

Research Gaps and Opportunities to Advance Women's Health

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Research Gaps and Opportunities to Advance Women's Health



- Lack of research on diseases affecting women and girls.
- Limited understanding of biological differences between sexes.
- Need for better ways to prevent, diagnose, and treat conditions that impact women differently.
- Investing in research benefits both women's health and society as a whole

Committee

Sheila P. Burke (Cochair)

Baker Donelson and John F. Kennedy
School of Government, Harvard
University

Alina Salganicoff (Cochair)

KFF

Neelum T. Aggarwal

Rush University Medical Center

Veronica Barcelona

Columbia University School of
Nursing

Alyssa M. Bilinski

Brown University School of Public
Health

Chloe E. Bird

Tufts Medical Center and RAND
Corporation

Susan Cheng

Cedars-Sinai Medical Center

Felina Cordova-Marks

University of Arizona College of
Public Health

Sherita H. Golden

Johns Hopkins University School of
Medicine

Holly A. Ingraham

University of California—San
Francisco School of Medicine

Robert M. Kaplan

Stanford University School of
Medicine

Nancy E. Lane

University of California, Davis Health
System

Jane E. Salmon

Hospital for Special Surgery and Weill
Cornell Medicine

Crystal Schiller

University of North Carolina at Chapel
Hill School of Medicine

Angeles Alvarez Secord

Duke University Health System

Methodius G. Tuuli

Brown University Warren Alpert Medical
School and Women & Infants Hospital

Bianca D.M. Wilson

University of California, Los Angeles
and California Center for Population
Research

NAM FELLOWS**Michelle P. Debbink**

University of Utah

Tracy E. Madsen

Brown University School of Public
Health

Background

- The U.S. leads the world in medical research, but breakthroughs in women's health are lacking.
- Basic differences between male and female biology are not well understood.
- Research on female-specific and common women's health conditions is underfunded.
- Advancing women's health research benefits overall scientific progress.

The Need for Women's Health Research



Healthy women are vital to a healthy society and growing economy.

- Women live longer than men but often have poorer health and more disabilities.
- Women's exclusion from research has created lasting gaps in health knowledge.
- Many barriers, such as finances, location, discrimination, and education, limit women's access to care.
- Advancing women's health benefits everyone's understanding of health.

Identifying Gaps and Opportunities in Women's Health Research



Information gathering meetings where the committee heard from researchers, patients, and other stakeholders



Review of primarily literature, past National Academies and other reports



Analysis of women's health research funding at the National Institutes of Health

“The gaps in women’s health research are large and at times feel overwhelming. My personal experiences are exacerbated by the frustrations of not being able to help my patients in more meaningful ways, by witnessing my peers and their daughter(s) suffering from so many gynecological conditions that remain with the same ineffective treatments that I offered to patients as an OB/GYN resident over 30 years ago.”

- PARTICIPANT AT COMMITTEE INFORMATION-GATHERING MEETING

Committee's Funding Analysis: Committee's approach to assess women's health research funding at NIH.

- The Research, Condition, and Disease Categorization (RCDC) system has several limitations.
- Instead of relying on RCDC, we analyzed NIH RePORTER data from 2013 to 2023 using multiple methods, including LLM. In April 2024, we downloaded over 800,000 grants.
- We only had access to publicly available grant data, such as titles, numbers, PI names, funding details, abstracts, and public health relevance—excluding grant proposals and progress reports.
- We examined overall funding by institutes, centers, offices, grant type, and women's health-related conditions.

Committee's Funding Analysis: NIH Spending on Women's Health Research

- Women's health research received 8.8% of NIH grants (2013-2023) and 7.9% in 2023
- Intramural research funding for women's health also remains low.

