



Chronic Conditions in Women: Perspectives Across the Life Course

Integrating Sex-Related Factors in the Development of Chronic and Multiple Chronic Conditions in Women

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Director, Office of Research on Women's Health
Bethesda, Md.

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1130 - 1230 ET





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

Presenter

Dr. Janine Austin Clayton, M.D., FARVO



Janine Austin Clayton, M.D., FARVO Associate Director for Research on Women's Health and Director of the Office of Research on Women's Health (ORWH) at the National Institutes of Health (NIH), is the architect of the NIH policy requiring scientists to consider sex as a biological variable across the research spectrum. This policy is part of NIH's initiative to enhance reproducibility through rigor and transparency. In 2021, Dr. Clayton was elected to the Board of Directors of the American Association for the Advancement of Science (AAAS). In 2024, Dr. Clayton was elected to become a member of the National Academy of Medicine (NAM).

Prior to joining the ORWH, Dr. Clayton was the Deputy Clinical Director of the National Eye Institute (NEI) for seven years. A board-certified ophthalmologist, Dr. Clayton's research interests include autoimmune ocular diseases and sex influences on health and disease. She is the author of more than 120 scientific publications, journal articles, and book chapters.

Dr. Clayton has received numerous awards, including the Senior Achievement Award from the Board of Trustees of the American Academy of Ophthalmology, and was named a Fellow of the Association for Research in Vision and Ophthalmology (FARVO). Dr. Clayton received the AMA Nathan Davis award for Outstanding Government Service in 2017. In 2021, Dr. Clayton was elected to the Board of Directors of the American Association for the Advancement of Science (AAAS). In 2023, Dr. Clayton received the American Medical Women's Association AMWA Presidential Award. In 2024, Dr. Clayton received the Society for Women's Health Research *Health Public Service Visionary Award* and was recognized as a Precision Medicine World Conference (PMWC) Luminary Honoree.



Disclosures

- Dr. Janine Austin Clayton has no relevant financial or non-financial relationships to disclose relating to the content of this activity.
- The views expressed in this presentation are those of Dr. Clayton and do not necessarily reflect the official policy or position of the Department of War, nor the U.S. Government.
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- Commercial support was not received for this activity.



Learning Modules



1

Opening
Remarks

2

Chronic
Conditions

3

Multimorbidity

4

NIH/ORWH
Research

5

Closing



Learning Objectives



At the conclusion of this activity, participants will be able to:

- 1 Summarize how ORWH supports biomedical research and its translation into primary care settings across the life course of women.
- 2 Compare how sex differences affect women's experiences with chronic and multiple chronic conditions.
- 3 Characterize women's health experiences across the life course: early adult, midlife, and mature adulthood.

Module 1: Opening Remarks



Key National Milestones for Women's Health Research (1 of 3)

1986



INCLUSION OF WOMEN IN STUDY POPULATIONS
P.T. 34; K.W. 0770000, 1014002
National Institutes of Health

Encourages Inclusion of Women in Clinical Trials

S.1 - National Institutes of Health Revitalization Act of 1993
Subtitle B--Clinical Research Equity Regarding Women and Minorities

PART I--WOMEN AND MINORITIES AS SUBJECTS IN CLINICAL RESEARCH

SEC. 131. REQUIREMENT OF INCLUSION IN RESEARCH.

Part G of title IV of the Public Health Service Act, as amended by section 101 of this Act, is amended by inserting after section 492A the following section:

INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH

1993



Advisory Committee on Research on Women's Health (ACRWH)
Coordinating Committee on Research on Women's Health (CCRWH)



Ensures women are included in NIH-funded clinical research

2016



Consideration of Sex as a Biological Variable in NIH-funded Research

Notice Number: NOT-OD-15-102

Key Dates

Release Date: June 9, 2015

Requires NIH-funded research to account for Sex as a Biological Variable (SABV)

SABV as part of study design

21st Century Cures Act

Public Law 114-255
114th Congress

An Act

To accelerate the discovery, development, and delivery of 21st century cures, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE; TABLE OF CONTENTS.

(a) SHORT TITLE.—This Act may be cited as the “21st Century Cures Act”.

2019



Updated guidelines to reflect individuals of all ages

2023



Establishment of OADR-ORWH

Amplify advancement of research for these conditions

(NIH, 2015)

(NIH, 1993.)

(<https://www.congress.gov/114/plaws/publ255/PLAW-114publ255.pdf>)



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Office of Research on Women's Health

Key National Milestones for Women's Health Research (2 of 3)

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(<https://www.congress.gov/bill/114th-congress/house-bill/34>)



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

Key National Milestones for Women's Health Research (3 of 3)

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Amplify advancement of research for these conditions

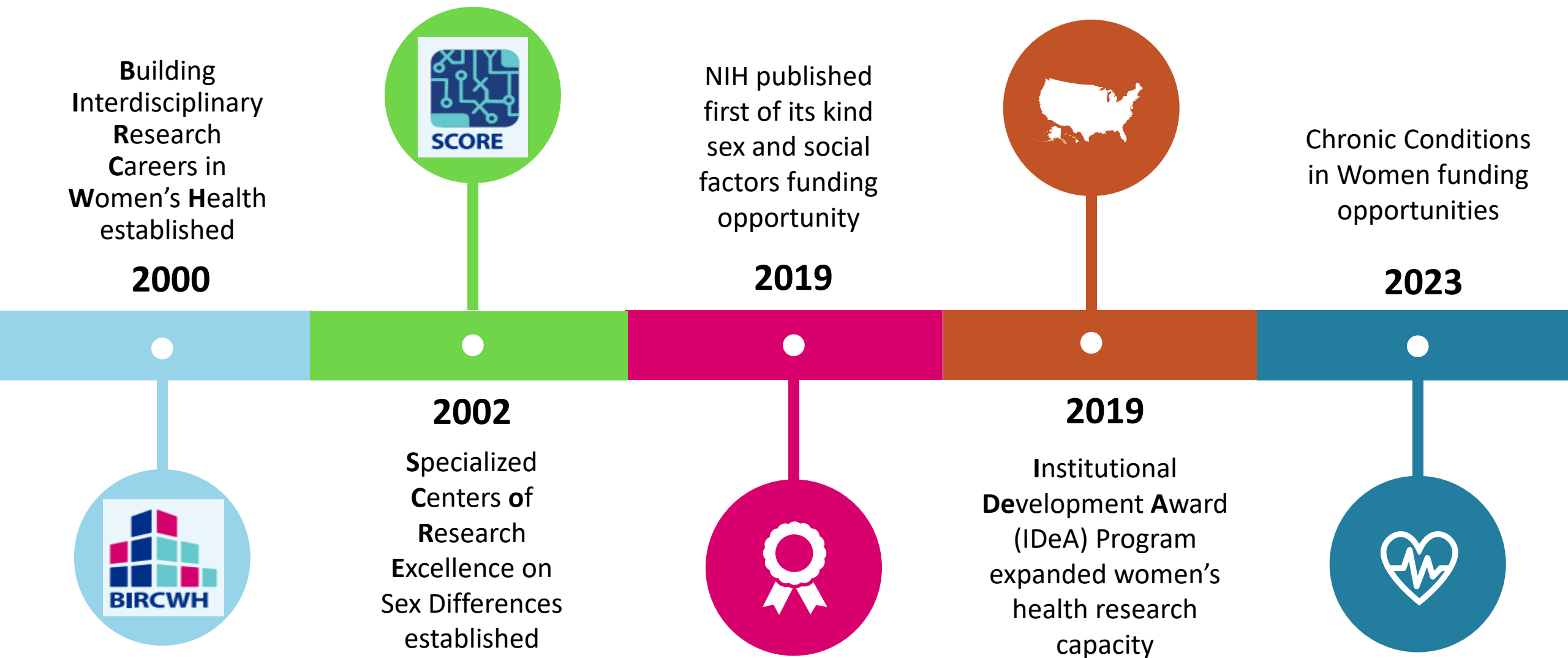
(NIH, 2015)

(NIH, 1993.)

(<https://www.congress.gov/bill/114th-congress/house-bill/34>)



Shaping the Landscape of Women's Health Research



ORWH Mission



Enhance and expand women's health research



Ensure women are well-represented in clinical research



Promote career advancement for women's health researchers

NIH Vision



Sex as a biological variable integrated into health research



Every woman receives evidence-based care



Women in science careers reach their full potential



NIH Inclusion Policies Expand Over the Years



“Insights garnered from this expanded inclusion approach could enhance **reproducibility** and **generalizability** of clinical study findings.” ¹

1993 NIH Revitalization Act

- Requires researchers to **include women** in clinical studies

NIH Inclusion Policy

- Women and underrepresented racial and ethnic minorities
- **Valid analysis** for different outcomes for Phase III clinical trials

21st Century Cures Act

- Expanded inclusion to **individuals of all ages**
- Created path to include **pregnant women and lactating women**
- Requires NIH-defined applicable Phase III Clinical Trials to report **sex-specific** results in ClinicalTrials.gov

(Bernard, Clayton, and Lauer, 2018)
(Public Health Service Act, 2016)
(NIH, 2025c)



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

ORWH is the NIH Nexus for Women's Health Research

NIH-Wide Strategic Plan for Research on the Health of Women

NIH Priorities:

1. Reproducibility and Rigor
2. Solution-Oriented Approaches
3. Training Future Biomedical Scientists
4. Unified NIH Funding Strategy
5. Scientifically Valid and Measurable Health Outcomes

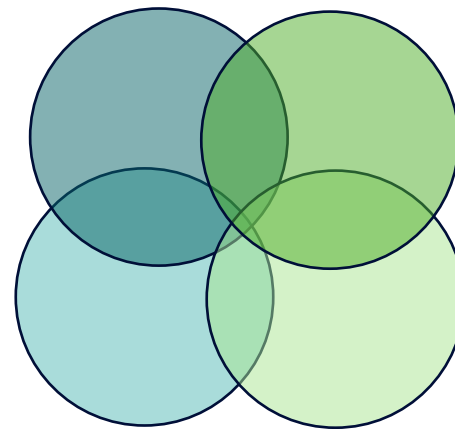
DPCPSI Priorities:

1. Transformative Science via Strategic Investments
2. Stronger Partnerships to Amplify NIH Mission
3. Data-driven Decision Making
4. Workforce Development and Programmatic Leadership
5. Accelerate Translation through Practical Solutions

NIH Institutes, Centers, & Offices

Impact

Synergy



Partnership

Innovation

Office of Research on Women's
Health

Driving NIH
Research Priorities

NIH-Wide Work
Groups

Strategic
Investments

Funding
Opportunities and
Initiatives

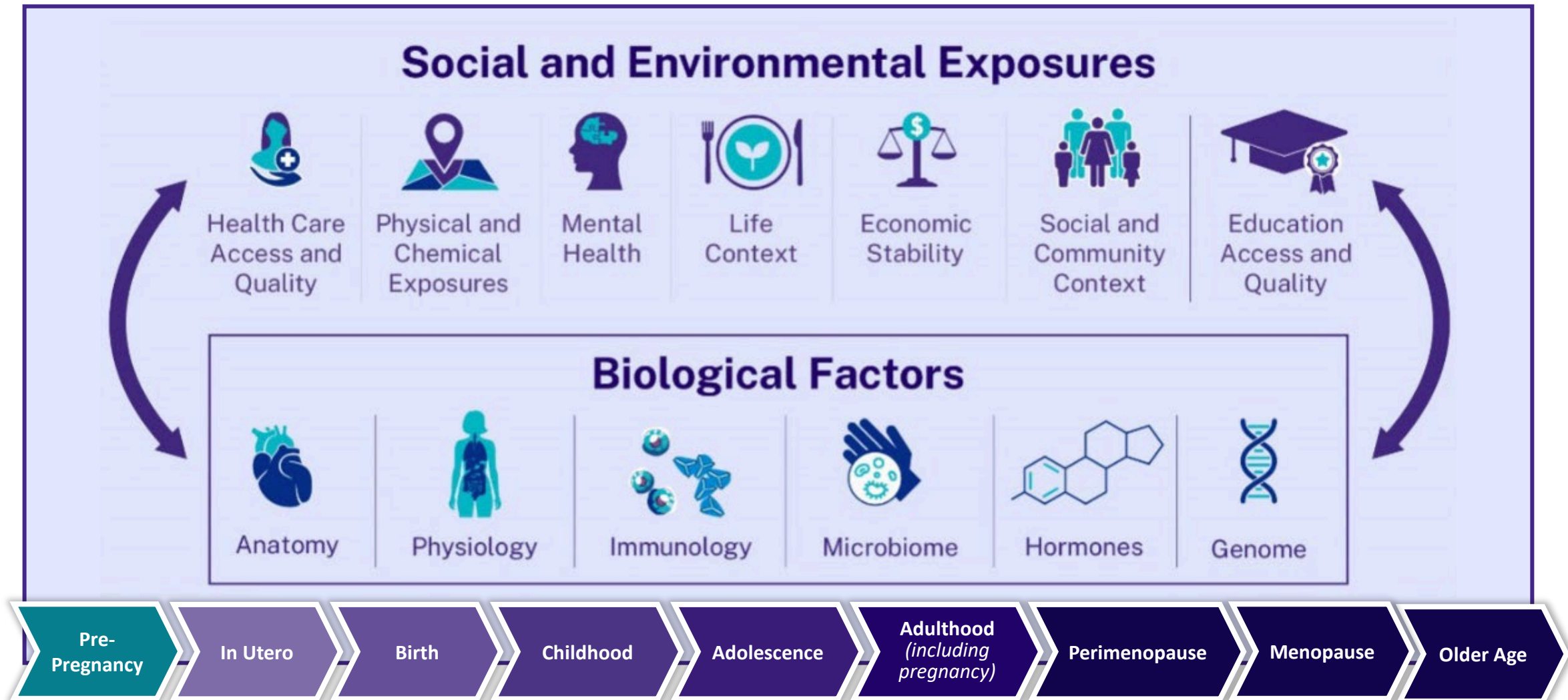
Workshops and
Meetings

N
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NIH Cross-Cutting Effort to Transform Women's Health Throughout the Life Course



(*Adapted from National Institutes of Health, Office of Research on Women's Health, 2024b)



The 4 Cs of Studying Sex to Strengthen Science



Consider

Design studies that take sex into account, or explain why it isn't incorporated



Collect

Tabulate sex-based data



Characterize

Analyze sex-based data



Communicate

Report and publish sex-based data

NIH Policy on **Consideration of Sex as a Biological Variable (SABV) in NIH-Funded Research**

“NIH expects that [SABV] 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.”



