

Advancing Research on Chronic Conditions in Women



*Committee on a Framework for the
Consideration of Chronic
Debilitating Conditions in Women*

Advancing Research on Chronic Conditions in Women



Consensus Study Report

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Office of Research on Women's Health



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Statement of Task



An ad hoc committee of the National Academies of Sciences, Engineering, and Medicine will:

- **Review the existing literature** on chronic debilitating conditions specific to women.



The review will consider:

- The **epidemiology** of chronic debilitating conditions including gender and racial and ethnic differences in clinical presentation and outcomes
- How the development and accumulation of chronic debilitating conditions in women are influenced by factors such as **menopause, aging-related skeletal muscle dysfunction** (loss of muscle mass, muscle strength, and muscle function), and **frailty**
- **Prevention, diagnosis, and treatment** of female-specific gynecologic conditions
- To the extent possible, the **social and economic impact** of chronic debilitating conditions.
- Assemble **evidence-based findings** on chronic debilitating conditions in women.
- The findings should incorporate the influence of **social determinants of health**, including but not limited to gender, race and/or ethnicity, socioeconomic status, sexual and gender minorities, and underserved rural populations.
- Produce a report that describes **current gaps**

Committee's Approach

Selection of Chronic Conditions



Statement of Task specifies **female-specific gynecologic** conditions and **aging-related skeletal muscle dysfunction**



Committee referred to conditions included in **NIH's Office of Research on Women's Health (ORWH)** framework



Committee considered **lived experiences** shared during information gathering sessions



Committee sought to include an array of conditions representing those the SOT specified

- female-specific and gynecologic conditions
- conditions related to skeletal/muscle dysfunction,
- conditions that predominately impact or affect women differently



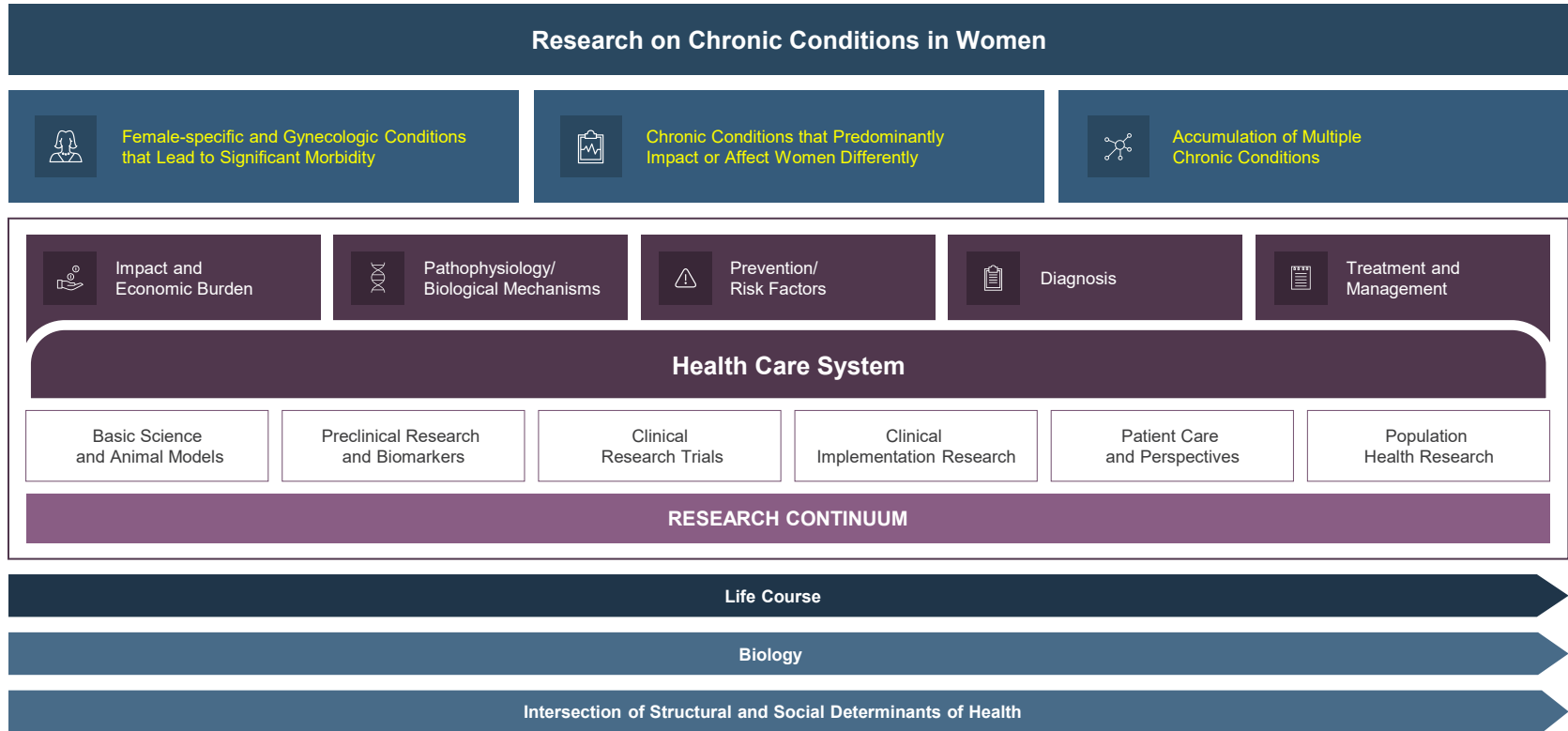
Substance use disorder and HIV included because they impact women differently

