Women in the United States experience a higher prevalence than men of many chronic conditions, including Alzheimer’s disease, depression, and osteoporosis; however, research has yet to fully explain these differences. Research is also lacking around female-specific conditions, such as endometriosis and pelvic floor disorders. Furthermore, women’s experiences related to these conditions—structural, social, and cultural factors—are poorly understood. All of this greatly hinders diagnosis, treatment, and prevention efforts, thus contributing to poorer health outcomes for women and substantial costs to individuals and for society.

The National Institutes of Health’s (NIH’s) Office of Research on Women’s Health asked the National Academies of Sciences, Engineering, and Medicine to convene a committee to identify current gaps in the science on chronic conditions and propose a research agenda. The resulting report, *Advancing Research on Chronic Conditions in Women*, presents the committee’s conclusions and research recommendations.

The committee reviewed several chronic conditions that are illustrative of female-specific and gynecologic conditions or that predominantly impact or affect women differently (see Box 1).

**CONCEPTUAL FRAMEWORK**

The conceptual framework (see Figure 1) developed by the committee depicts the research continuum, how findings may translate into interventions, and the influence of structural and social determinants of health across the life course.
BOX 1
Chronic Conditions Reviewed in the Report

Female-Specific and Gynecologic
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)

Autoimmune Diseases
Systemic lupus
Multiple sclerosis (also affects the neurocognitive system)

Musculoskeletal
Osteoporosis
Sarcopenia

Neurocognitive
Alzheimer’s disease

Pain Disorders
Migraine/headache
Chronic pain
Fibromyalgia
Myalgic encephalomyelitis/chronic fatigue syndrome

Cardiometabolic Disease
Cardiovascular disease
Stroke
Metabolic (Type 2 diabetes, metabolic syndrome, obesity)

Mental Health
Depression
Substance use disorder

Infectious Disease
Human immunodeficiency virus

Research on Chronic Conditions in Women

Impact and Economic Burden
Pathophysiology/Biological Mechanisms
Prevention/Risk Factors
Diagnosis
Treatment and Management

Basic Science and Animal Models
Preclinical Research and Biomarkers
Clinical Research Trials
Clinical Implementation Research
Patient Care and Perspectives
Population Health Research

Life Course
Biology
Intersection of Structural and Social Determinants of Health

FIGURE 1 The committee’s conceptual framework for organizing this report.
A RESEARCH AGENDA TO ADVANCE THE UNDERSTANDING OF CHRONIC CONDITIONS IN WOMEN

The committee identified several research gaps in prevention, diagnosis, treatment, and management of chronic conditions. The research agenda directs NIH and other relevant agencies to take actions, including measuring the impact and economic burden of chronic conditions in women; studying the biological pathways; the role of female-specific factors such as reproductive milestones, life experiences, trauma, and lifestyle behaviors; developing better diagnostic tools specific to women; studying multiple chronic conditions; researching the impact of inequities; and supporting more women-centric research.

Data to Improve Understanding of the Impact of Chronic Conditions in Women

Limited data on chronic conditions hinders a comprehensive understanding of their impact on women. Many chronic conditions are understudied in women, and national surveillance systems do not capture or publish data on female-specific and gynecologic conditions (see Conclusions 1 and 1.2 in the report). Therefore, the report recommends research to:

- Improve estimates of the impact of and expand data collection on chronic conditions that are female-specific and gynecologic, and that predominantly impact or affect women differently. Research should characterize and report differences in chronic condition presentation by gender, race and ethnicity, sexual orientation, and the various structural and social determinants as well as assess their economic impact (see Recommendations 1.1 and 1.2 in the report).

Sex-Specific Biological Research Focused on Women

Understanding the biology of chronic conditions is imperative for diagnoses and developing treatment and prevention strategies. Some progress has been made—but further progress is needed (see Conclusion 2 in the report). Therefore, the report recommends supporting research to:

- Understand the independent and interacting roles of gonadal hormones and sex chromosome genes that cause sex differences (see Recommendation 2.1 in the report).

- Understand the causes of female-specific and gynecologic conditions as well as conditions that present with pain and how chronic conditions are affected by inflammation, immune system, and environmental exposures that can lead to changes in gene expression (see Recommendation 2.2 in the report).

- Understand the genetic drivers of differing symptoms for female-specific and gynecologic conditions, including ensuring that the data supporting such research are diverse (see Recommendation 2.3 in the report).

- Develop and improve existing animal models for understanding physiological processes in female-specific and gynecologic conditions; develop preclinical systems (in vitro models, cell systems, omics); and improve understanding of molecular consequences of prolonged inflammation and the prenatal and maternal environments (see Recommendation 2.4 in the report).