Effective 01/25/2016
SABV Policy Notice: NOT-OD-15-102

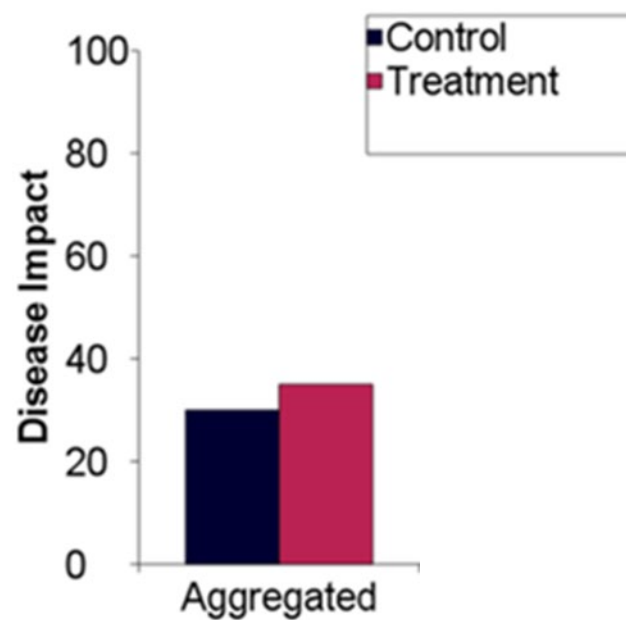


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Importance of Disaggregating Data by Sex

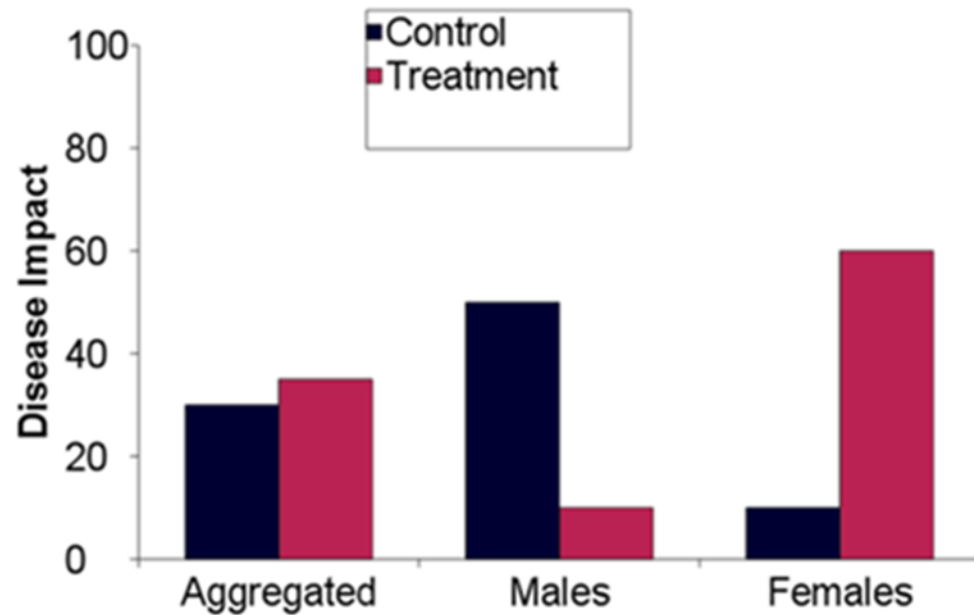
Example Scenario



Study results not disaggregated by sex

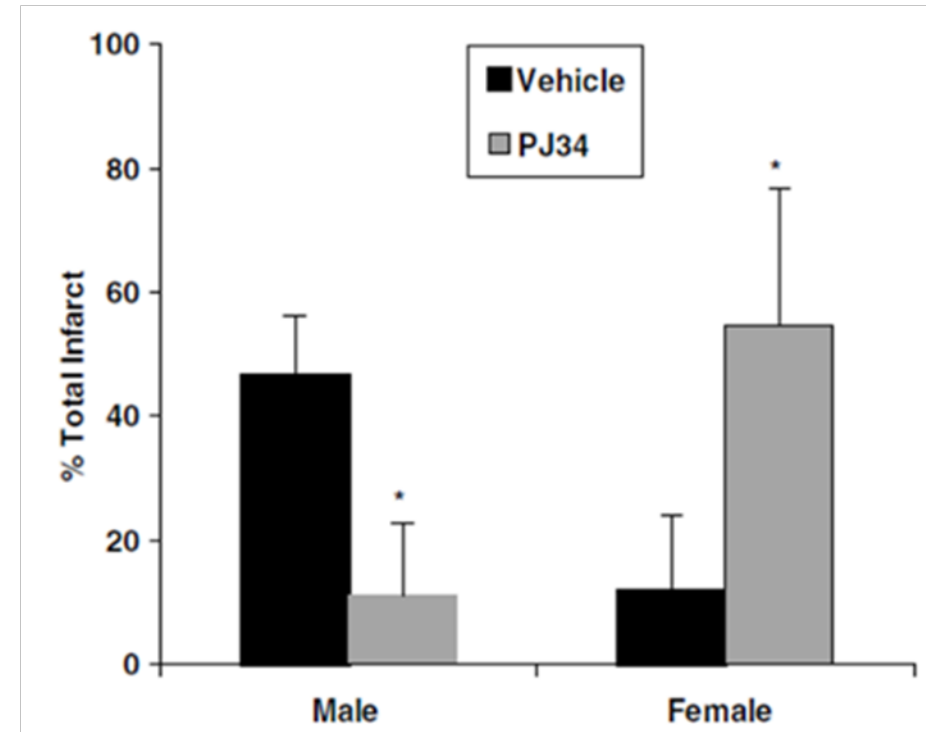
Disaggregating Results by Sex Reveals Stark Differences “Hiding in Plain Sight”

Example Scenario



Study produced novel findings due to disaggregating results by sex

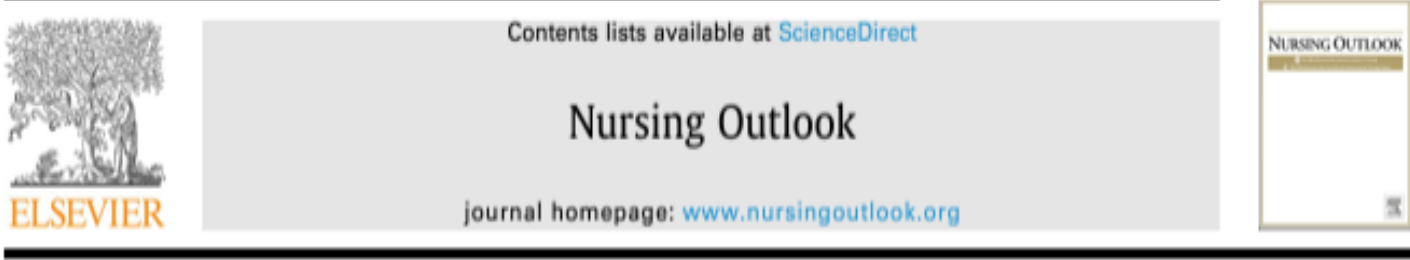
Ischemic Stroke Study Results



Reduced infarction
(obstruction of blood
supply)

Increased ischemic
(stroke) damage

Biological Sex Shapes Health and Disease Across the Life Course



The image shows the cover of the journal 'Nursing Outlook'. On the left is the Elsevier logo featuring a tree and a person. To its right, it says 'Contents lists available at ScienceDirect'. The journal title 'Nursing Outlook' is prominently displayed in the center. Below the title is the journal homepage URL: 'www.nursingoutlook.org'. On the right side of the cover is a small thumbnail of the journal's front cover. Below the journal cover information, the article title 'Ensuring accountability for consideration of sex as a biological variable in research' is shown. To the right of the title is a 'Check for updates' button. Below the title is a list of authors: Elizabeth A. Kostas-Polston, PhD, FAANP, FAAN^{a,*,1}, Margaret Bevans, PhD, RN, FAAN^{b,1}, Tamra L. Shea, PhD, RN, CNE^c, Kelly McGlothen-Bell, PhD, RN, FAWHONN^d, Mary A. Nies, PhD, FAAN, FAAHB^e, Ivy M. Alexander, PhD, FAANP, FAAN^f, Versie Johnson-Mallard, PhD, FAANP, FAAN^g, Janine Austin Clayton, MD, FARVO^h.

Ensuring accountability for consideration of sex as a biological variable in research

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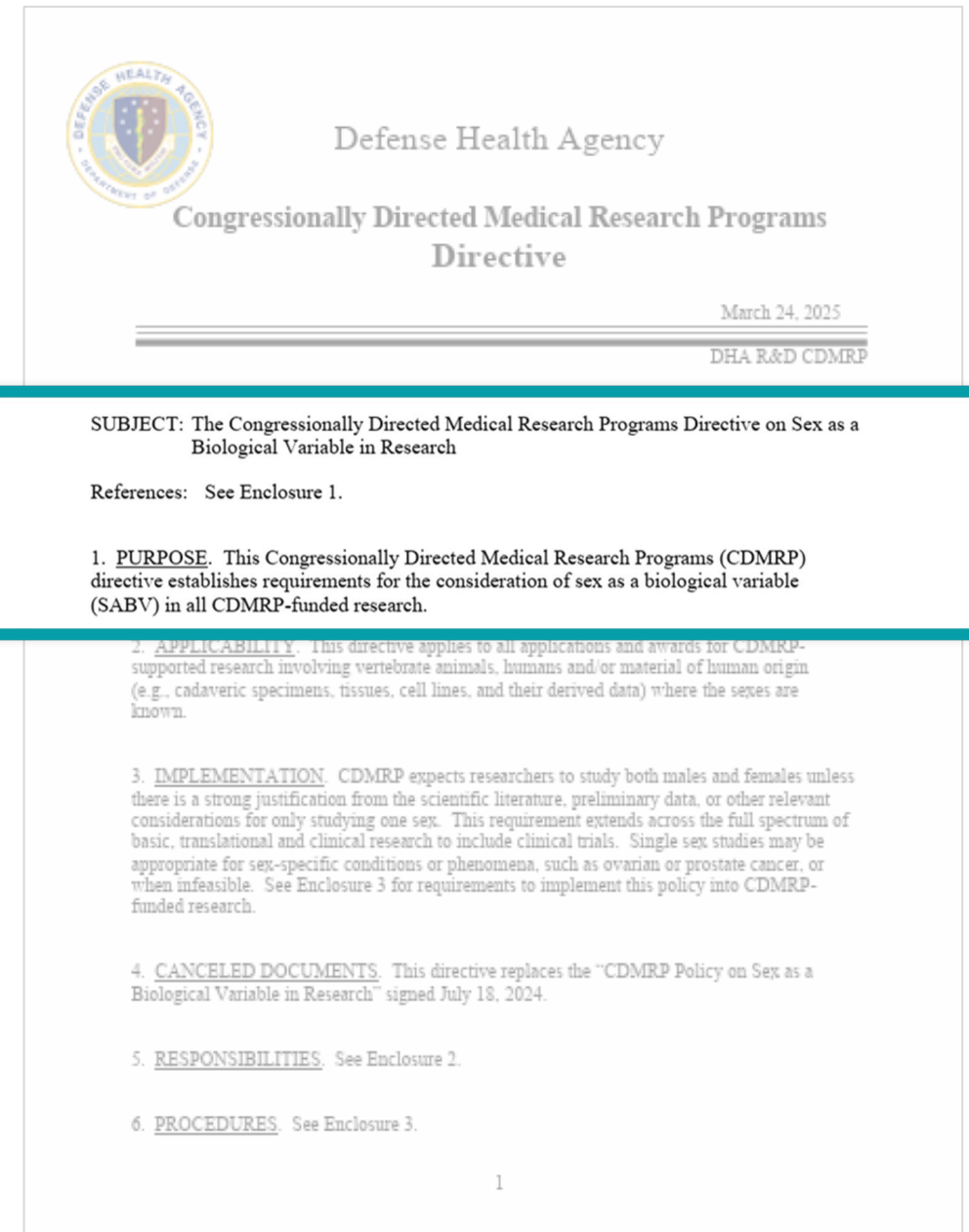
(Kostas-Polston, 2024)

ICMJE INTERNATIONAL COMMITTEE of
MEDICAL JOURNAL EDITORS

(<https://www.icmje.org/recommendations>, n.d.)/

Congressionally Directed Medical Research Programs Released Directive on Sex as A Biological Variable

- This Congressionally Directed Medical Research Programs (CDMRP) Directive establishes requirements for the consideration of **Sex as a Biological Variable** in all CDMRP-funded research
- Extends across the full spectrum of basic, translational, and clinical research to include clinical trials



ORWH Signature Programs Advance the Study of Women's Health



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

- BIRCWH is the ORWH signature career development effort, with **25 active programs** spanning **28 states** across **48 institutions**
- ORWH invested in **over 890 scholars**, with NIH's Institute, Center, or Offices (ICOs) contributing more than **\$15M** annually
- The Veterans Affairs (VA)-**BIRCWH** partnership launched its **inaugural cohort in FY26**, extending its reach to veteran populations



Specialized Centers of Research Excellence (SCORE) on Sex Differences

- Only NIH Centers program dedicated to **disease-agnostic** sex differences research
- **15 funded centers** with **8 ICOs** serving as national translational research hubs
- Each SCORE center includes basic, translational, clinical and career enhancement cores (CEC)

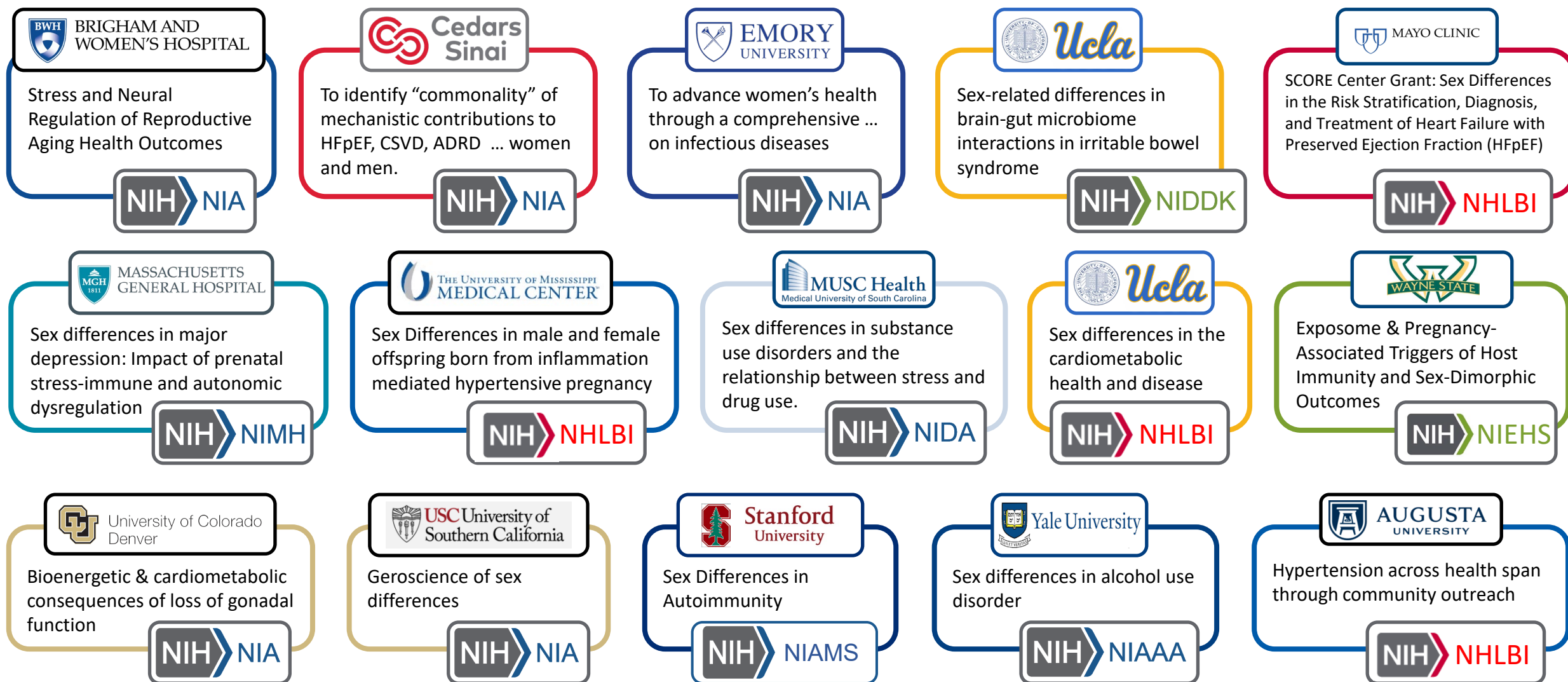


Women's Health Research in Institutional Development Award (IDeA) Programs

- Expands geographic reach and capacity building in states with historically low NIH funding
- Now active in **21 of 23 IDeA states plus Puerto Rico**
- Includes **90 administrative supplements** and **4 COBRE awards**
- **Every \$1 of NIH-funded research generates \$2.57 in local economic activity***