Committee's Approach

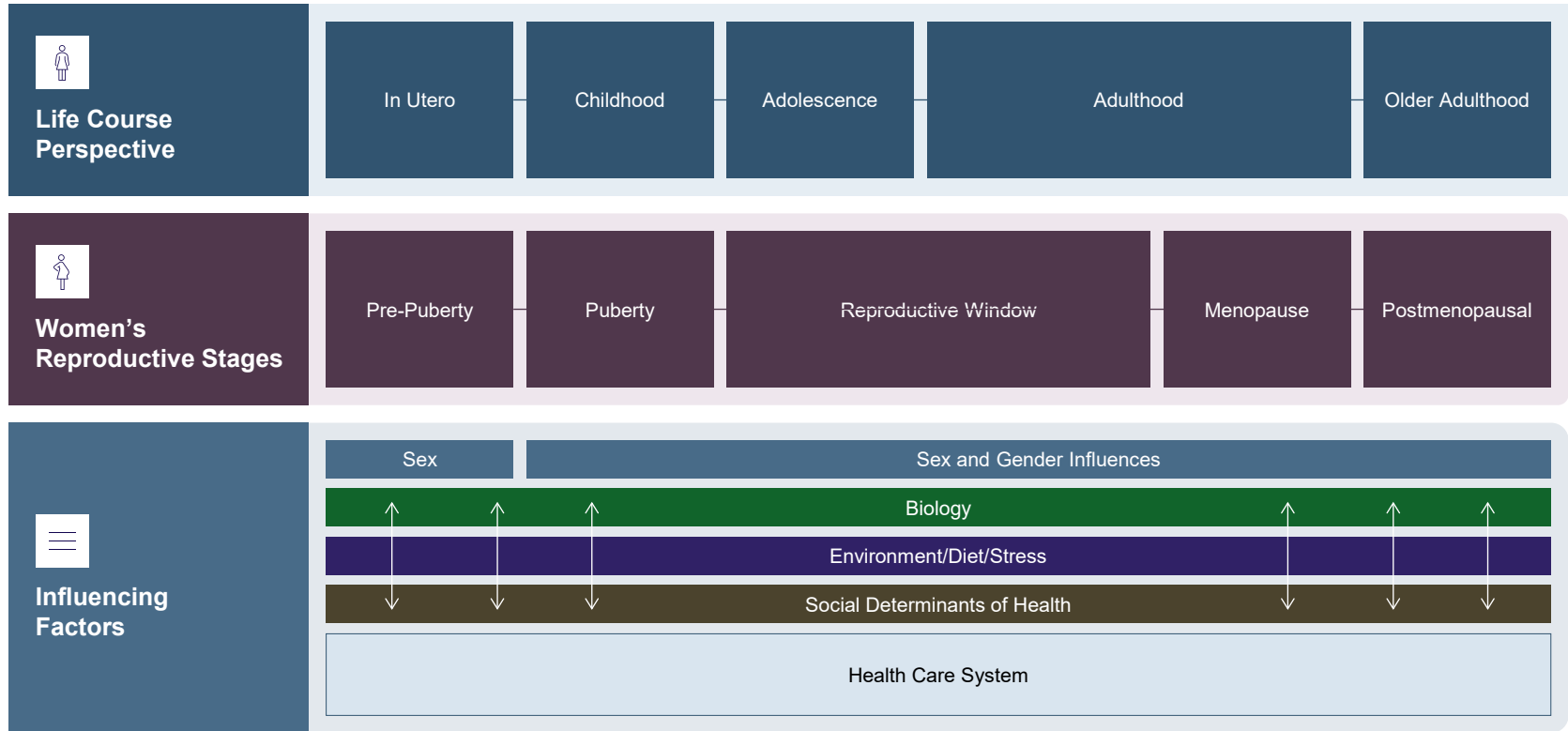
Chronic Conditions Reviewed in this Report