Reproductive Milestones Research from Menarche to the Menopause Transition

Reproductive milestones throughout the life course—including menstruation, pregnancy, and menopause—play a large role in the development of chronic conditions; however, significant knowledge gaps exist in how they impact such conditions (see Conclusion 3 in the report). Therefore, the report recommends research to:

- Better understand how specific reproductive milestones, including the menstrual cycle, adverse pregnancy outcomes, and premature/early menopause, affect chronic conditions as well as characterize these in racial and ethnic groups and LGBTQIA+ women (see Recommendation 3.1 in the report).
• More effectively address biology, prevention, evaluation, and treatment of symptoms during perimenopause, menopause, and post-menopause and the relationship between menopause and chronic conditions (see Recommendation 3.2 in the report).

Research on Trauma, Social Identities, and Structural and Social Determinants of Health

Health disparities exist within chronic conditions that impact women. Structural and social determinants of health (see Conclusion 4 in the report); lifestyle behaviors (see Conclusion 6 in the report); and early life experiences, societal gender expectations, and trauma (see Conclusion 5 in the report) are poorly understood and can significantly impact condition onset, symptoms, and duration. The report recommends research to:

• Understand how various social identities interact with structural and social determinants of health to influence chronic conditions in women (see Recommendation 4 in the report).

• Explore the role of traumatic experiences as risk factors in women (see Recommendation 5 in the report).

• Investigate how health-promoting lifestyle behaviors can influence and be influenced by chronic conditions, as well as their interactions with structural and social determinants of health (see Recommendation 6 in the report).

Research to Enhance Sex- and Gender-Specific Diagnostic Tools

Women may have different chronic condition presentation than men, and failure to differentiate symptoms by sex and gender can contribute to misdiagnosis or underdiagnosis (see Conclusion 7 in the report). Therefore, the report recommends research to:

• Develop diagnostic tools that are sex- and gender-specific, that can distinguish conditions with similar symptoms, and explore a multilevel approach to diagnosing chronic conditions in women that incorporate the patient lived experience (see Recommendation 7 in the report).

Research on Multiple Chronic Conditions in Women

Women tend to develop multiple chronic conditions, but research studying single diseases is prioritized, limiting understanding around etiology, diagnosis, treatment, and care. Studies of multiple chronic conditions have been hampered by a lack of existing standardized definitions and diagnostic approaches (see Conclusion 8 in the report). Therefore, the report recommends supporting research to:

• Understand the biological pathways involved in developing multiple chronic conditions related to aging (cellular senescence) and inflammation and develop animal models that examine co–occurrence of chronic conditions (see Recommendation 8.1 in the report).

• Develop measurement tools, including those incorporating female–specific and gynecologic conditions, and review and validate tools to aid in the development of a standardized definition (see Recommendation 8.2 in the report).

• Develop approaches that appropriately study multiple chronic conditions and ensure the representation of women with multiple chronic conditions in studies (see Recommendation 8.3 in the report).

• Develop evidence–based treatment and management guidelines for women with multiple chronic conditions, examine how negative effects of polypharmacy contribute to other chronic conditions, design tools to improve daily functioning and quality of life, and integrate longitudinal models of care for women with multiple chronic conditions (see Recommendation 8.4 in the report).

Centering Women to Address Disparities in Health Care Access and Research

A health equity lens is critical as inequities in care arise from gender biases and structural sexism (see Conclusion 9 in the report), which can result in negative outcomes such as dismissal of symptoms, underdiagnosis, or misdiagnosis. In addition, women–centric research strategies can help ensure more effective and equitable
health outcomes (see Conclusion 10 in the report). To address these issues, the report recommends research to:

- Understand gender differences in access and use of health care services, including how structural sexism influences health policies; develop methods for assessing various forms of discrimination encountered by women; and assess and validate diagnostic tools to be appropriately used in diverse racial and ethnic groups (see Recommendation 9 in the report).

- Recruit and engage women from diverse backgrounds and populations, including those with multiple chronic conditions; use novel techniques for incorporating women who have not yet sought care due to obstacles in accessing health care services or because their conditions are in a preclinical stage; use community-based research approaches; and account for sex and gender in studies where appropriate (see Recommendation 10 in the report).

The committee’s research agenda aims to bridge gaps in the scientific understanding of the etiology of chronic conditions and the interface of biological and social factors that influence the trajectory of these conditions. Ultimately, research outcomes would lead to greater diagnostic rigor, better data on the impact of these conditions, more effective therapeutic interventions, and woman-centered care that will benefit women, families, and communities.

To learn more about this report, visit www.nationalacademies.org/chronic-conditions-in-women.