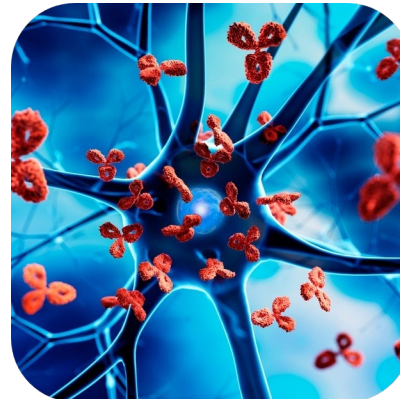
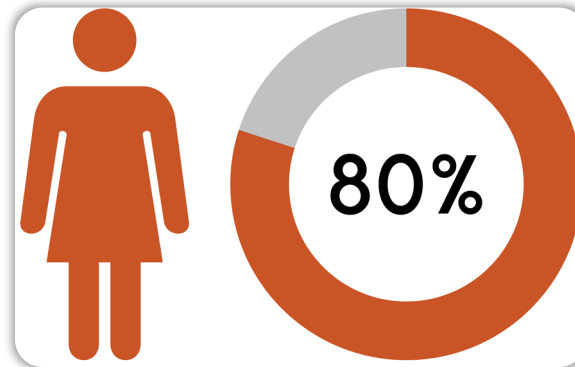


Current SCORE Programs Apply SABV to Broad Range of Topics



Office of Autoimmune Disease Research (OADR-ORWH)

8% of the U.S. Population is Living with an Autoimmune Disease, **80% are Women!**



Established in 2023, OADR-ORWH works to:

- Coordinate development of a multi-institute and center (IC) strategic research plan
- Identify emerging areas of innovation and research opportunity
- Coordinate and foster collaborative research across ICs
- Annually evaluate the NIH autoimmune disease research (ADR) portfolio
- Provide resources to support planning, collaboration, and innovation
- Develop a publicly accessible central repository for ADR

Access the full strategic plan online:

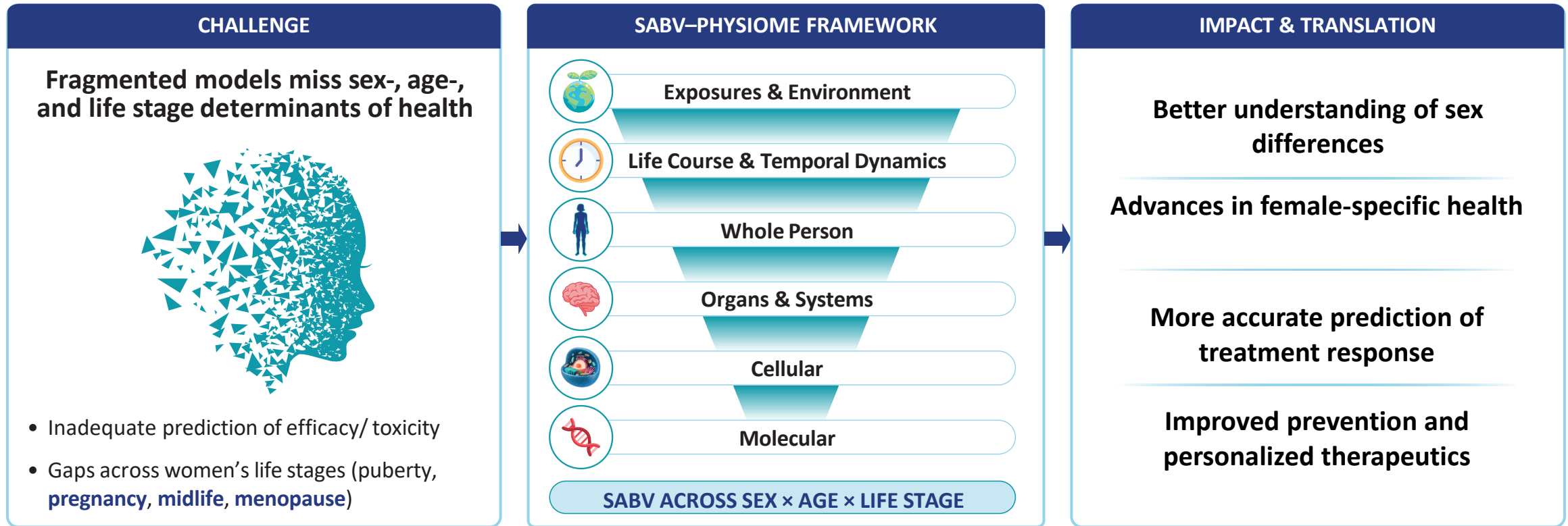
<https://orwh.od.nih.gov/OADR-ORWH/Strategic-Planning-for-ADR>

Module 2: Chronic Conditions



A Sex-Specific Whole Person Framework for Precision Therapeutics Across the Life Course

SEX AS A BIOLOGICAL VARIABLE (SABV) – INTEGRATED ACROSS ALL SCALES



**Life-stage
informed**



**Mechanistic &
predictive**



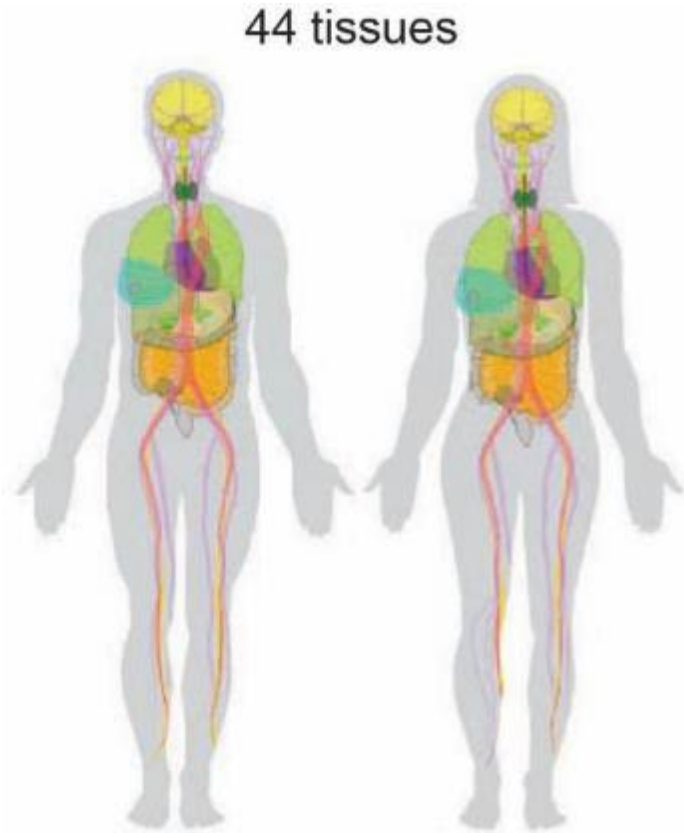
**Drug discovery
& safety**



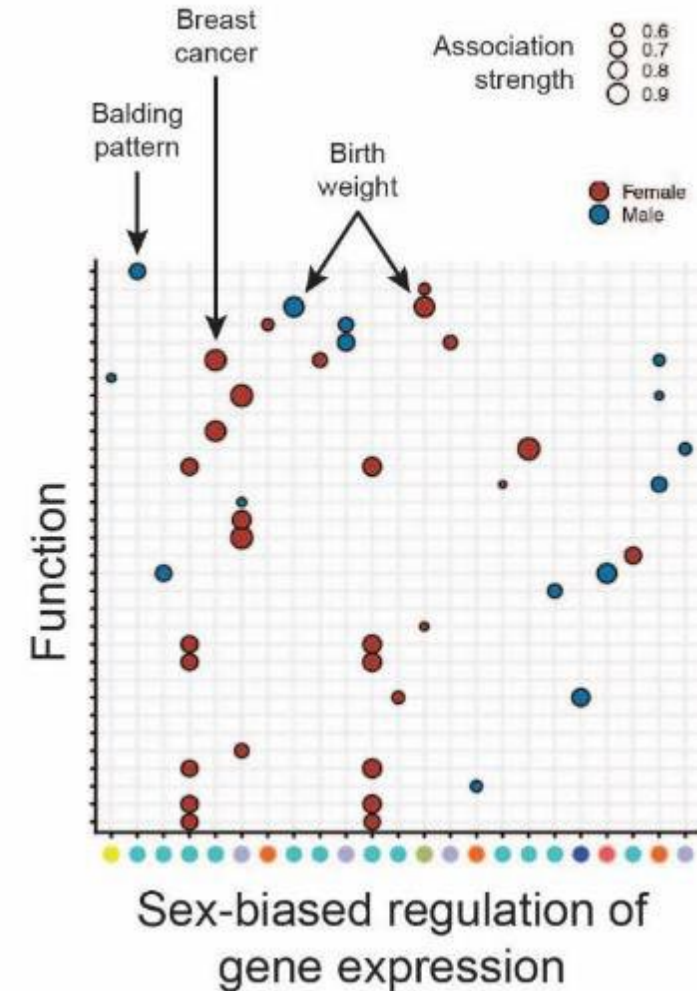
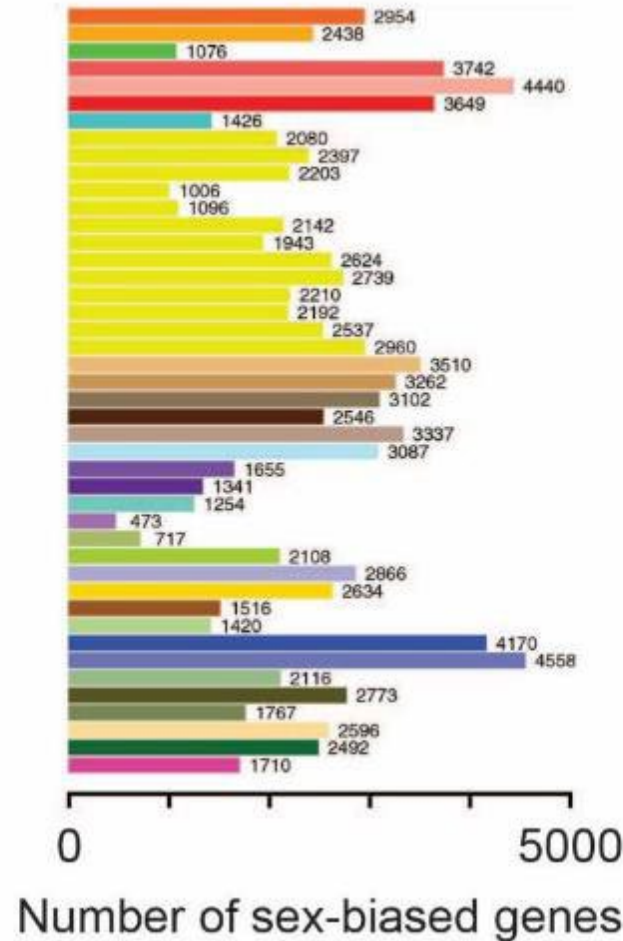
**Better health for
women and men**



NIH-Funded Genotype-Tissue-Expression (GTEx) Found Sex Differences in >13k Genes, Linked to >50 Bodily Traits & Functions



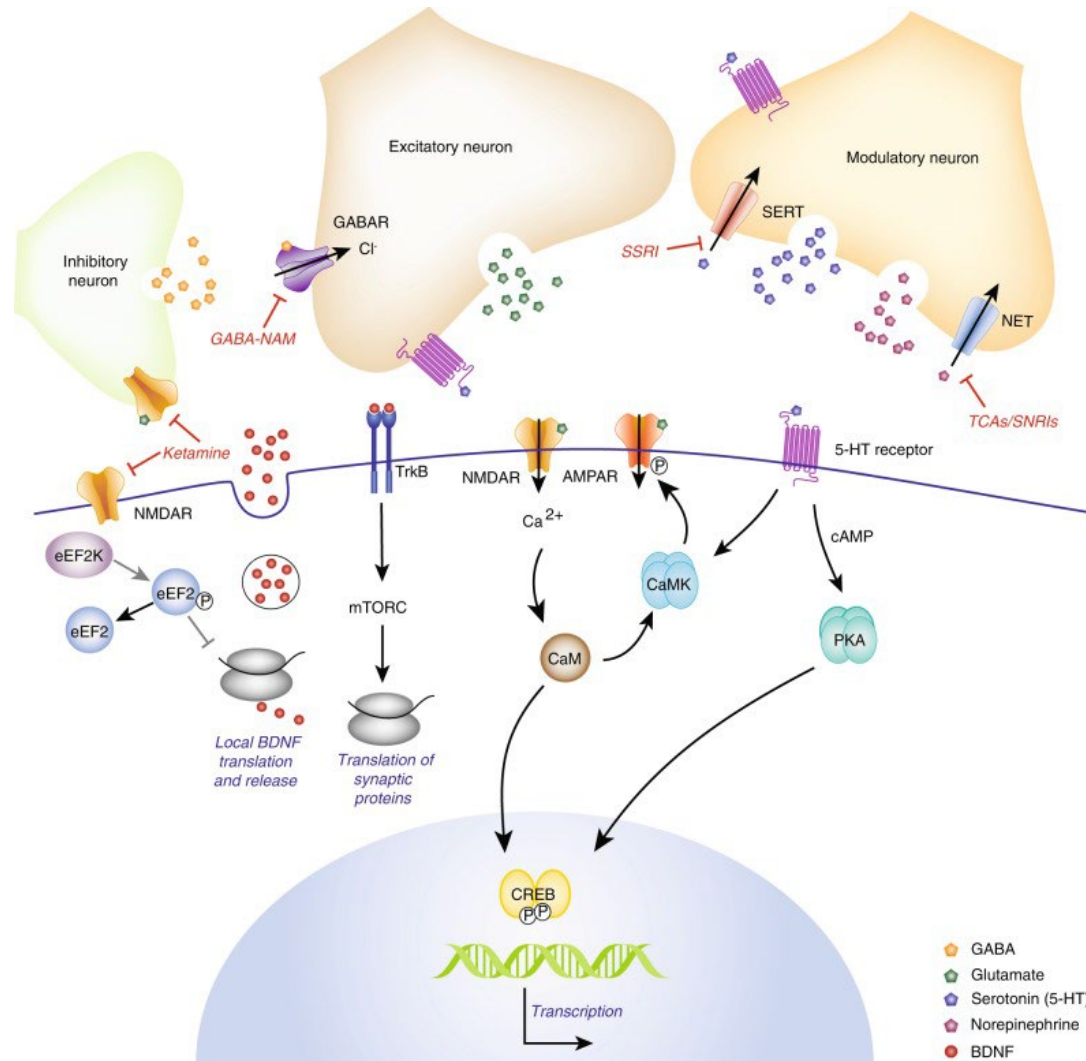
37% of all Genes Exhibit Sex-Biased Expression in at Least One Tissue



Sex-Related Differences: Mental Health

Antidepressant Efficacy

- One example of how **sex** influences mental health is that the sex hormones estrogen and progesterone play a role in increasing the activity of **key signaling molecules** (including dopamine and serotonin) that affect mood.