Box S-1 Chronic Conditions Reviewed in the Report	
Female-Specific and Gynecologic¹ Endometriosis/dysmenorrhea/chronic pelvic pain Uterine fibroids Infertility Vulvodynia Pelvic floor disorders (including urinary incontinence and pelvic organ prolapse) Menopausal symptoms (including exogenous hormone use)	Pain Disorders Migraine/headache Chronic pain Fibromyalgia Myalgic encephalomyelitis/chronic fatigue syndrome
Autoimmune Diseases Systemic lupus Multiple sclerosis (also affects the neurocognitive system)	Cardiometabolic Disease Cardiovascular disease Stroke Metabolic (Type 2 diabetes, metabolic syndrome, obesity)
Musculoskeletal Osteoporosis Sarcopenia	Mental Health Depression Substance use disorder
Neurocognitive Alzheimer's disease	Infectious Disease Human immunodeficiency virus

The Committee's Conceptual Framework



Factors that Contribute to Chronic Conditions in Women



Key Report Definitions



Chronic
Conditions



Sex
and Gender



Woman



Structural and Social
Determinants of Health

Report Definitions

Chronic Conditions



The committee refers to “**chronic conditions in women**”:

Conditions that last 1 year or more and require ongoing medical attention or limit self-care, independent living, social interactions, or quality of life*



The committee chose to remove the word “debilitating,” as it may negate the experiences of women who live with chronic conditions and have developed coping mechanisms that help them function more fully.

* Source: HHS (U.S. Department of Health and Human Services). 2010. *Multiple chronic conditions—a strategic framework: Optimum health and quality of life for individuals with multiple chronic conditions*. Washington, DC: U.S. Department of Health and Human Services.

Report Definitions

Women, Sex and Gender



Women:

Any individual who considers themselves to be a **woman** or was **assigned female sex** at birth



Sex and Gender:

Biological differences are generally classified as **sex** differences, whereas those associated with the social environment are considered **gender** differences.

Report Definitions

Structural and Social Determinants of Health

Structural determinants of health:

“Macrolevel factors, such as laws, policies, institutional practices, governance processes, and social norms that shape the distribution (or maldistribution) of the social determinants of health across and within social groups.”*

Social determinants of health:

Conditions in which people are born, grow, work, play, worship, live, and age, along with the wider set of forces and systems shaping the conditions of daily life.
These are grouped into 5 domains: **education, health access & quality, economic stability, neighborhood & built environment, and social & community context.**

Summary Highlights of Report Recommendations

This report includes (in no order of priority):

→ **10** overarching **conclusions**

→ **18** **recommended areas of research**

Needed to advance research on chronic conditions in women

NATIONAL ACADEMIES Sciences
Engineering
Medicine

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on Chronic Conditions
in Women



Consensus Study Report

Recommendations: A Research Agenda for the Future



The committee identified key research gaps that NIH and other relevant agencies that fund research should support to advance the understanding of chronic conditions in women. Based on the committee's conclusions, it recommends the following areas of research to help fill these gaps.