NIH Spending on Women's Health Research is a Small Fraction of Overall Grant Spending

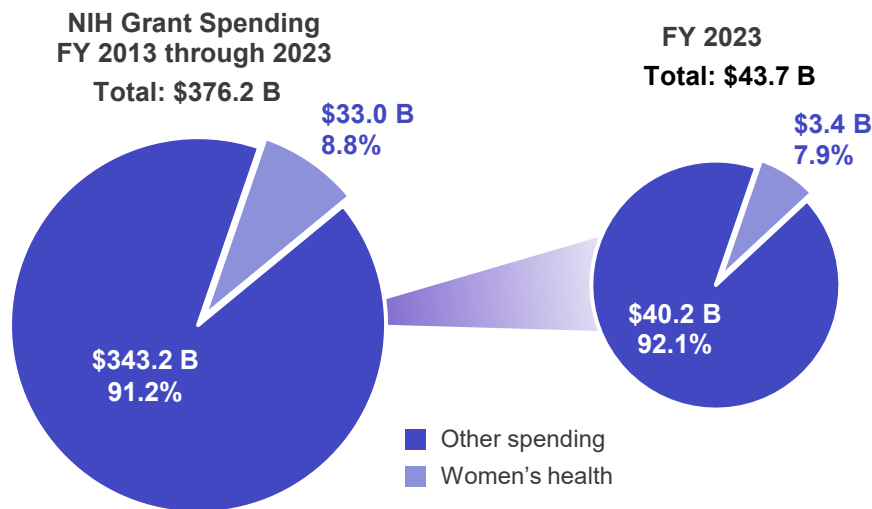


FIGURE. Total NIH grant funding on women's health research, FY 2013–2023 and for FY 2023.

SOURCE: Committee analysis.

Committee's Funding Analysis: Distribution of NIH Funding for Women's Health

- **Grants funded to study conditions relevant to women's health favored certain conditions.**
 - Top 10: breast cancer and some female-specific cancers, pregnancy and infertility, and perimenopause and menopause, as well as conditions that also affect men, such as HIV/AIDS, diabetes, and depressive disorders.
- **Low levels of funding for many female-specific conditions.**
 - Endometriosis, fibroids, pelvic floor disorders, polycystic ovary syndrome, postpartum depression, uterine cancer, vulvodynia, and others.
 - Yearly funding has been flat over the last decade for many of these conditions.

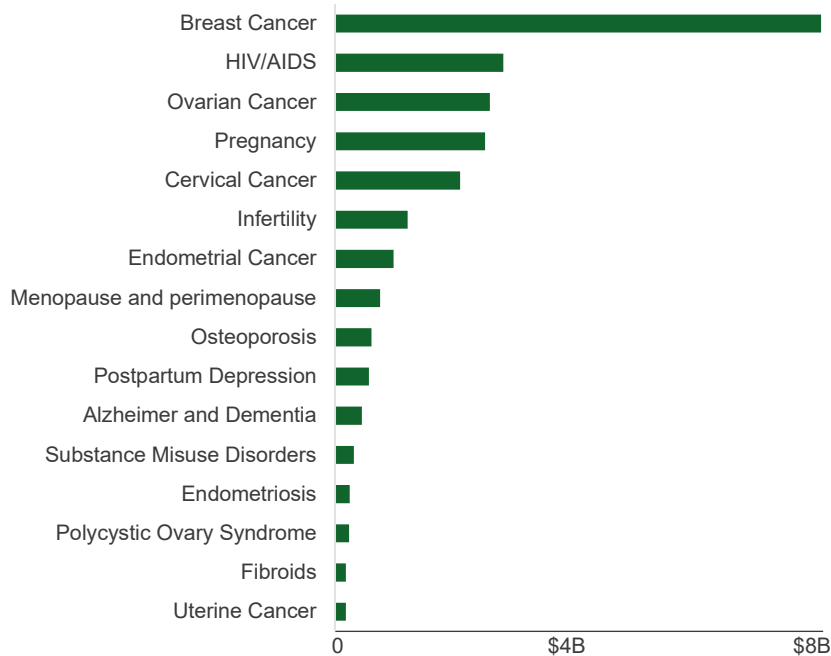


FIGURE NIH grant funding for select conditions relevant to women's health, FY 2013–FY 2023.
SOURCE: Committee funding analysis.