Context

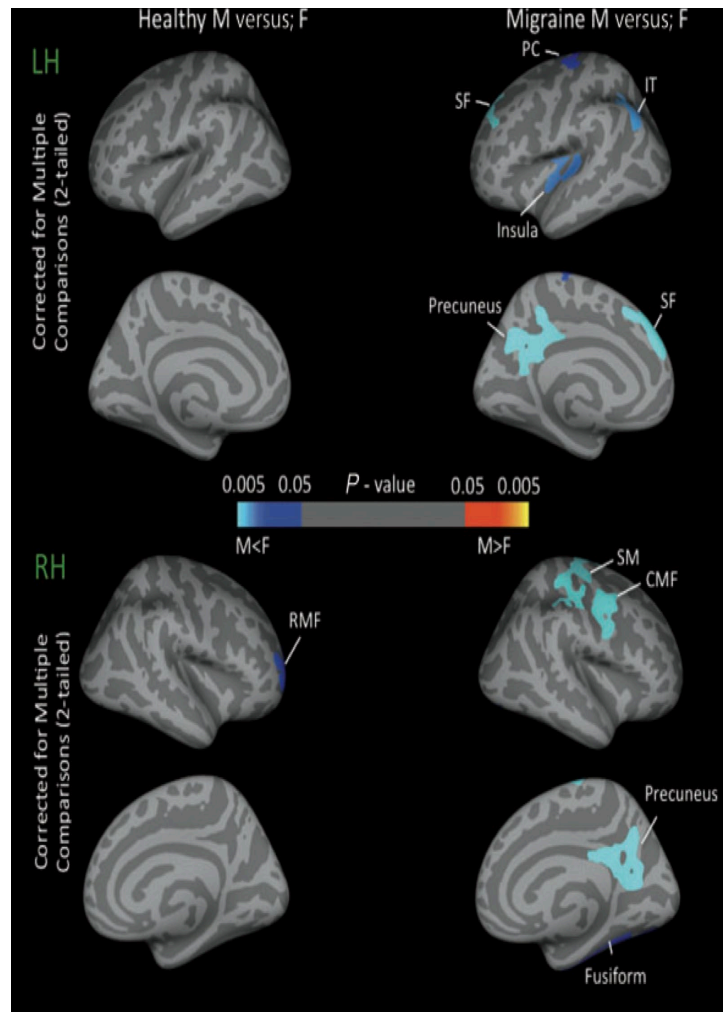
- Situational factors (e.g., violence) are associated with an increase in post-traumatic stress, anxiety, and depressive disorders in women.

Sex-Related Differences: Experience of Chronic Pain

Presents and
Progresses
Differently in
Women



Brains of female (right)
and male migraine
sufferers differ



Nervous System

Women have greater sensitivity and more chronic pain than men

Women respond differently to pain

- Estrogen can increase or decrease pain perception
- Women seek out pain relief more often than men

Differences in pain relief

- Women respond to opioid pain relievers at lower doses than men
- μ -opioid analgesics (morphine, fentanyl, methadone) are more effective in women

(Berkley J., 1997) (Miaskowski, C. et al., 2000)



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Office of Research on Women's Health

Another example of “One-Size-Does-Not-Fit-All”

Current Thinking

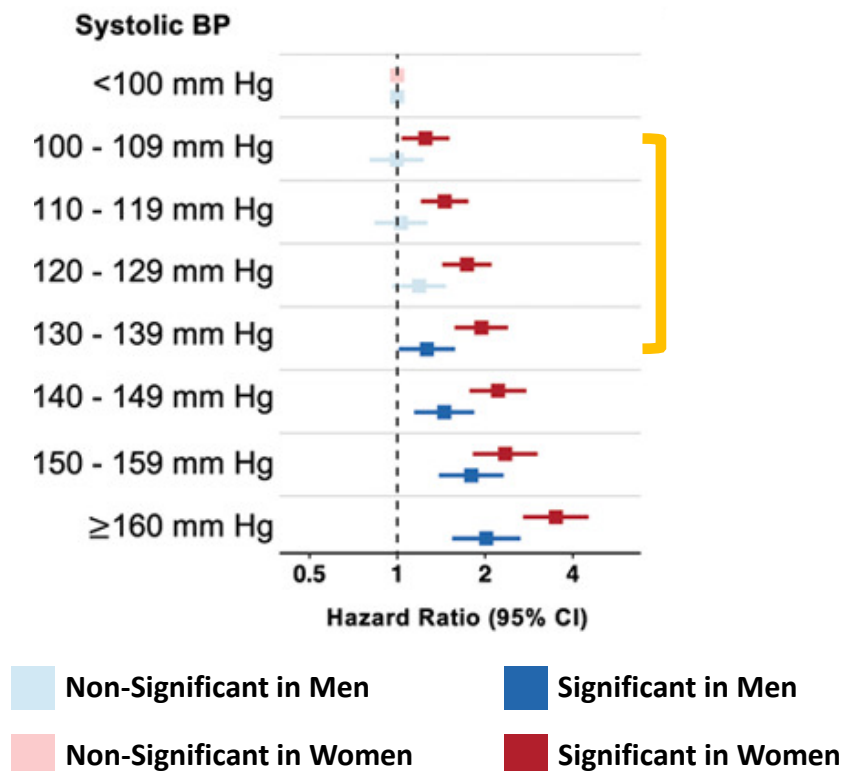
Established blood pressure (BP) guidelines state that women and men have the **same normal healthy range of BP** (i.e., systolic upper limit of 120 mmHg)

- Above threshold is associated with risk for heart attack, heart failure, stroke

Specialized Centers of
Research Excellence
on Sex Differences



CARDIOVASCULAR DISEASE



Revisit hypertension treatment guidelines that **do not account** for sex differences

Recent Findings

In fact, women have a **lower “normal” systolic BP range** (SBP) compared to men (110 v. 120)

- Researchers observed increasing Cardiovascular disease (CVD) risk beginning at lower thresholds of SBP for women than for men

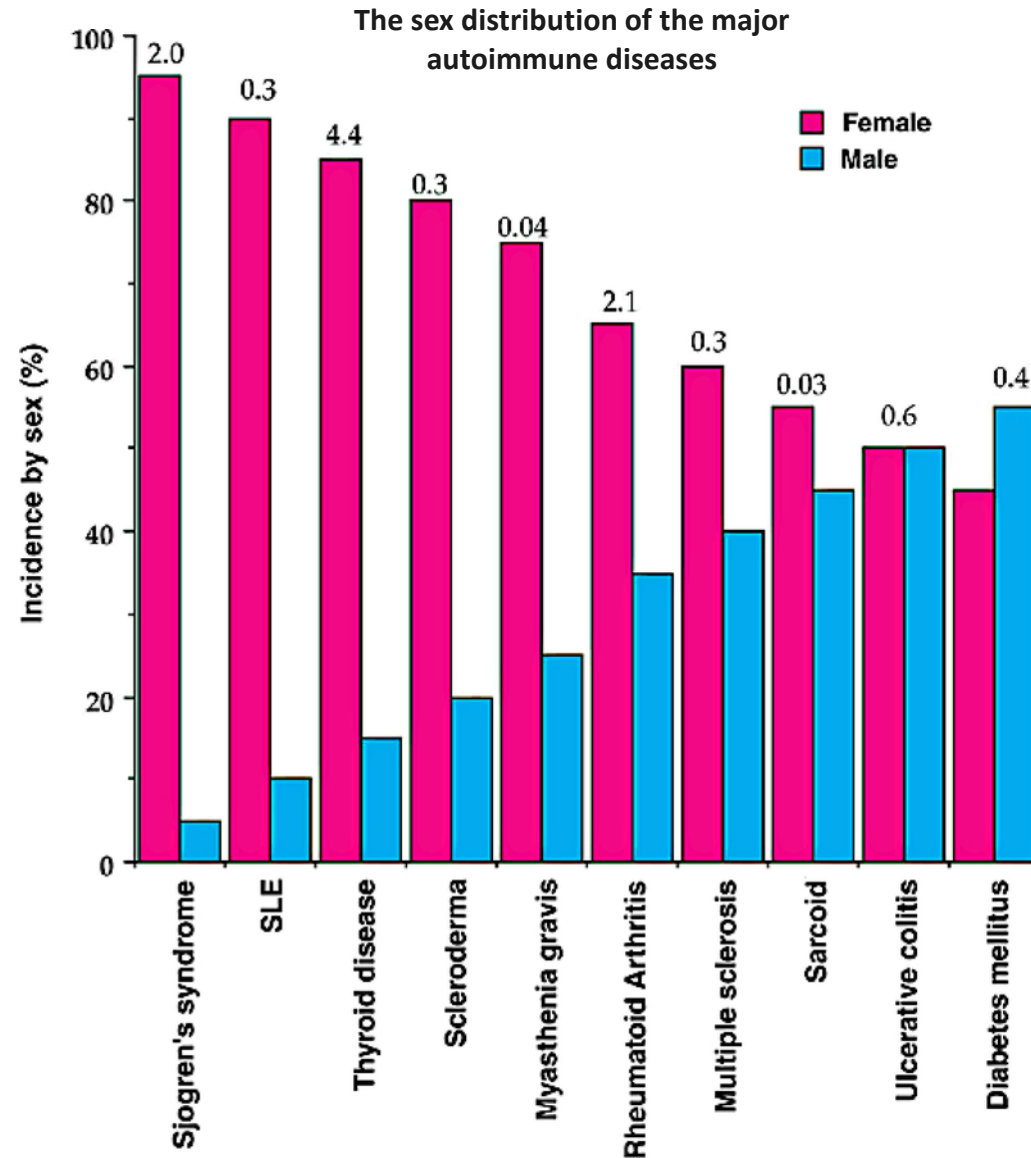


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Office of Research on Women's Health

Sex-Related Differences: Autoimmune Disorders

Disproportionate Effects

- The **female immune system** is generally more robust than the male system, e.g., with higher levels of circulating antibodies and greater cytokine release in response to infection.



Context

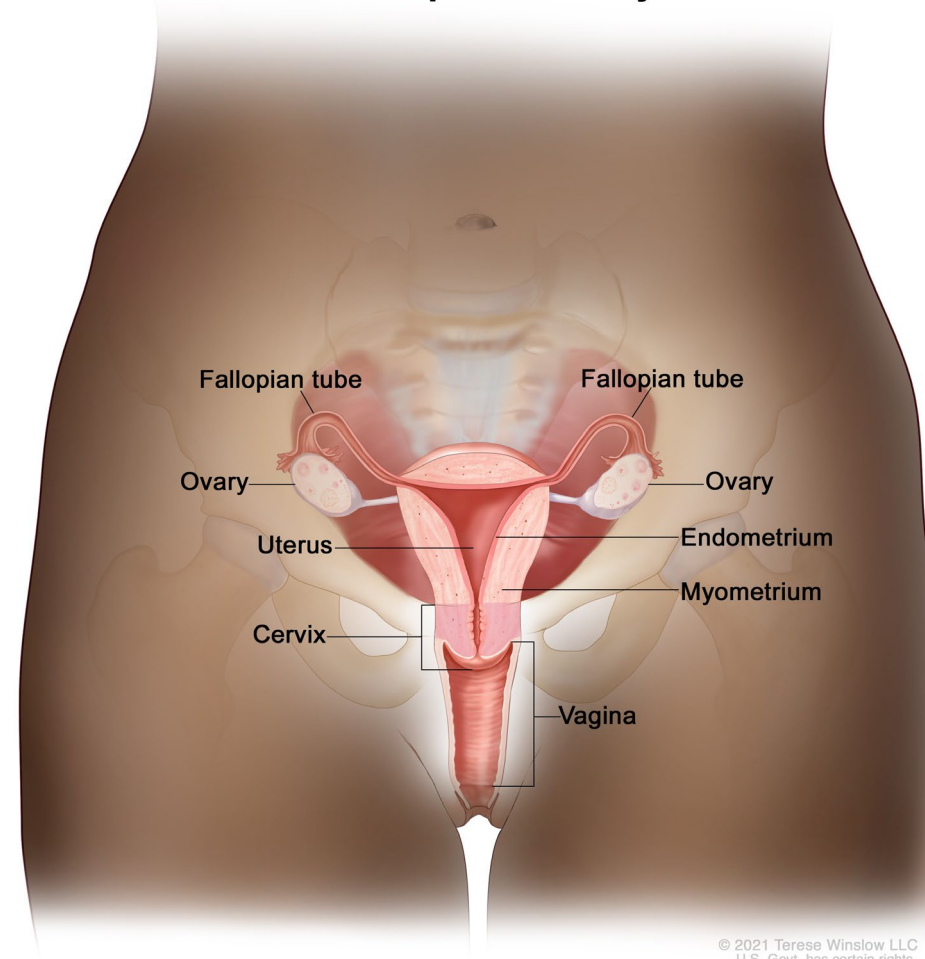
- Symptoms in women may be interpreted as non-physiological leading to delayed diagnoses.

Female Specific Conditions: Endometriosis

Clinical Impact

- Endometriosis is a chronic gynecological disease that affects approximately 1 in 10 women of reproductive age.
- Symptoms of severe pelvic pain, infertility, fatigue, and abnormal menstruation can cause significant negative effects on an individual's physical and mental health, including interactions with their family, friends, and health care providers.

Female Reproductive System



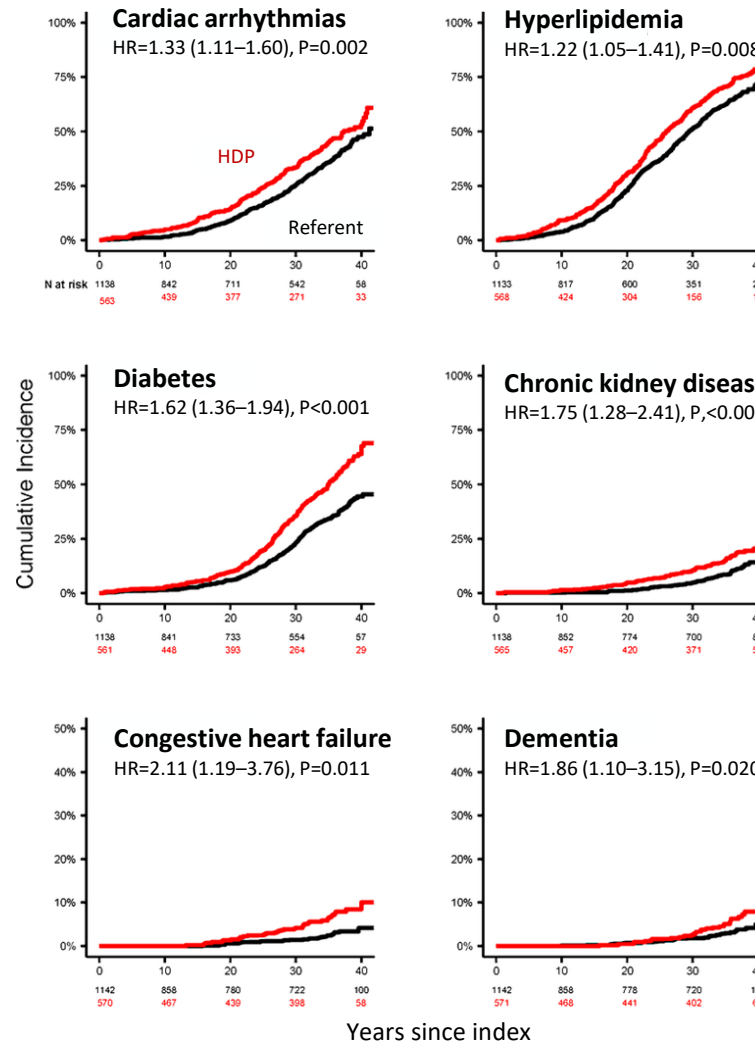
Gaps in Clinical Recognition

- Limited understanding around menstrual disorders and pain presentation has been associated with delayed diagnosis of endometriosis for as long as 11 years from the onset of symptoms, postponing treatment and the alleviation of symptoms.