The **Impact** of Chronic Conditions on Women



Disparities and Life Experiences



Understanding the **Biology and Pathophysiology** of Chronic Conditions in Women



Diagnosis and Treatment



Multiple Chronic Conditions



Female-Specific Factors in the Development of Chronic Conditions



Inequities and Women-Centered Research

Recommendation 1:

The Impact of Chronic
Conditions on Women



Conclusion 1:

Chronic conditions continue to have a significant impact in women. Limited data hinders understanding and underreporting promotes inaccurate findings.

Rec 1.1

NIH and other relevant research agencies should support research to improve estimates of the impact of chronic conditions in women. Specifically, research is needed to more accurately:

- A** Diagnose and reduce misclassification of female-specific and gynecologic conditions
- B** Diagnose chronic conditions that predominantly impact or affect women differently
- C** Characterize differences in chronic condition presentation by gender, race and ethnicity, and the various structural and social determinants that these women experience or are affected by
- D** Assess of the economic impact (direct and indirect) and quality of life

Rec 1.2

NIH and other relevant research agencies should support national surveillance and population-based studies to expand data collection activities to include female-specific and gynecologic conditions and female-predominant conditions not currently included.

Recommendation 2:

The Biology &
Pathophysiology of Chronic
Conditions in Women



Conclusion 2:

Some progress has been made in understanding pathophysiology and biologic mechanisms, but further progress is needed.

NIH AND OTHER RELEVANT RESEARCH AGENCIES SHOULD SUPPORT RESEARCH

Rec 2.1

To understand the independent and interacting roles of gonadal hormones and sex chromosome genes causing sex differences and chronic conditions affecting women more than men.

Rec 2.2

To develop a better understanding of how inflammatory and immune system pathways affect the development of chronic conditions in women and support research to:

- A Understand the basic etiology of female-specific and gynecologic chronic conditions
- B Elucidate the role inflammation and immune system pathways and environmental exposures play in the etiology
- C Elucidate how epigenetic alterations change gene expression as a consequence of exposures to alter cellular function and contribute to the etiology
- D Understand the etiological mechanisms of chronic conditions that include pain

NIH AND OTHER RELEVANT RESEARCH AGENCIES SHOULD SUPPORT RESEARCH

Rec 2.3

To better understand the genetic drivers of subtypes and symptom heterogeneity of female-specific and gynecologic conditions and ensure that databases used in such studies are diverse given subpopulation differences

Rec 2.4

To address the lack of suitable animal models and other preclinical systems for exploring the biological mechanism underlying chronic conditions in women, as well as:

- A** Develop or improve experimental animal models to gain better insights into biological and physiological processes that lead to female-specific and gynecologic conditions
- B** Develop in vitro models, cell systems, organoid systems, and fluidic models to better understand the pathobiology of chronic conditions
- C** Utilize systems biological analysis to understand the interactions of genomes, transcriptomes, proteomes, and epigenomes contributing to chronic conditions
- D** Improve understanding of how sex hormones, sex chromosome genes, and their epigenetic regulators affect the etiology and progression of chronic conditions
- E** Improve understanding of the molecular mechanisms/consequences of prolonged inflammation and the prenatal and maternal environments which alter cellular function and affect chronic conditions

Recommendation 3:

Female-Specific Factors
and Chronic Conditions



Conclusion 3:

Reproductive milestones imposed dramatic changes in a woman's body and functioning can influence the risk of developing certain chronic conditions across the life course.