Examples of Increasing Prioritization of Low-Funded Women's Health Conditions

RADx® Tech ACT Endo Challenge

- Launched in August 2024
- Collaboration between the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) and the National Institute of Biomedical Imaging and Bioengineering (NIBIB)
- Focus on advancing non-invasive diagnostics for endometriosis

Specialized Centers for Research on Health Disparities in Uterine Leiomyoma

- In June 2024, NICHD and the NIH Office of Research on Women's Health (ORWH) announced the awarding of funds for two of these centers
- Represents a \$15 million investment in the advancement of research on uterine fibroids

Committee's Funding Analysis: Distribution of NIH Funding for Women's Health

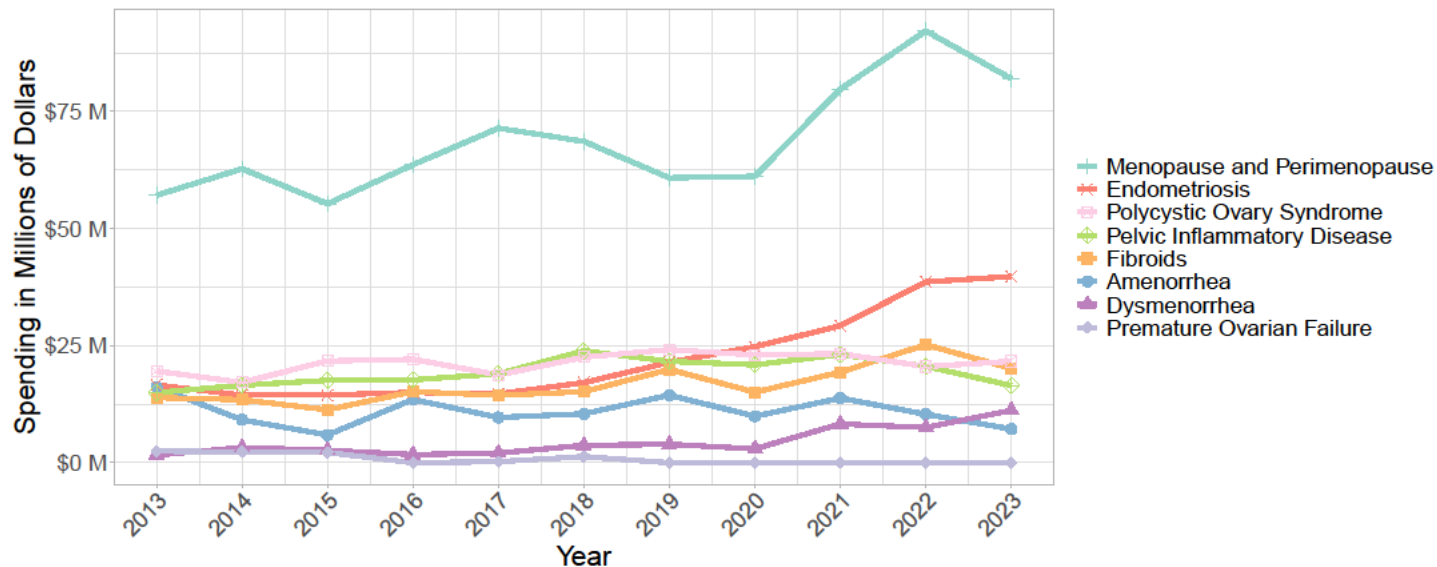


FIGURE. NIH grant funding for women's health research, FY 2013 through 2023, for select female-specific health conditions.
SOURCE: Committee analysis.