Female-Specific Conditions: Hypertensive Disorders of Pregnancy

Pregnancy

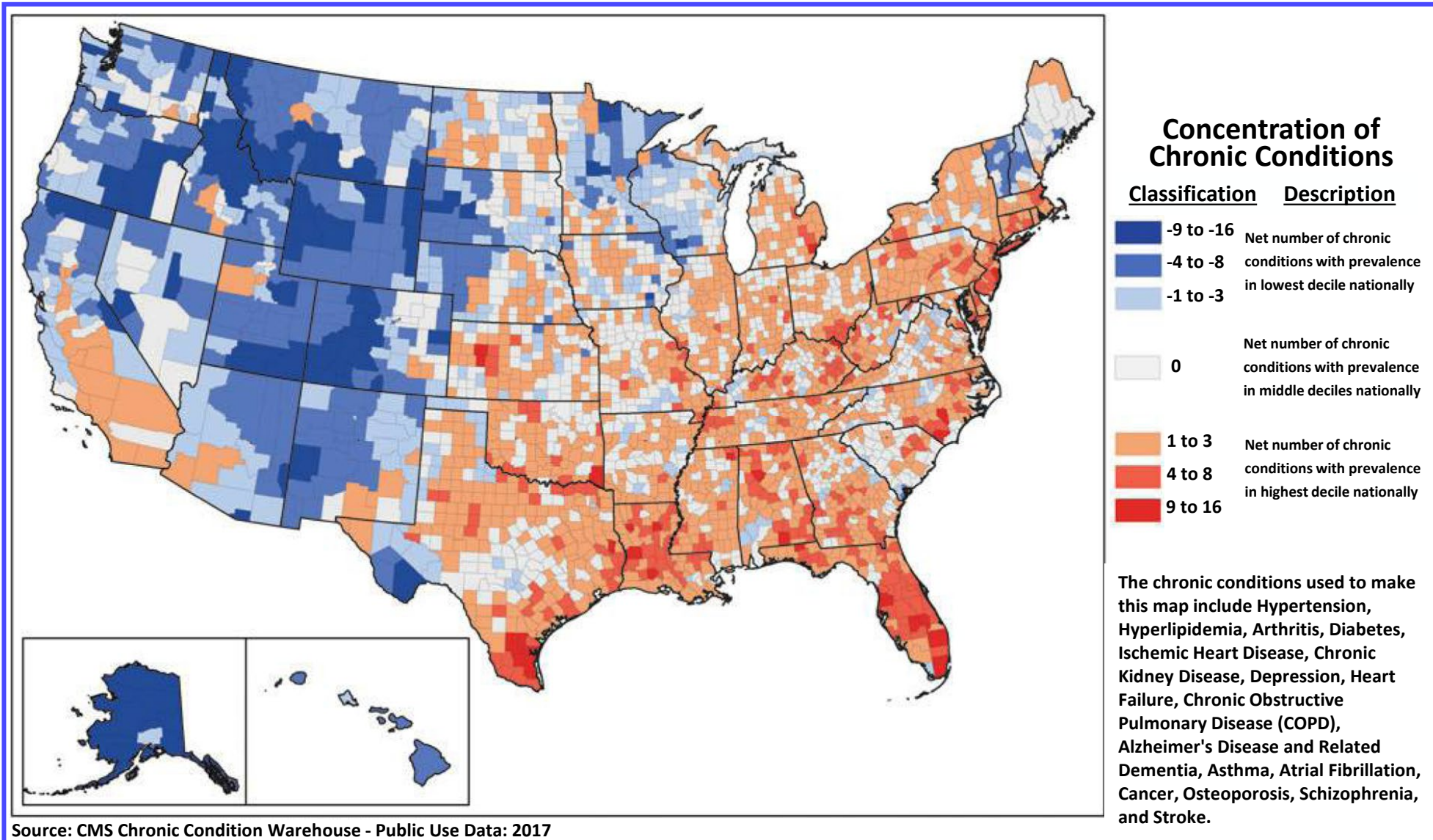
- Hypertensive disorders of pregnancy (HDP) are characterized by elevated blood pressure during pregnancy or the postpartum period and affect approximately 1 in 6 **women** during their reproductive years. HDP remains a leading cause of maternal and fetal morbidity and mortality worldwide.



Long-Term Health

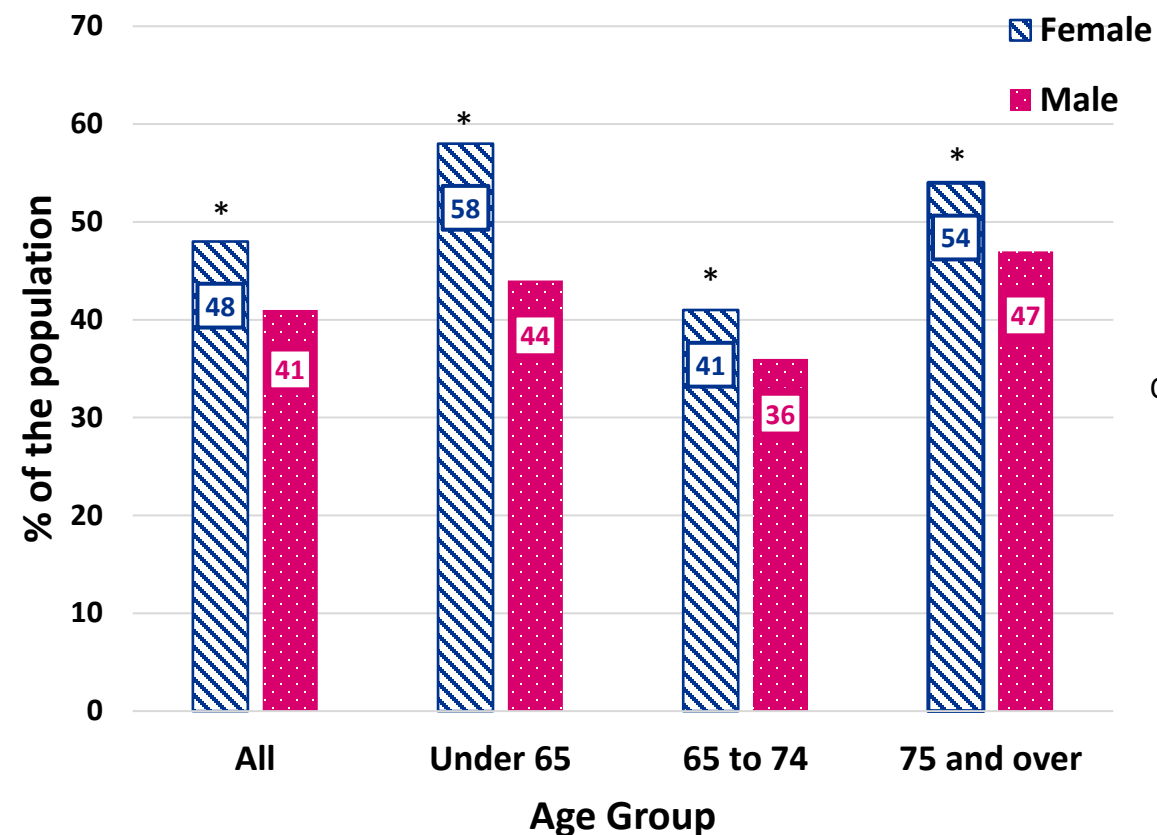
- Women with a history of HDP have significantly increased risks for **stroke (2.27x)**, **coronary artery disease (1.89x)**, **cardiac arrhythmias (1.62x)**, and **chronic kidney disease (2.41x)**. These women also develop multiple chronic conditions earlier in life, indicating accelerated aging that requires long-term surveillance and prevention.

An Increasing Burden of Chronic Conditions: US Counties with Highest Concentration of Chronic Conditions

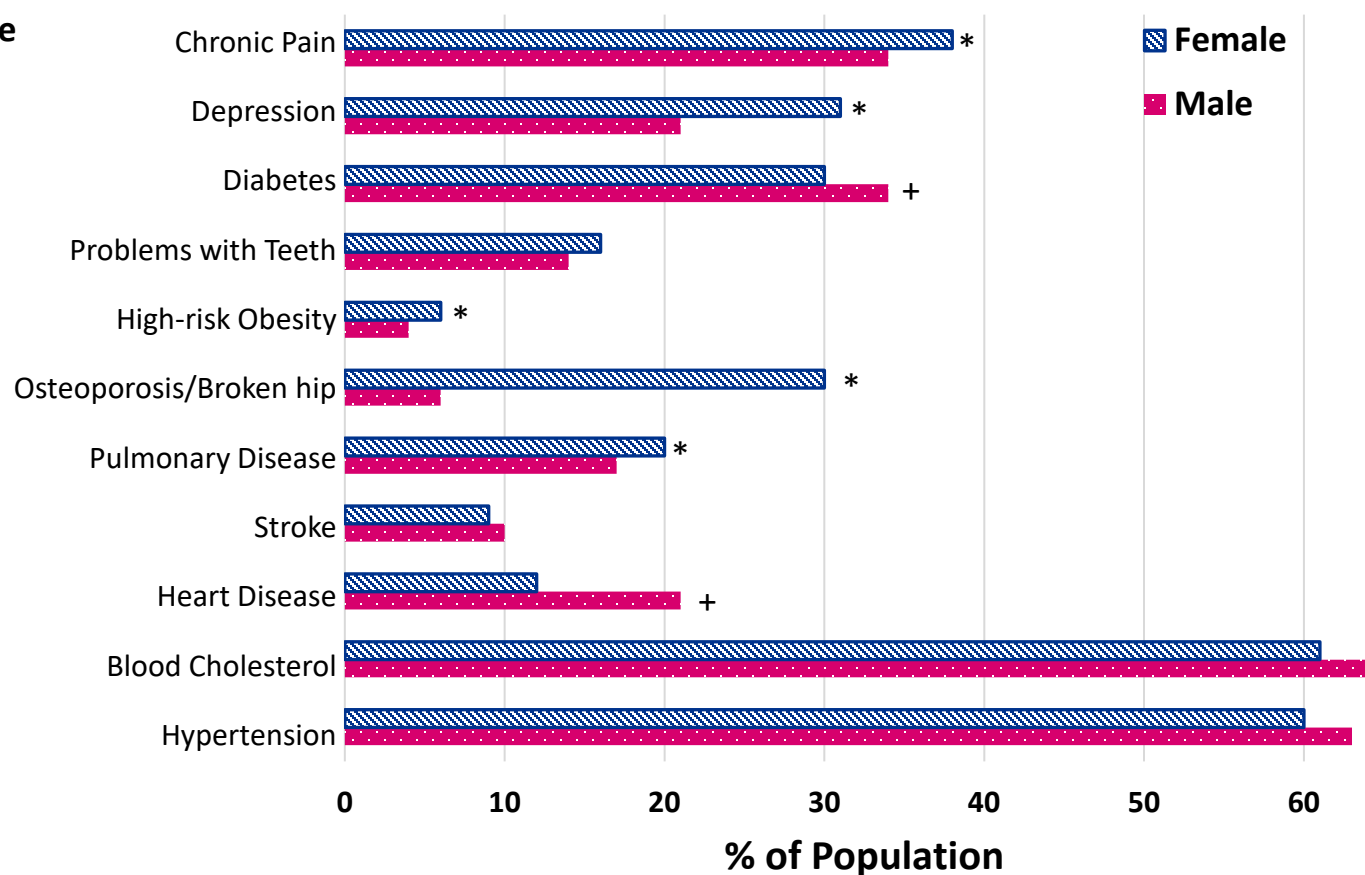


Nearly 50% of Medicare Beneficiaries Live with Multiple Chronic Conditions

Medicare Beneficiaries with 4+ Chronic Conditions (2022)



Medicare Beneficiaries with Chronic Conditions by Sex (2022)



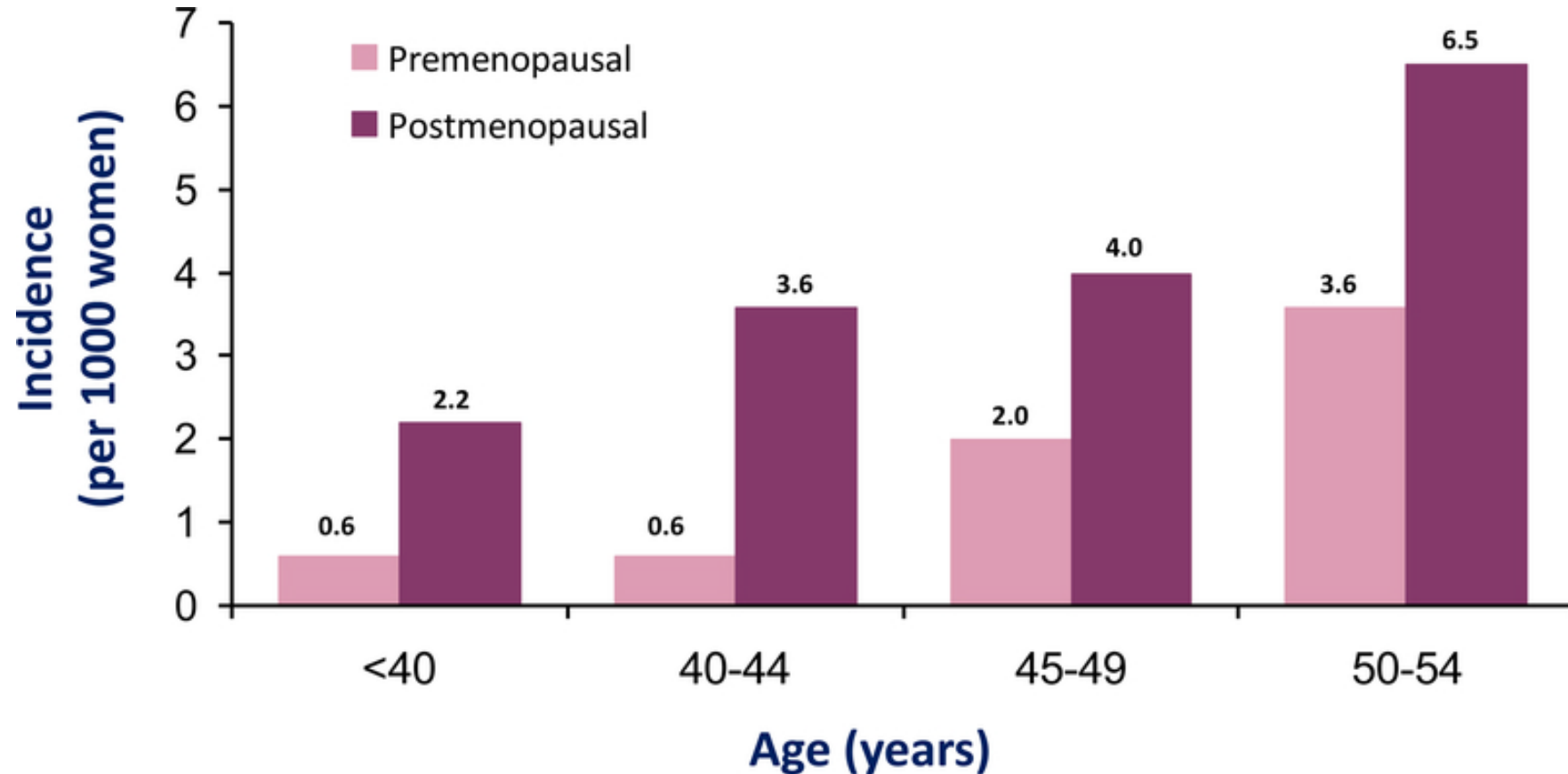
* Significantly higher difference in women/female.