Rec 3.1

NIH and other relevant research agencies should support research to better understand the exact mechanisms hormonal fluctuations play in the development of chronic conditions in women, as well as:

- A** Elucidate the importance of age of menarche
- B** Understand the role of menstrual cycle regularity/irregularity, length, and menstrual cycle phases over the life course
- C** Understand how the length of the reproductive window, parity, and breastfeeding influence
- D** Understand the link between adverse pregnancy outcomes
- E** Examine the role of migraines during pregnancy and their link to negative pregnancy outcomes
- F** Explore the effect of exogenous hormones
- G** Understand the effects of premature menopause and early menopause, both spontaneous and iatrogenic, on the risk
- H** Better understand and characterize reproductive milestones in racial and ethnic groups of women as well LGBTQIA+ women

Rec 3.2

To develop new and better approaches for addressing the symptoms that affect women during perimenopause, menopause, and postmenopause, NIH and other relevant research agencies should support research to:

- A** Understand the biological mechanisms underlying the timing and the manifestation of menopausal symptoms, including vasomotor symptoms
- B** Improve methods of evaluating and diagnosing perimenopause and menopause
- C** Investigate and evaluate the effectiveness of a range of management and treatment options for treating menopausal symptoms, including pharmacological and nonpharmacological therapies, and preventing future chronic conditions
- D** Examine the relationship between menopause and the risk of developing or exacerbating chronic conditions. Special attention should be given to musculoskeletal conditions that lead to frailty in women
- E** Investigate preventive measures for mitigating the effect of menopause on chronic conditions

Recommendation 4-6:

Disparities &
Life Experiences

Conclusion 4:

Structural and social determinants of health influence the development, progression, and management of chronic conditions in women.

Rec 4: NIH and other relevant research agencies should support research to understand how multiple social identities (race and ethnicity, cultural norms, gender identity, sexual orientation) interact with structural and social determinants of health to influence chronic conditions in women across the life course

Conclusion 5:

Early-life experiences and societal gender expectations may expose women to traumatic events throughout their lives that can adversely affect their health

Rec 5: NIH and other relevant research agencies should support research to explore the role of traumatic experiences as risk factors in the development of chronic conditions throughout the life course

Conclusion 6:

Lifestyle behaviors can decrease the risk of chronic conditions, and chronic condition can minimize the ability to engage in positive lifestyle behaviors. Lifestyle behaviors across the life course are not well studied.

Rec 6: NIH and other relevant research agencies should support research to improve the understanding of the role of lifestyle behaviors on the development of chronic conditions in women

Recommendation 7:

Diagnosis and
Treatment in Women



Conclusion 7:

Women may present differently than men for many chronic conditions.

NIH AND OTHER RELEVANT RESEARCH AGENCIES SHOULD SUPPORT RESEARCH

Rec 7

To improve early and accurate detection and diagnosis of chronic conditions in women, more specifically:

- A** To develop sex- and gender-specific diagnostic tools for conditions in which there are clear differences in the clinical presentation
- B** To develop diagnostic tools that can more accurately distinguish between chronic conditions that share similar symptoms
- C** To explore a multilevel approach to the diagnosis of chronic conditions in women that includes identifying biological markers, developing diagnostic tools that capture variation in symptom manifestation and incorporate the lived experience, and engaging with health systems

Recommendation 8:

Multiple Chronic
Conditions in Women



Conclusion 8:

Women tend to develop multiple chronic conditions across the life course. Standardized definitions and diagnostic approaches are lacking for multiple chronic conditions.

NIH AND OTHER RELEVANT RESEARCH AGENCIES SHOULD SUPPORT RESEARCH:

Rec 8.1

To 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, and support research:

- A** To understand the biological mechanisms involved in the development of multiple chronic conditions in women, including aging-related mechanisms and inflammation
- B** To further investigate the role of cellular senescence in the development of multiple chronic conditions and how reversal or prevention, through senolytic therapies, can potentially delay the development of age-related chronic conditions
- C** To develop animal models that examine the co-occurrence of specific chronic condition groups

Rec 8.2

To improve the diagnosis of multiple chronic conditions in women, including:

- A** To develop new measurement tools for multiple chronic conditions that include female-specific and gynecologic conditions to more fully understand the impact in women
- B** To review and validate diagnostic or measurement tools for multiple chronic conditions to aid in the development of a standardized definition

Rec 8.3

Since research approaches that use single-disease models hinder the ability to understand pathophysiology, treatment, prevention, and management of multiple chronic conditions in women, NIH and other relevant agencies should support:

- A The development of research approaches that appropriately study multiple chronic conditions in women
- B Research that ensures the representation of women with multiple chronic conditions in research designs

Rec 8.4

To improve the treatment and care of women with multiple chronic conditions, research is needed to:

- A Develop evidence-based treatment and management guidelines for women with multiple chronic conditions
- B Examine negative effects of polypharmacy that can contribute to developing other chronic conditions
- C Design tools that incorporate measures of daily functioning and quality of life to improve the assessment of the impact of multiple chronic conditions in women
- D Design and test integrated and longitudinal models of care for women with multiple chronic conditions

Recommendation 9:

Inequities & Women-
Centered Research



Conclusion 9:

A health equity lens is important for improving health care access, care, and outcomes, including patient-centered outcomes in women.

Rec 9

NIH and other relevant research agencies should support research to address inequities that continue to exist for women in the health care setting, specifically:

- A** Elucidate gender differences in access and use of health care services, taking into consideration the effects of structural sexism on health policies, inequities in health resource distribution, and social determinants of health
- B** Develop methods for assessing discrimination encountered by women when accessing health care services for chronic conditions
- C** Assess and validate diagnostic tools for appropriate use in diverse racial and ethnic groups

Recommendation 10:

Inequities and Women-
Centered Research



Conclusion 10:

Women-centric research strategies can help ensure that research activities address the unique health needs of women leading to more effective and equitable health outcomes.

Rec 10:

NIH and relevant funding agencies should support research that is women-centric. Studies should account for sex and gender and include a diversity of women in the research process. Researchers should:

- A** Recruit women from different backgrounds and underserved rural populations to better define the full spectrum of preclinical and clinical disease presentation
- B** Involve women with multiple chronic conditions, including their communities, in the design, implementation, and dissemination of research findings
- C** Use novel techniques for engaging and incorporating women who have yet to seek care due to obstacles in accessing health care services or because conditions are in a preclinical stage
- D** Use community-based research approaches to improve relevance, acceptability, and centering of women's needs and outcomes
- E** Account for sex and gender in studies where appropriate and standardize measures for capturing these variables accurately

Summary: A Research Agenda for the Future



The committee's research agenda aims

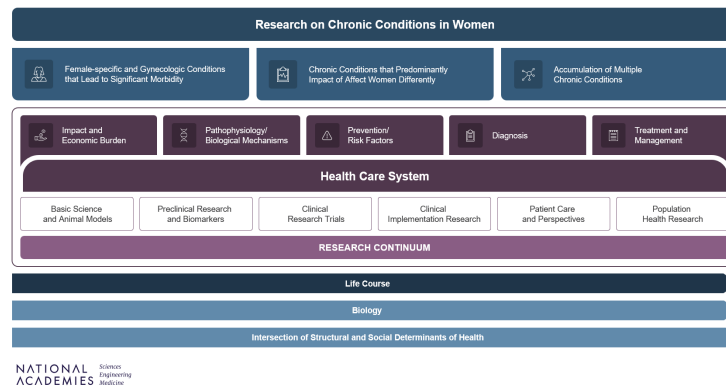
- To bridge gaps in the scientific understanding of the etiology of chronic conditions over the life course and
- the interface of biological and social factors that influence their trajectory.

Ultimately, research outcomes would lead to

- Greater diagnostic rigor,
- better data on the impact of these conditions, and
- more effective therapeutic interventions and woman-centered care.



The Committee's Conceptual Framework



5

To learn more about the Committee or to access the report, please visit:

<https://www.nationalacademies.org/our-work/framework-for-the-consideration-of-chronic-debilitating-conditions-in-women>

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