Committee's Funding Analysis: Distribution of NIH Funding for Women's Health

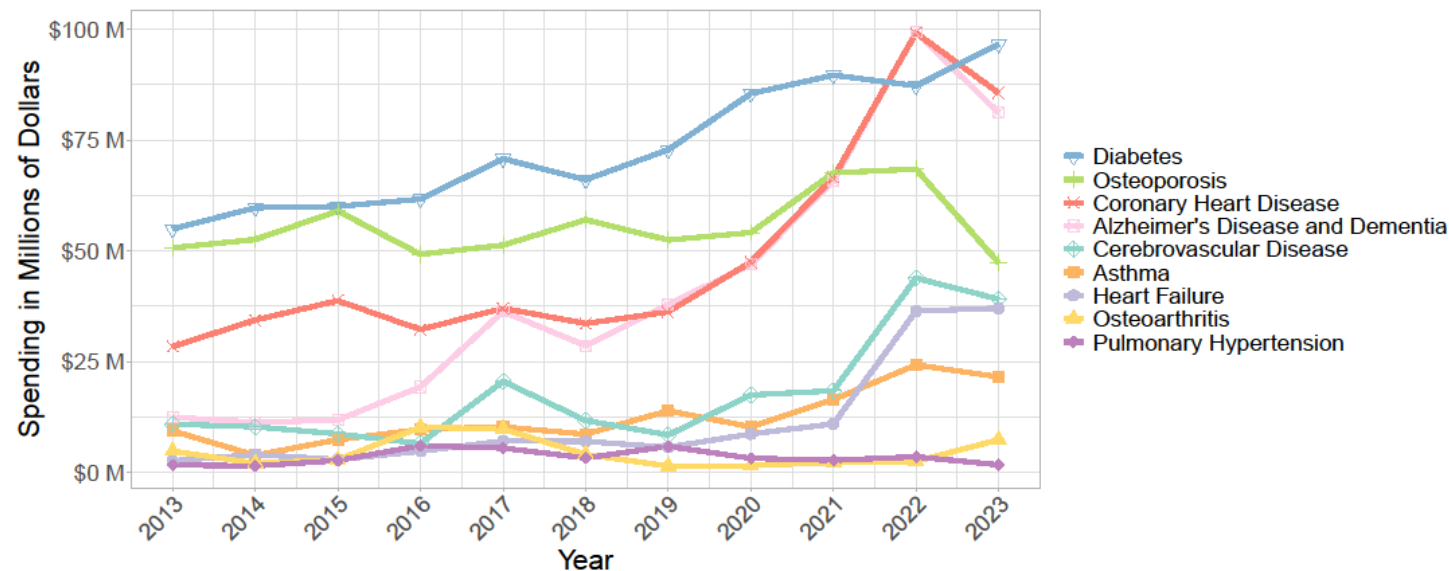


FIGURE. NIH grant funding for women's health research, FY 2013 through 2023, for prevalent chronic diseases.

SOURCE: Committee analysis.

Gaps and Opportunities in Women's Health Research



Priorities for Advancing Women's Health Research

Recommendation 8 describes areas for prioritization needed to advance WHR across the research spectrum, specifically in basic, preclinical, clinical, population, and implementation science research.

- Considerations across the research continuum include:
 - Quality of Life: Address conditions like depression, endometriosis, fibroids, IBS, osteoarthritis, osteoporosis, and PCOS.
 - Early Mortality: Focus on CVD and female-specific cancers.

Priorities in Women's Health Research

Basic Research

- Study hormonal profiles and female physiology to understand sex-based differences in disease risk, pathology, and progression.

Preclinical & Clinical Research

- Investigate causes of female-specific and gynecologic chronic conditions.
- Collect and analyze sex- and gender-specific data to improve treatment efficacy and assess side effects.

Priorities in Women's Health Research

Population Research

- Population-level research that studies how policies at the system, payor, local, state and national levels affect women's health

Implementation Science Research

- Implementation science research that develops and tests strategies for implementing innovative health care services delivery approaches

Sex as a Biological Variable (SABV)

Why It Matters

- Many studies overlook sex and gender differences, limiting insights.
- Most health research is based on male physiology due to historical exclusion of women in clinical trials.

NIH SABV Policy (2016)

- Requires inclusion of both sexes in studies (unless justified otherwise).
- Mandates consideration of biological sex in study design, analysis, and reporting.

Impact

- Leads to discoveries that improve understanding of sex-based differences (e.g., drug metabolism, treatment responses).

Challenges & Benefits of SABV Implementation

Key Considerations

- Overall uptake and application of SABV policy in practice has not been optimal.
- Although there are limitations for broad implementation, the benefits of incorporating SABV in research far outweigh the challenges researchers may face.

Sample Size & Cost

- Some researchers assume larger sample sizes increase costs, but often, only minimal changes are needed.
- Incorporating SABV can reduce the need for follow-up studies, improving efficiency and scientific impact.

Basic Science Implications

- Inclusion of heterogeneous female models (e.g., intact ovaries, ovariectomized, older females) may require tailored cohort sizes and increased funding.
- Highlights the need for NIH funding to support sex-diverse research.