+ significantly higher difference in men/male.

(Centers for Medicare & Medicaid Services., 2024)



Postmenopausal Women Are At Significantly Higher Risk For Cardiovascular Disease



It is critical to address the role of menopause in the health of midlife women in the context of preventing, diagnosing, and treating chronic conditions



Women's Health Across the Life Course

Primary Care Providers Responsible for Supporting Women's Health Across The Life Course:

Social Stresses—Preventive Health—Sexual and Reproductive Health—Behavioral Health—Palliative Care

Early Adulthood
15-44



Most frequent diagnosis:

1. Normal Pregnancy	13.0%
2. Pregnancy & GYN*	5.4%
3. Acute URI	3.2%
4. Gen Med Exam	3.1%

* Complications/Non-normal

upper respiratory infection (URI)

Middle Adulthood
45-64



Most frequent diagnosis:

1. Essential HTN	5.3%
2. Arthropathies	4.4%
3. Diabetes	3.6%
4. Rheumatism*	3.1%

* Exclude the back

hypertension (HTN)

Mature Adulthood
65+



Most frequent diagnosis:

1. Essential HTN	7.8%
2. Arthropathies	4.8%
3. Cataract	4.2%
4. Malignant neoplasm	3.6%

Women's Health Experiences: Early Adulthood 15-44



Women's Health in Focus

Primary Care Provider may utilize younger women's entry into healthcare system to navigate pathways to education and resources to address:

**Rising
Cardiovascular Risks**

**Fertility & Maternal
Health**

**Intimate Partner
Violence**

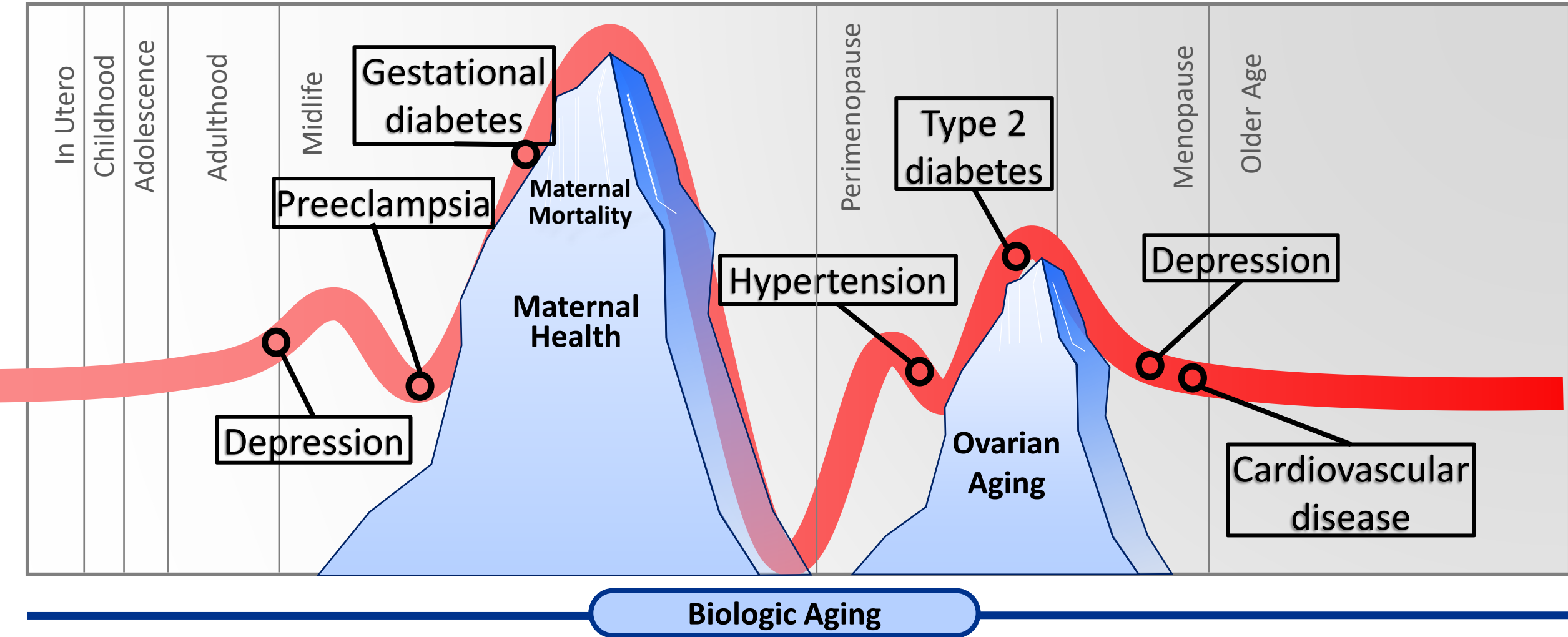
Translational Research Highlight: *Essential Hypertension*

- ❑ Pregnancy complications, such as **hypertensive disorders of pregnancy** (gestational hypertension and preeclampsia) and gestational diabetes mellitus (GDM), are associated with **cardiovascular morbidity and mortality** later in life.
- ❑ Studies suggest the likelihood of progression of gestational diabetes to Type 2 diabetes (T2D) or from **prehypertension to hypertension** varies among populations.
- ❑ The risk for development of T2D and HTN is within years of the pregnancy complication not decades.

Research Opportunities

- ❑ Consider ways to **optimize postpartum primary care**.
- ❑ Implement solutions to enhance patient engagement in primary care settings.

Perimenopause: A Systems-Level Inflection Point in Women's Health Trajectories



Women's Health Experiences: Middle Adulthood 45-64

Sex Differences in Type 2 Diabetes



Diagnosis:

Men diagnosed younger and at lower body mass index (BMI); women have higher risk factor burden at diagnosis



Cardiovascular Risk:

Women have higher relative risk of CVD complications and mortality; younger women at particularly high risk



Women's Key Risk Factors:

Gestational diabetes history, Polycystic ovary syndrome (PCOS), early menopause, high testosterone; psychosocial stress more impactful



Treatment Gap:

Women less likely to receive guideline-recommended CVD risk reduction; report more medication side effects



Prediabetes Pattern:

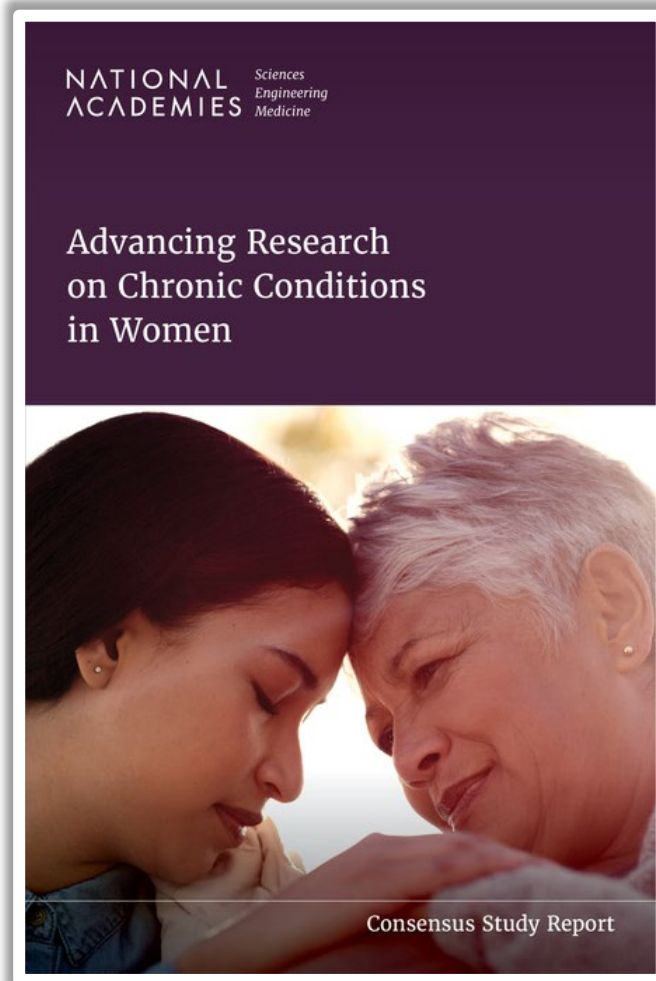
Impaired glucose tolerance more common in women; impaired fasting glucose more common in men



Clinical Implication:

Sex-specific prevention and management strategies urgently needed

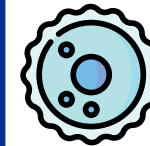
The NASEM's Conceptual Framework for Research on Chronic Conditions in Women



Research on Chronic Conditions in Women



Female-specific and Gynecologic Conditions that Lead to Significant Morbidity
Pregnancy and Menopause



Chronic Conditions that Predominantly Impact Women
Autoimmune Disease



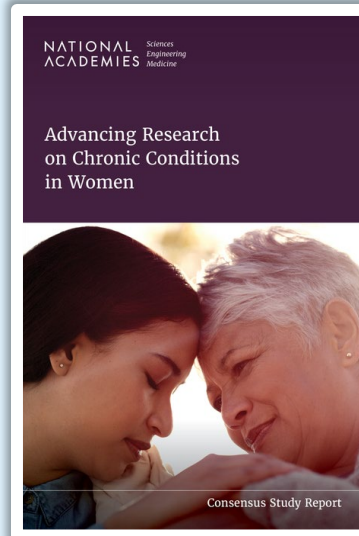
Chronic Conditions that Impact Women Differently
Cardiovascular Disease



Accumulation of Multiple Chronic Conditions

Recommendations to Advance NIH Research on Chronic Disease in Women

- Improve estimates of the **impact** of chronic conditions in women.
- Understand the independent and interacting roles of gonadal hormones and sex chromosome genes causing **sex differences** and chronic conditions affecting women more than men.
- Understand the exact mechanisms hormonal fluctuations play in the development of **female-specific** chronic conditions in women.
- Explore the role of traumatic experiences as risk factors in the development of chronic conditions throughout the **life course**.



- Understand the role of lifestyle **behaviors** on the development of chronic conditions.
- Understand the cellular processes that have been postulated to be possible targets that could play a role in preventing or ameliorating **multiple chronic conditions** in women.
- Improve early and accurate **detection and diagnosis** of chronic conditions in women.
- Understand the cellular processes that could play a role in preventing or ameliorating **multiple chronic conditions** in women.

ORWH is Catalyzing the Transformation of Women's Health to Fill Gaps in Knowledge



Carrie Mahoney, Ph.D.
Harvard University, MA

Orexins and Severity of Menopausal Symptoms

(NIA and ORWH)



Fiona Baker, Ph.D.
SRI International, CA

Thermoregulatory Physiology of Menopausal Hot Flashes

(NIA and ORWH)



Jodi Flaws, Ph.D., M.S.
University of Illinois at Urbana-Champaign, IL

Phthalates, Oxidative Stress, and Hot Flashes in Aging Women

(NIA and ORWH)



Karen P Jakubowski, Ph.D.
University of Pittsburgh, PA

Investigating Intimate Partner Violence in the Context of Sleep Among Survivors

(NHLBI and ORWH)



Mercedes Bravo, Ph.D.
Duke University, NC

Innovative Data Science and Geospatial Methods in Hypertensive Disorders of Pregnancy and Blood Pressure Over Time

(NHLBI and ORWH)



Nicole De Nisco, Ph.D.
University of Texas at Dallas, TX

The Impact of Estrogen Hormone Therapy Modality on Urobiome Dynamics In Postmenopausal Women

(NIA and ORWH)



Thomas Leung, M.D., Ph.D.
University of Pennsylvania, PA

Innate Lymphoid Cells and Tertiary Lymphoid Structures in Sarcoidosis

(NIAMS and ORWH)



Zhina Sadeghi, M.D.
University Of California-Irvine, CA

Anti-Fibrogenic Therapy to Target Aging-Associated Urethra Dysfunction

(NIA and ORWH)

★ = Female-specific condition



NIH Advances Research to Illuminate Understudied Chronic Diseases in Women



Bertha Chen, M.D.
Stanford University, CA

Cellular Mechanisms in The Vagina of Women With Recurrent Vaginal Prolapse After Prolapse Surgery

(NICHD)



Rebecca Shelby, Ph.D.
Duke University, NC

Improving Outcomes for Women Experiencing Premature or Early Menopause After Cancer: Development and Pilot Testing of a Novel Intervention

(NCI)



Rebecca Seguin-Fowler, Ph.D.
Texas A&M Agrilife Research, TX

Deep in the Heart for Women: A Community-Engaged Intervention Study to Catalyze a Culture of Health in Rural South Texas

(NHLBI)



Omid Veisheh, Ph.D.
Rice University, TX

Bioengineered Lymphatic Regenerating Platform for Treatment of Breast Cancer Related Lymphedema

(NHLBI)



Sathish Venkatachalem, Ph.D.
North Dakota State University, ND

Estrogen Signaling in Chronic Asthma

(NHLBI)



All awards are funded through:
RFA-OD-23-014 (R01) and RFA-OD-23-013 (R21)



= Female-specific condition



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

Chronic Disease Funding Opportunities Have Been Key to Filling the Gaps in Chronic Disease Research

Cancer-Related Women's Health & Translational Innovation

- **Cervical cancer prediction***, **breast cancer survivorship***
- **Bioengineering and intervention development***

Molecular & Inflammatory Mechanisms

- Immune activation, host-pathogen interactions, neuroimmune mechanisms, epigenetics, connective tissue disorders
- Sex-informed disease mechanisms across pulmonary, ocular, and rheumatic conditions
- Cellular, fibrotic, and nociceptive mechanisms

Infectious Disease–Reproductive Biology Intersections

- **Menstruation*** and sexually transmitted infection (STI) susceptibility

All awards are funded through:
RFA-OD-23-014 (R01) and RFA-OD-23-013 (R21)

Cardiovascular, Pulmonary & Metabolic Health Across the Life Course

- **Pregnancy-related risk***, **rural women's heart health***
- Data science, geospatial methods, community-engaged research
- Sleep

Reproductive Aging, Menopause & Hormone Biology

- **Genitourinary syndrome of menopause***, **thermoregulation***, **estrogen signaling***
- Environmental exposures, neuroendocrine regulation
- **Endometriosis***, **prolapse**, pelvic pain, **urethral dysfunction***

Psychosocial, Environmental & Modifiable Health and Healthcare System Factors

- Intimate partner violence, environmental drivers of health outcomes
- Integrated social, behavioral, and exposomic approaches
- Food insecurity

