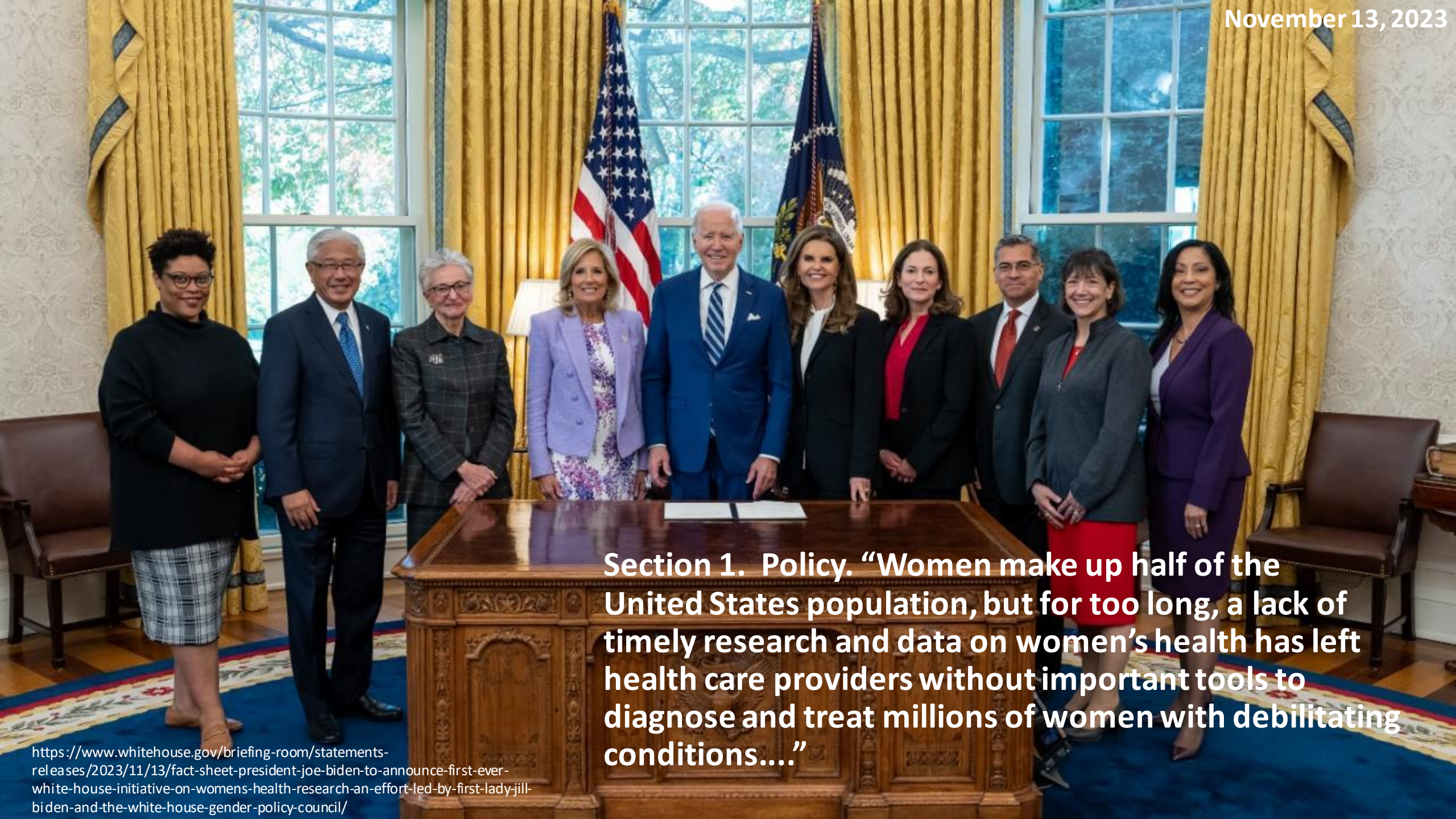
Crosscutting Themes Identified: Where Research is "Urgently Needed"

1. **Implementing best practices** – evidence-based and more holistic, patient-centered care
2. **Addressing care inequities –** especially among populations with overlapping identities
3. **Intentional research** – two components:
   - ➢ Historic overreliance on male clinical research participants left significant gaps regarding female-specific disorders and diseases more common in women
   - ➢ Despite Sex As a Biological Variable (SABV) policy, gaps remain in basic and translational understanding of sex differences



https://orwh.od.nih.gov/about/newsroom/events/55th-meeting-advisory-committee-research-womens-healthconsensus-conference

November 13, 2023



Section 1. Policy. “Women make up half of the United States population, but for too long, a lack of timely research and data on women’s health has left health care providers without important tools to diagnose and treat millions of women with debilitating conditions….”

https://www.whitehouse.gov/briefing-room/statements-releases/2023/11/13/fact-sheet-president-joe-biden-to-announce-first-ever-white-house-initiative-on-womens-health-research-an-effort-led-by-first-lady-jill-biden-and-the-white-house-gender-policy-council/

Section 2. Establishment.
There is established, within the Office of the First Lady, a White House Initiative on Women's Health Research (Initiative).

Section 3: Membership.
The Initiative shall be led by a Chair designated by the President who shall hold a dual role in the Office of the First Lady and on the staff of the White House Gender Policy Council.

Section 4: Mission and Functions. The mission of the Initiative is to advance women's health research in U.S.

Section 5: Recommendations to the President. Within 45 days of the date of this memorandum, the members of the Initiative or their designees shall provide recommendations to the President, through the Chair, on concrete actions that agencies and offices can take to advance women's health research.