SABV vs. Sex Differences Research



Key Differences

- **SABV:** Requires considering sex as a variable in NIH-funded studies but does not replace dedicated sex differences research.
- **Sex Differences Research:** Focuses on identifying sex-based variations in conditions or treatments, often requiring larger sample sizes and funding.

Why It Matters

- Integrating sex into study design enhances findings that benefit both sexes.
- True sex differences research assesses biological mechanisms driving differences.

More Info

- A 2-pager on SABV is available on the project [website](#)

Gaps and Opportunities in Women's Health Research



Chromosomes & Women's Health: Gaps & Opportunities

X vs. Y Chromosome Research

- Females (XX) silence one X chromosome to prevent excess gene expression.
- Research has mainly focused on the Y chromosome, leaving X-silencing effects on women's health understudied.

Genome-Wide Association Studies (GWAS)

- GWAS helps identify genetic disease markers but often **excludes sex chromosomes**, limiting insights into sex-specific health risks.

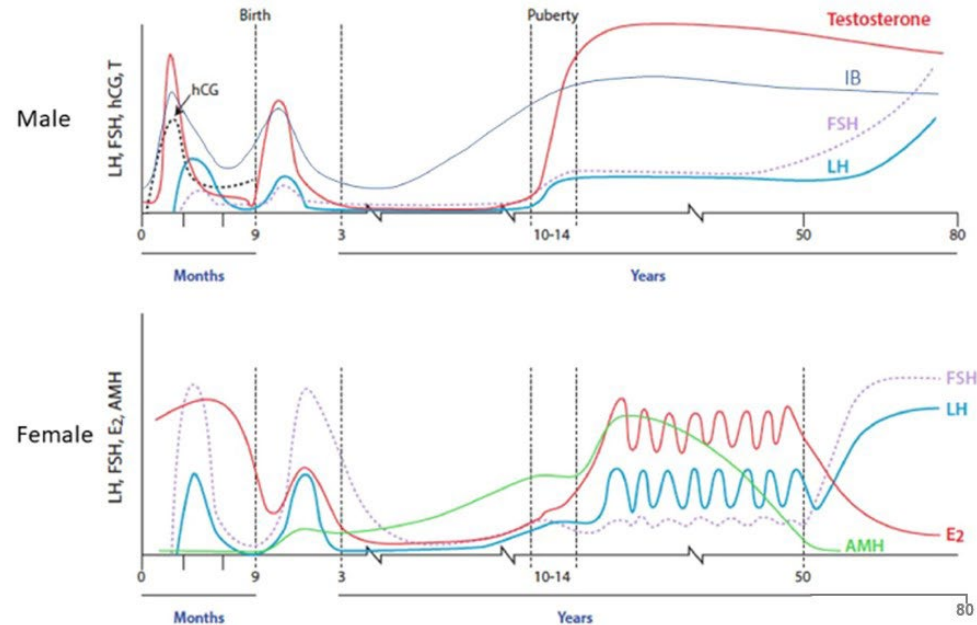
Gaps and Opportunities in Women's Health Research: Chromosomes and Health

Key Findings

- A protein linked to **X-silencing** interacts with other proteins, contributing to autoimmune diseases more common in women (Dou et al., 2024).
- Highlights the role of **basic science** in explaining why **women are disproportionately affected** by autoimmune disorders.
- Understanding **X-linked proteins** may lead to breakthroughs in other conditions.

Gaps and Opportunities in Women's Health Research: Female Sex Hormones

- Female physiology is more dynamic due to hormone fluctuations throughout the reproductive life-span.



Female Sex Hormones: Gaps & Opportunities

Why It Matters

- Hormonal complexity has led to the exclusion of women from studies, yet understanding it is crucial for **women's physical & mental health**.
- **All organ systems** have receptors for ovarian sex hormones, influencing overall physiology.

Key Examples

- **Menopause:** Declining estrogen levels cause **hot flashes, bone loss, insomnia, depression, vaginal atrophy, and weight gain**.
- **Depression:** Ovarian hormones play a key role in regulating mood during reproductive years.

Physical Health Conditions: Gaps & Opportunities

Cardiometabolic Disease

- Links exist between **sex hormones & cardiometabolic disease**, but mechanisms remain unclear, limiting treatment insights.