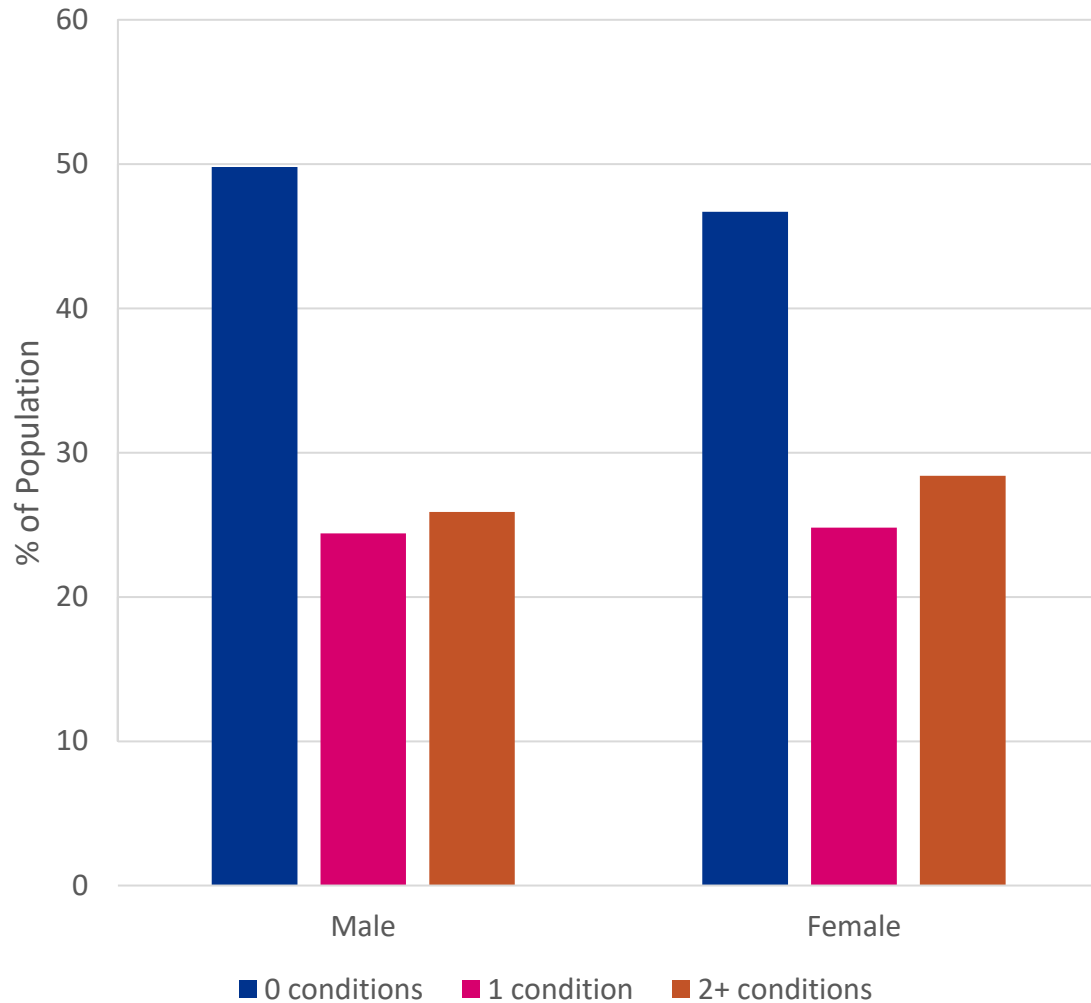
* **Female-specific conditions**



Module 3: Multimorbidity

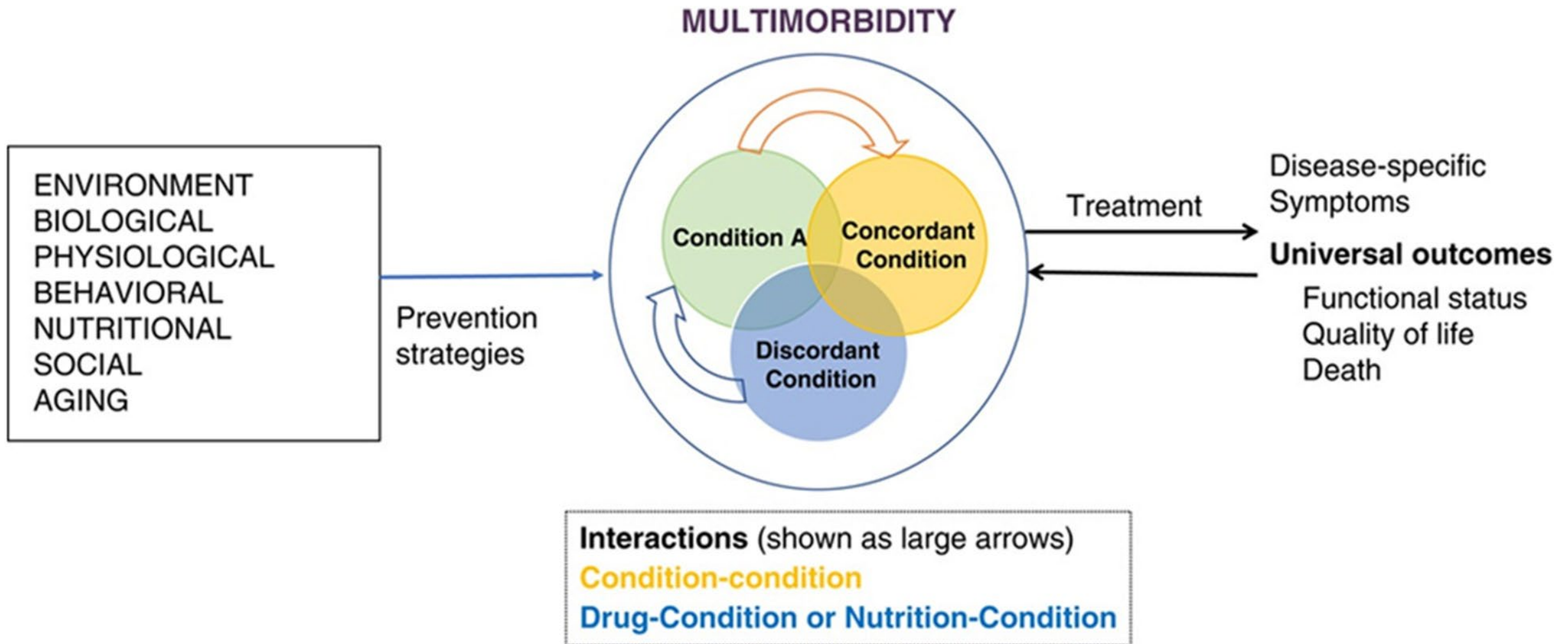


Multiple Chronic Conditions (Multimorbidity)



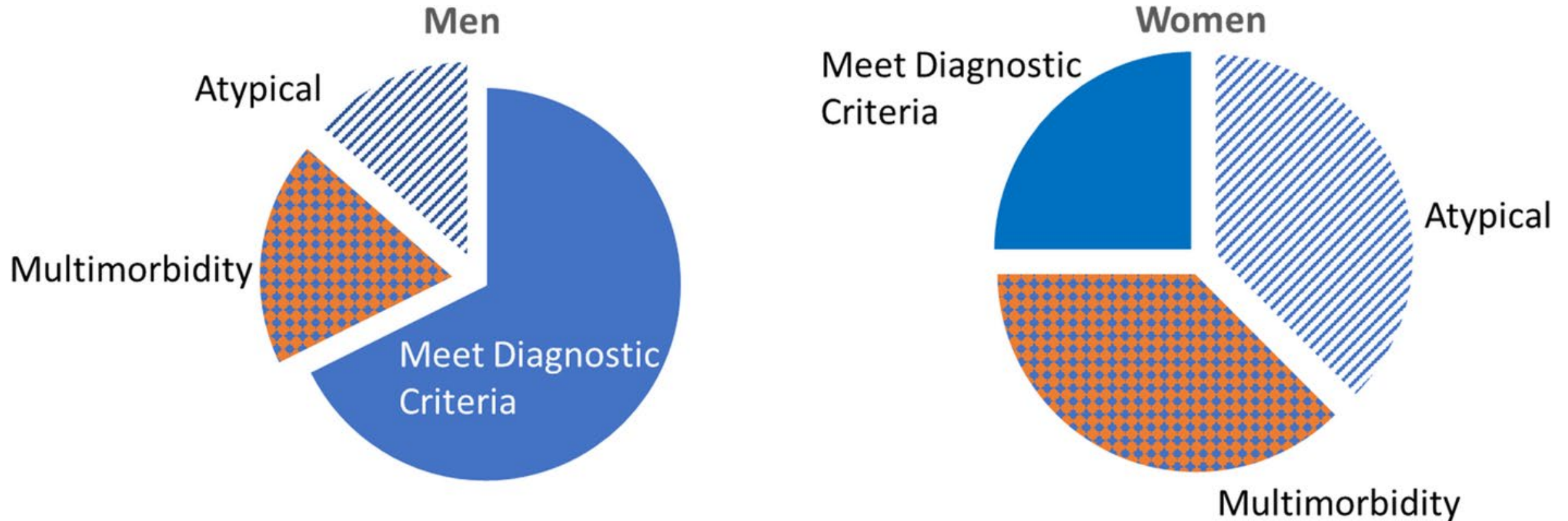
- Multimorbidity is the co-occurrence of two or more chronic conditions in one individual
- Multimorbidity is more common in women
- Interactions between conditions are poorly understood in women

A Model and Research Framework for Multimorbidity

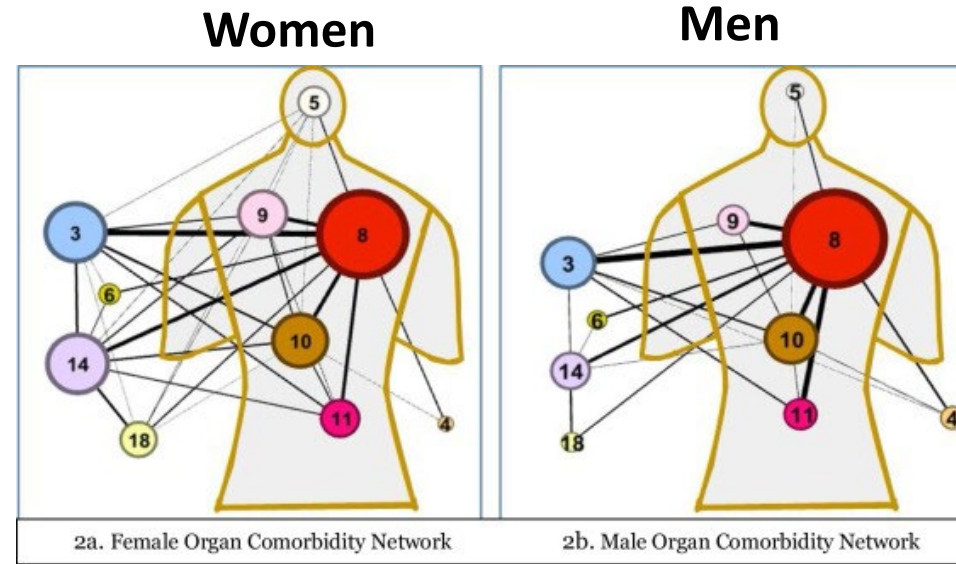


Sex Differences in Diseases Impacts Research Participation

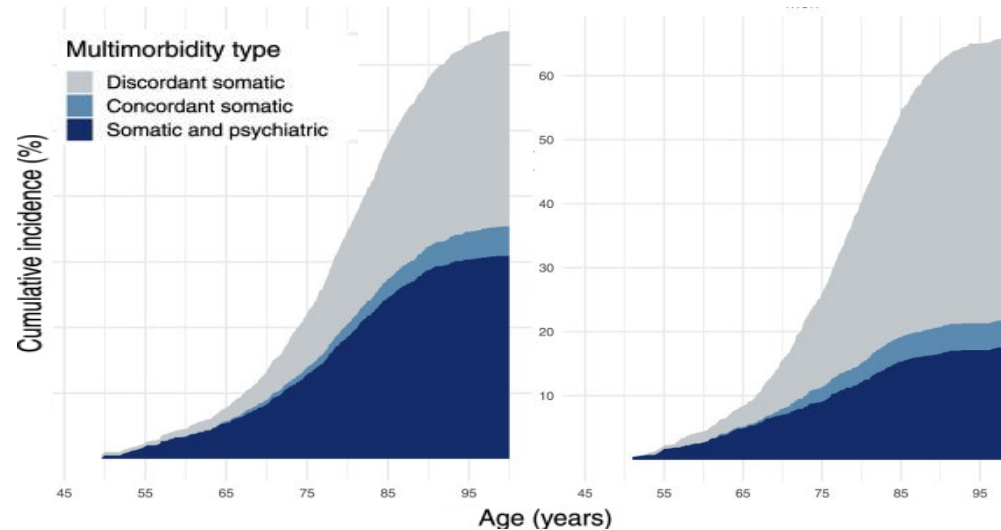
Exclusion of subjects with multimorbidities decreases validity and generalizability of research findings



Multimorbidity is More Complex in Women



- The pattern of **accumulating** morbidity, meaning which initial chronic conditions are diagnosed and how conditions are additive, differs by sex.
- The “networks” of morbidity in women more frequently cross **multiple** organ systems.



(St Sauver JL, et al., 2015)
(Velek P, et al., 2022)
(Kalgothra P, et al., 2017)

Menopause at the Intersection of Multimorbidity

U.S. Government Accountability Office (GAO) Report – June 2026

Providers and Their Roles in Menopause Care within the VHA

Key Clinicians for Menopause Care



Primary Care

- Counsels veterans on symptoms and impact of menopause on other diseases
- Discusses medications and lifestyle changes with veterans
- Makes referrals to other specialties as needed



Gynecology

- Provides similar menopause care services as primary care providers
- May provide specialty evaluation and management for complex menopause cases

Specialty Care



Pelvic Floor Physical Therapy

- Supports management of menopause symptoms related to the muscles at the base of the pelvis which support bladder, bowel, and sexual functions



Radiology

- Provides diagnostic and screening relevant to perimenopausal and menopausal veterans



Mental Health

- Helps patients manage mental health menopause symptoms in relation to other mental health conditions
- Collaborates with primary care team on medication management



Nutrition Counseling

- Helps patients with menopause-related weight gain or body composition changes with a focus on maintaining muscle and bone health



Endocrinology

- Helps veterans manage impact of hormone changes on other diseases caused by hormone imbalances



Complementary and Integrative Health

- Provides mind-body practices such as acupuncture, meditation, Tai Chi and yoga, which are shown to help with menopause symptoms



Clinical Pharmacy

- Reviews and adjusts menopause medications in the context of other medications, patient history, and contraindications



Musculoskeletal/Orthopedics

- Diagnoses and manages menopause-related musculoskeletal issues



Cardiology

- Monitors and manages increased risk to cardiovascular health due to menopause



Social Work

- Provides social needs screenings, mental health support, health literacy related to managing menopause symptoms, and connects veterans to community resources



Sleep Medicine

- Manages sleep disorders prevalent in menopause



Urology

- Evaluates and treats bladder and urinary conditions that occur during menopause

Source: GAO analysis of Veterans Health Administration (VHA) descriptions of care providers and their roles; RaulAlmudi/stock.adobe.com (illustrations). | GAO-26-107853

Women veterans may face additional risks due to greater post-traumatic stress disorder symptoms and military sexual trauma

- Both are associated with menopausal symptoms of fatigue, sleep disorders, vasomotor symptoms and urinary or vaginal symptoms.

GAO identified opportunities to strengthen care:

- **Use identified performance measures to monitor implementation of menopause guideline recommendations:** Low rates of documented menopause/perimenopause diagnoses (**6%–20%**), and hormone therapy prescribing (**3%–35%**) for veterans aged 45–64.
- **Provider education:** Menopause the **#1 requested area for additional education** among respondents to VHA's 2024 national needs assessment.
- **Patient education:** **60%** of women veterans responding to GAO's questionnaire had not received VHA menopause education or resources.

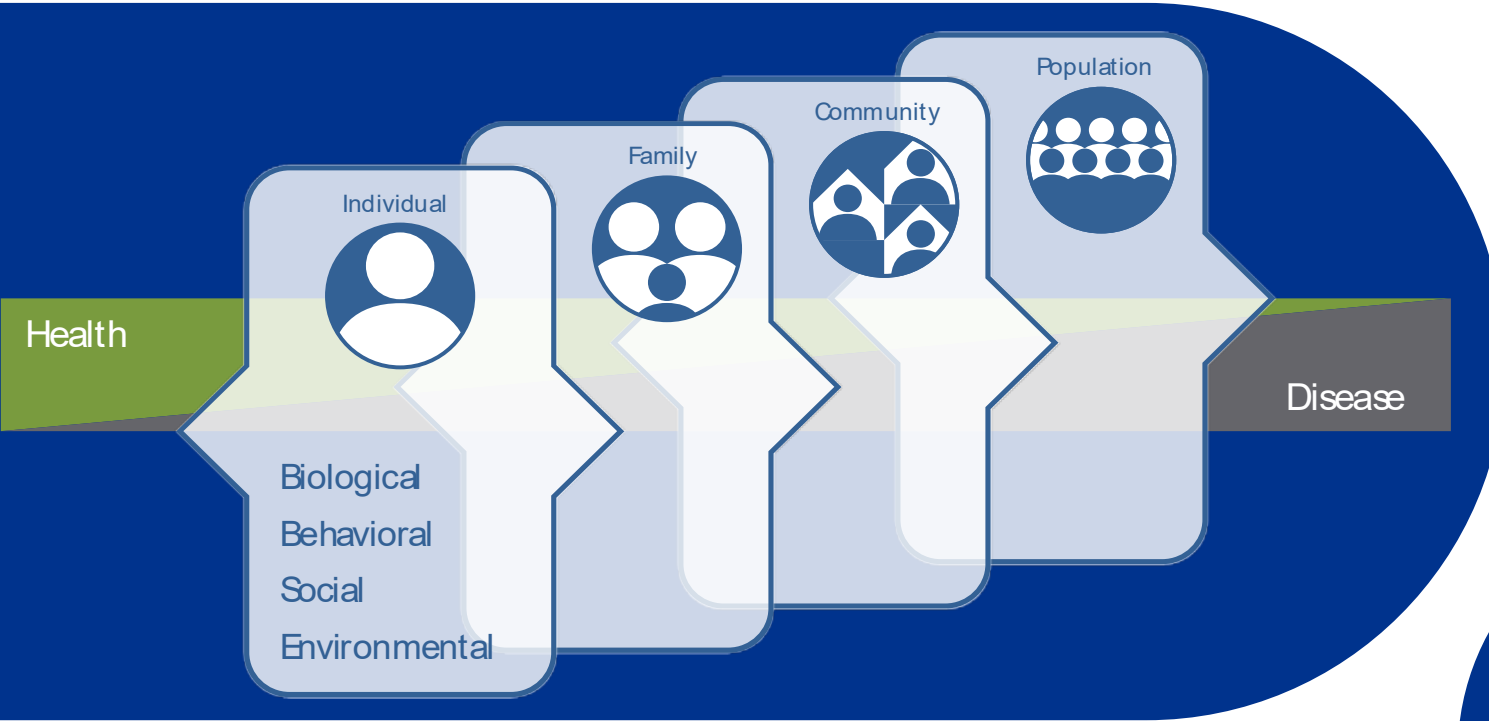
(Thomas, J. L., Blanken, A. E., Huang, A. J., Maguen, S., Gibson, C. J., & Sumner, J. A., 2024)

(Travis, K. J., Huang, A. J., Maguen, S., Inslicht, S., Byers, A. L., Seal, K. H., & Gibson, C. J., 2024)



Paradigm Shift: From Multi-Morbidity to the Whole Person

Decoding Health and Mapping the Integrated Human Physiome



Whole Person Physiome Research and Coordination Center (WPP-RCC)

Aims to transform health research by modeling how multiple body systems interact to support whole-person health, **female and male**, shifting focus from disease treatment to prevention, resilience, and optimal function.

Principal Investigator: Michael Snyder, Ph.D.
Professor, Stanford University

“By organizing healthy physiological function into a whole-body knowledge network, researchers will be able to explore scientific questions about health in a new way.”

Helene M. Langevin, M.D.
Former Director | NCCIH

Participating ICOs:

NCCIH, NHLBI, NIA, NIAAA, NIAID, NIBIB, NIDCR, NIDDK, NIDA, NIEHS, NIMH, NINR, NCI, DPCPSI, ODP, OBSSR, ODS, ODSS, **ORWH**

Module 4: NIH/ORWH Research



Enhancing Women's Health Research Through Collaboration



Aligning Women's Health Efforts Across NIH and United States Government Agencies

Increase access and collaboration to **close research gaps** with **new women's health research, survey tools, analyses, and insights**

Enhance data collection and transparency in reporting of NIH support of female-specific diseases and conditions with standardized methodology

Enhance cross-disciplinary collaboration by improving data harmonization across studies through the use of **Common Data Elements**

Enhanced Reporting for Women's Health Research: NIH Research, Condition, and Disease Categorization (RCDC)



Starting with reporting of FY 2024 expenditures, the NIH has transitioned from the manual *Women's Health* category to the automated *Women's Health Research* category to:

- Enhance **accuracy** and **consistency** in reporting
- Better **distinguish research** focused on improving the health of women across the life course

ORWH In the Spotlight: Enhanced Reporting for
Women's Health Research
<https://bit.ly/4sIKERA>

FY 2025 NIH Categorical Spending Data
<https://grants.nih.gov/news-events/nih-extramural-nexus-news/2026/06/new-fy-2025-nih-categorical-spending-data-available>



The NIH Women's Health Central Resource

**INFORMATION ABOUT ADVANCEMENTS
ON NIH WOMEN'S HEALTH RESEARCH**

- **SINGLE PLACE TO FIND**

- Research Projects
- Health Topic Information
- Research Funding Opportunities
- Clinical Trials
- Medical Literature

- **FOR**

- Patients, caregivers, researchers, medical professionals, and the public

- **FEATURING**

- Additional health topics
- Enhanced search capabilities
- Common Data Elements Repository (CDE-R)

NIH Discover Women's Health Research Resource



*For health conditions that uniquely,
disproportionately, and/or differently affect
women across their life course*

<https://discoverwhr.nih.gov/>

Supported by NLM and ORWH



DiscoverWHR Expands to Include Prevalent Women's Health Issues



- Breast Cancer*
- Cervical Cancer*
- Ovarian Cancer*



- Endometriosis
- Hypertensive Disorders of Pregnancy*
- Vulvodynia*



- Exercise*
- Nutrition*



- Alzheimer's Disease*
- Anxiety*
- Attention Deficit
- Bipolar Disorder*
- Depression*
- Hyperactivity Disorder (ADHD)
- Insomnia*
- Migraine*
- Schizophrenia*



- Female Infertility*
- Pelvic Floor Disorders*
- Pelvic Inflammatory Disease (PID)*
- Polycystic Ovary Syndrome (PCOS)



- Uterine Cancer*
- Uterine Fibroids*
- Obesity*
- Gestational Diabetes Mellitus (GDM) *



- Autoimmune Diseases**
- Hidradenitis Suppurativa (HS)*
 - Lupus
 - Multiple Sclerosis (MS)*
 - Rheumatoid Arthritis
 - Scleroderma
 - Type 1 Diabetes*



- HIV (Human Immunodeficiency Virus)
- HPV (Human Papillomavirus)



- Cardiovascular Disease*
- Chronic Liver Disease (CLD)*
- Myocardial Infarction*
- Osteoporosis*
- Chronic Pain*
- Stroke*
- Menopause
- Chronic Kidney Disease
- Chronic Obstructive Pulmonary Disease*
- Alcohol Use Disorder*
- Intimate Partner Violence (IPV) *

Featured Topics

Chronic Conditions

Find out how NIH is helping to advance research on how chronic conditions, such as [cardiovascular disease](#), [depression](#), [endometriosis](#), and [PCOS](#), impact women.

[Explore Chronic Conditions →](#)

NIH Common Data Element Repository (CDE-R)

* New Topic Areas

Women's Health: Early Adulthood 15-44

ORWH-supported

Developing Targeted Interventions and Next-Generation NAMs to Improve Metabolic and Reproductive Health for Women in Early to Mid-Adulthood

Scientific Output

Title: Resistant Starch Treatment of Polycystic Ovary Syndrome: Impact on Cardiometabolic Dysfunction and the Gut Microbiome

Institution: University of Pennsylvania

PI: Anuja Dokras, MD, MHCI, PhD

<https://reporter.nih.gov/search/vljnvRQ4ME2eTm3F8mhe3w/project-details/11377590>



Title: NAMs for Clinical Translation of Therapeutics for Systemic Gynecology Diseases

Institution: Massachusetts Institute Of Technology

PI: Linda Griffith, PhD

<https://reporter.nih.gov/search/Zrq7HNQMy0uRRmPKyGH9dw/project-details/11305605>



Women's Health: Middle Adulthood 45-64

ORWH-supported

Driving Innovative
Solutions to Enhance
Menopause-Related
Genitourinary and
Cardiometabolic
Health in Midlife
Women

Scientific Output

***Title: Regenerative Biomaterial for Combating
Genitourinary Syndrome of Menopause***

Institution: University of California, San Diego

PI: Marianna Alperin, MD, MS

https://reporter.nih.gov/search/yqDenjSBbE6P1aII1Tmf_Q/project-details/11187044



***Title: Changes In Cardiometabolic Tissue Gene
Regulation and Omics Profiles with Menopause***

Institution: University of California, San Francisco

PI: Elizabeth Theusch, PhD

<https://reporter.nih.gov/search/6amKNf8sY0SKXc768r3qjA/project-details/10872907>



Women's Health: Mature Adulthood 65+

ORWH-supported

Improving
Cardiovascular
Function and Slowing
Neurodegeneration
in Women 65+
Through
Non-Pharmacologic
Therapies and
Precision Cellular
Approaches

Scientific Output

Title: Heat Therapy to Improve Functional Performance in Heart Failure with Preserved Ejection Fraction (HFpEF)

Institution: Purdue University

PI: Daniel Hirai, PhD

<https://reporter.nih.gov/search/4-fMrWu2s0Gn2aPczxbItA/project-details/11177923>



Title: Assessing Cellular Aging in Old and Rejuvenated Neurons from Alzheimer Patients

Institution: Salk Institute for Biological Sciences

PI: Fred Gage, PhD

<https://reporter.nih.gov/search/PqW0Qsgr-0qsbhoi98cB5w/project-details/11297619>



Module 5: Closing



**FINAL
THOUGHTS**

MILITARY WOMEN'S HEALTH WEBINAR SERIES

The first federal webinar series dedicated to military women's health, created through partnership between ORWH and the Uniformed Services University Military Women's Health Research Program.

OUR IMPACT



4,812

REGISTRANTS
over 12 months



2,137

LIVE ATTENDEES
engaged across the country



20+

EARNED CME CREDIT
across 3 events



9

WEBINARS
Covering the full spectrum of
women's health across the
life course



100s

WATCHED ONLINE
through on-demand
recordings

ADVANCING NIH'S MISSION



Strengthening partnerships
across the biomedical
research enterprise



Maximizing the value of
federal resources and
minimizing duplication



Expanding access to
scientific knowledge
and professional
education



Accelerating the
dissemination and
translation of research



Improving the
health of women
and the nation



LEARN MORE. WATCH. SHARE.

All webinars are available on demand.

https://www.youtube.com/playlist?list=PLr4mqJimfflK_fYFvDa5G-Rqsmu-zqaE-





E-Learning Course: Chronic Conditions in Women

A Practical Guide for Healthcare Providers and Patients



Purpose

- Bridge gaps in provider–patient communication during the clinical encounter
- Improve access to evidence-based women’s health information
- Translate NIH research resources into clinical practice



Course Structure

- 10 paired modules (Provider + Patient tracks)
- Focus on major chronic conditions affecting women:
 - Cardiovascular disease, Diabetes, Chronic pain, Autoimmune diseases, and more



Provider Modules

- Clinically relevant sex differences
- Differences in symptoms and presentation
- Diagnostic considerations
- Treatment implications



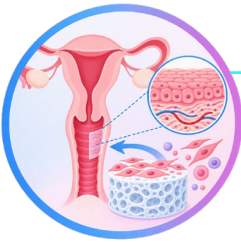
Patient Modules

- Self-awareness of symptoms and risk
- Health literacy support
- Empowerment in clinical interactions

Computational Modeling of Hormone Homeostasis Program Launch

September 14, 2026

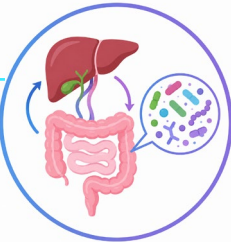
*Enabling sex-specific therapeutic efficacy and toxicity evaluation and
transforming women's health outcomes*



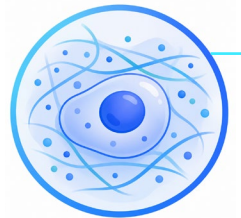
The Virginia Polytechnic Institute team will develop a physics-informed computational model that simulates how vaginal tissue grows, remodels, and responds to mechanical stress across the lifespan.



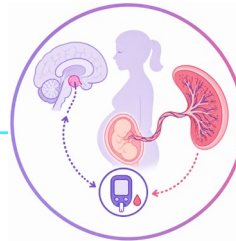
The Michigan State University team will develop an *in silico* platform of female reproductive endocrinology to predict metabolic therapeutic response across the female reproductive lifespan.



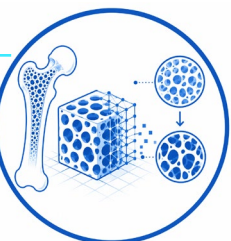
The University of Virginia team will model how the microbiome influences estrogen metabolism and how estrogen is processed and recycled by the body in a connected system linking gut, liver, and vaginal physiology. **Co-funded by the Office of Research Innovation, Validation and Application (ORIVA)*



The Montana State University team will develop a computational model of articular chondrocytes to understand how differences in male and female metabolism produce specific proteins and unintended off target drug effects.



The Morgan State University team will develop a digital twin of the hypothalamus, placenta, and gastrointestinal tract for pregnant women.



The University of California, San Francisco team will model how hormone homeostasis in both males and females influences skeletal responses to osteoporosis therapies and endocrine treatments.



Division of Program Coordination, Planning, and
Strategic Initiatives
Office of Research on Women's Health



THANK YOU!



Key Takeaways and Review



- 1 NIH policy is that SABV be factored into research designs, analyses, and reporting in vertebrate animal and human studies.
- 2 NIH/ORWH developed a multidimensional framework that examines how intersecting factors affect women's health across the life course.
- 3 Midlife marks a pivotal moment with the onset of chronic conditions among women.
- 4 Multimorbidity is more common in women, but interactions between conditions are poorly understood in women.



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THANK YOU. QUESTIONS?