Fibroids

- Leading cause of **hysterectomy in the U.S.**, yet little is known about their pathophysiology.
- **Research gaps and Opportunities:**
 - Focus has been on **estrogen's role**, with limited study of other hormonal and non-hormonal factors.
 - Unclear why **fibroids are more prevalent in Black females**.

Endometriosis: Gaps & Opportunities

Uncertainties & Barriers

- **Cause, risk factors, and true prevalence** remain unclear.
- **No nonsurgical diagnostic method** exists.

Treatment Challenges & Opportunities

- **Hysterectomy & hormonal treatments** can impact fertility.
- **Increases risk** of ovarian cancer & chronic pain conditions (e.g., IBS).
- **More research needed** on fertility-preserving treatments & pathophysiology.

Polycystic Ovary Syndrome (PCOS): Gaps & Opportunities

Health Impacts

- Most common **endocrine disorder in women** and a leading cause of infertility.
- Linked to **CVD, Type 2 diabetes, fatty liver disease, endometrial hyperplasia, and cancer**, often influenced by body fat levels.

Key Research Opportunities

- **No cure & no FDA-approved therapies.**
- Need to explore **genetic, epigenetic, and environmental factors.**
- Assess **long-term cardiovascular, metabolic, and cognitive risks.**
- Develop **mitigation & curative strategies.**

Mental Health & Women's Hormones: Gaps & Insights

Hormonal Influence on the Brain

- **Estrogen receptors** are widespread in neuronal & non-neuronal brain cells (e.g., microglia, astrocytes).
- **Rodent models** show ovarian steroids affect brain activity & behaviors (e.g., feeding, mating, maternal instincts).

Key Research Opportunity

- **Unclear why** hormonal fluctuations contribute to **female-specific affective disorders** across life stages.

Pubertal Depression: Gaps & Insights

Increased Risk in Women

- Depression risk rises at **mid-puberty** and persists throughout reproductive years.

Key Research Opportunities

- **Ovarian steroids** may play a role, but findings are mostly **correlational**.
- **Few preclinical models** exist to study neuroendocrine mechanisms.

Premenstrual Dysphoric Disorder (PMDD): Gaps & Insights

Impact of Hormonal Changes

- Can trigger **mood & behavior changes** (e.g., impulsivity, irritability, anxiety, sadness).
- **Sex steroids** alter gene expression & brain blood flow, contributing to symptoms.

Key Research Opportunities

- **Why some women** experience epigenetic changes from estradiol & progesterone is unknown.
- **Need for better diagnosis & clinical management.**
- PMDD **excludes cases of premenstrual exacerbation** of chronic depression, despite similar symptom severity.

Perinatal Depression (PND): Research Opportunities

What It Is

- A major depressive disorder occurring **during pregnancy or within 3 months postpartum**.

Key Research Opportunity

- Research on the **complex & multifactorial causes** to identify clear biological pathways.
- Identify ways to **prevent** PND and **increase access** to existing treatments.

Menopause and Cognition: Research Opportunities

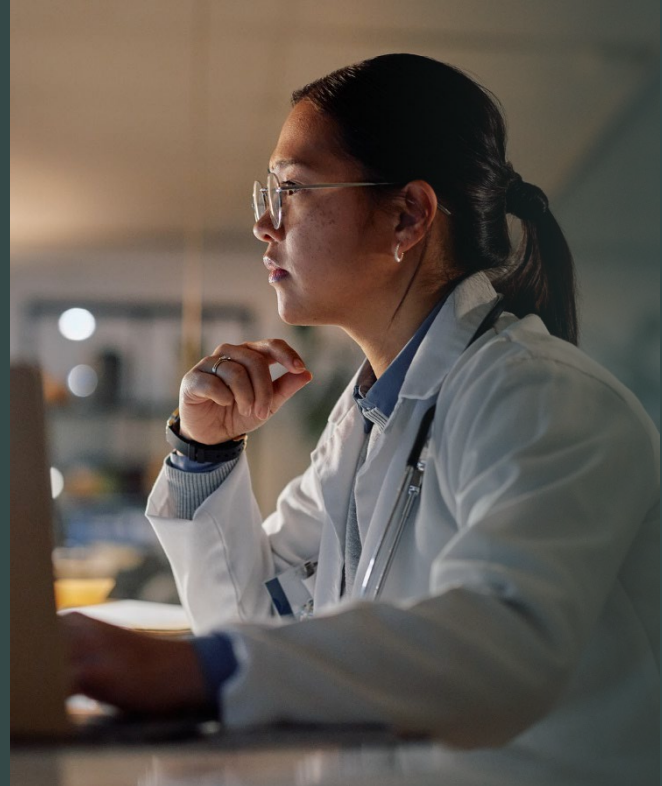
Cognitive Changes During Menopause:

- Many women experience memory lapses, difficulty concentrating, and "brain fog" during menopause.
- These cognitive changes can affect daily functioning and overall well-being.

Research Gaps and Opportunities:

- The biological mechanisms linking menopause to cognitive decline are not fully understood.
- Historically, women have been underrepresented in cognitive health research, leading to gaps in knowledge.
- Promote studies aimed at developing strategies to mitigate cognitive decline during menopause.

Expanding, Training, Supporting, and Retaining the Women's Health Research Workforce



NIH Workforce Programs in Women's Health Research

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

- **Objective:** Trains early-career faculty to develop research skills in **women's health & sex differences**.
- **Key Benefits:**
 - Provides **protected time** for research, writing, and securing peer-reviewed funding.
 - Encourages **collaboration across disciplines** to advance women's health research.
 - Supports career development through **mentorship & networking**.

Women's Reproductive Health Research (WRHR)

- **Objective:** Enhances research capabilities of **newly trained OB/GYNs**.
- **Key Benefits:**
 - Offers **state-of-the-art education & hands-on experience** in reproductive health research.
 - Covers **basic science, translational, and clinical research**.
 - Prepares researchers for **independent funding & leadership roles** in women's health.

NIH Workforce Programs in Women's Health Research

Research Scientist Development Program (RSDP)

- **Objective:** Trains **reproductive physician-scientists** in cutting-edge **cell & molecular technologies** to address key issues in obstetrics and gynecology.
- **Key Benefits:**
 - Focus on **basic science skill development** for early-career faculty.
 - Provides **mentored research opportunities** to advance independent careers.
 - Encourages **innovation in reproductive health research**.

Specialized Centers of Research Excellence (SCORE) on Sex Differences

- **Objective:** NIH-funded **national research hubs** for sex and gender studies.
- **Key Benefits:**
 - **Facilitates collaboration** between academia, private industry, & federal agencies.
 - Enhances research on **biological sex differences** in women's health.
 - Supports **multidisciplinary & translational research** to address complex health disparities.

Conclusions & Future Directions

Key Gaps in Women's Health Research

- **Limited understanding** of basic female physiology.
- **Understudied conditions** that affect women disproportionately or differently than men.

Opportunities for Advancement

- Research can drive **better prevention, diagnosis, & treatment**.
- Potential breakthroughs will **benefit both women's health & society overall**.

The Role of Workforce Programs

- Programs like **BIRCWH, SCORE, WRHR, & RSDP** have successfully supported women's health researchers.
- **NIH should expand initiatives** to further prioritize women's health research.

To access the report and supporting materials, visit

www.nationalacademies.org/womens-health-research

For more information, contact:

Amy Geller, Study Director

WomensHealthResearch@nas.edu



Backup Slides

The Committee's Recommendation on Women's Health Research Workforce Programs

NIH should augment existing programs and develop new grant initiatives specifically designed to promote interdisciplinary science and career development in areas related to women's health. NIH should:

- Expand the **Building Interdisciplinary Research Careers in Women's Health (BIRCWH)** program to 40 centers over 5 years; increase funding to \$1.5 million annually per center,
- Expand the **Specialized Centers of Research Excellence (SCORE) on Sex Differences** to 17 centers over the next 5 years; increase funding to \$2.5 million annually per center,
- Fund additional **multi-project program grants**, with or without built-in training components, that focus on women's health research (e.g., P and U grants),
- Expand the **Women's Reproductive Health Research (WRHR)** program to 20 centers over 2 years; increase funding to \$500,000 annually per center, and
- Expand the **Research Scientist Development Program (RSDP)** to support 10 scholars with full support for 5 years at \$1.25 million annually.