### NIH FACT SHEETS ON Women's Health Research





# Table of Contents

Introduction	2
NIH ICO Funding Code Abbreviations	3
Autoimmune Diseases and Women's Health	ŧ
Cancer and Women's Health6	5
Cardiovascular Disease and Women's Health	3
Dementia and Women's Health	)
HIV and Women's Health	2
Maternal Morbidity and Mortality14	ł
Menopause	5
Mental Health and Women's Health	3
Substance Misuse, Substance Use Disorder, and Women's Health	)
Violence Against Women and Trauma22	2
Selected Women's Health NIH Activities—FY22 and FY2324	ļ
References	5



### | Introduction

This collection of **NIH Fact Sheets on Women's Health Research** provides health and disease data on women with relevant discussions of how sex and/or gender differences and female-specific considerations may play a role in shaping the health status of women. The health and disease topics were selected given their alignment with key issues of morbidity and mortality for women.

The fact sheets outline the state of the science for women's health on autoimmune diseases, cancer, cardiovascular disease, dementia, HIV, maternal morbidity and mortality, menopause, mental health, substance use disorder, and violence against women and trauma. Accompanying health- and disease-specific discussions, scientific gaps and opportunities for further study, and current National Institutes of Health (NIH) activities (e.g., active projects, programs, collaborations, and initiatives) are highlighted.

These fact sheets are a product of the NIH Coordinating Committee for Research on Women's Health. The women's health research funding data and figures included were derived in collaboration with the NIH Office of Extramural Research (OER), using draft Fiscal Year 2023 Research, Condition, and Disease Categorization (RCDC) data. Taken together, these fact sheets characterize the women's health research landscape and identify opportunities for interdisciplinary and multifaceted research strategies to address women's health research topics.

### **NIH ICO Funding Code Abbreviations**

Funding data for the fact sheets are displayed using NIH institute, center, and office (ICO) abbreviations. The abbreviations within the fact sheet are detailed below:

<u>FIC</u>	NIH Fogarty International Center
<u>NCATS</u>	National Center for Advancing Translational Sciences
NCCIH	National Center for Complementary and Integrative Health (formally NCCAM)
<u>NCI</u>	National Cancer Institute
<u>NEI</u>	National Eye Institute
<u>NHGRI</u>	National Human Genome Research Institute
<u>NHLBI</u>	National Heart, Lung, and Blood Institute
<u>NIA</u>	National Institute on Aging
<u>NIAAA</u>	National Institute on Alcohol Abuse and Alcoholism
NIAID	National Institute of Allergy and Infectious Diseases
<u>NIAMS</u>	National Institute of Arthritis and Musculoskeletal and Skin Diseases
<u>NIBIB</u>	National Institute of Biomedical Imaging and Bioengineering
NICHD	<i>Eunice Kennedy Shriver</i> National Institute of Child Health and Human Development
<u>NIDA</u>	National Institute on Drug Abuse
NIDCD	National Institute on Deafness and Other Communication Disorders

<u>NIDCR</u>	National Institute of Dental and Craniofacial Research
<u>NIDDK</u>	National Institute of Diabetes and Digestive and Kidney Diseases
<u>NIEHS</u>	National Institute of Environmental Health Sciences
<u>NIGMS</u>	National Institute of General Medical Sciences
<u>NIMH</u>	National Institute of Mental Health
<u>NIMHD</u>	National Institute on Minority Health and Health Disparities
<u>NINDS</u>	National Institute on Neurological Disorders and Stroke
<u>NINR</u>	National Institute of Nursing Research
<u>NLM</u>	National Library of Medicine
<u>OADR-</u> <u>ORWH</u>	Office of Autoimmune Disease Research in the Office of Research on Women's Health
<u>OAR</u>	Office of AIDS Research
<u>OBSSR</u>	Office of Behavioral and Social Sciences Research
<u>OD</u>	Office of the Director, NIH
<u>ODP</u>	Office of Disease Prevention
<u>ORWH</u>	Office of Research on Women's Health



## Autoimmune Diseases and Women's Health

**Background:** Autoimmune diseases are characterized by the immune system erroneously attacking self-antigens, cells, and/ or organs. Common autoimmune diseases include rheumatoid arthritis (RA), psoriasis, systemic lupus erythematosus (SLE), multiple sclerosis, inflammatory bowel disease, and type 1 diabetes.

- Autoimmune diseases encompass an estimated 80–150 conditions and affect approximately 5–8% of the population, an estimated 25–31 million Americans.<sup>1,2,3</sup>
- Autoimmune diseases are the third most common category of diseases in the U.S., after cancer and cardiovascular disease.
- Of the patients diagnosed with autoimmune disease, 80% are women.<sup>1,2,4</sup>
- Prolonged latency periods challenge efforts to identify potential exposures or other etiologies that contribute to disease pathogenesis.<sup>5,6</sup>

• Large population-based cohorts have shown an increasing prevalence of autoimmune diseases over time.<sup>7</sup>

Specific considerations relevant to women's health: Many autoimmune diseases are more prevalent in women; however, the exact cause of this increased prevalence is not fully understood. Several female-specific factors are thought to contribute to the increased prevalence of autoimmune disorders among women. Hormonal and physiological changes, such as the onset of puberty, pregnancy, and menopause, can increase the risk and/or severity of systemic autoimmune conditions.<sup>8,9</sup> Pregnancy represents a unique immunologic state in which tolerance of the fetus must be balanced with preservation of the maternal immune system.<sup>10</sup> During pregnancy, autoimmune disease may wax or wane-for example, RA improves substantially in most patients, whereas SLE is associated with several complications of pregnancy including preeclampsia.<sup>11</sup> Sex differences in immune cell responses leading to differences in immune biology in women may contribute to the higher rates of autoimmune disease in

women.<sup>2,12</sup> In female XX mammalian cells. the Xist long noncoding RNA randomly inactivates one of the X chromosomes, where a significant number of immunerelated genes are located.<sup>13</sup> Escape from inactivation leads to mosaicism of the female X-chromosome resulting in significant sex differences in the immune system.14,15 Environmental and occupational exposures (e.g., smoking, sunlight, contact with chemicals) vary by gender and may drive or accentuate sex differences through changes in hormonal or epigenetic effects.<sup>1</sup> Exposure to vicarious racism may result in heightened disease activity and contribute to racial disparities in SLE.<sup>16</sup>

### Scientific gaps and opportunities: In 2022, a National Academies of Sciences, Engineering, and Medicine report identified specific research gaps across and within autoimmune diseases that include diagnostics, therapeutics, and outcomes.<sup>2</sup> The heterogeneity across and within autoimmune diseases continues to challenge surveillance

FY23 Women's Health Funding: Autoimmune Disease



The women's health funding figures included in these Fact Sheets were derived with assistance from the Office of Extramural Research using draft RCDC data.

efforts and hampers our understanding of disease-specific pathogenic mechanisms. Further investigation of factors that contribute to autoimmunity, such as etiologic factors (including hormones, genetic factors, environmental factors, and the microbiome) require the use of a matrixed approach so that complex interactions can be studied fully. Interventions to reduce disparities in access to care and therapeutic options for autoimmune diseases are also needed.

**Current NIH activities:** Currently, multiple NIH institutes, centers, and offices (ICOs) support autoimmune research, in alignment with their individual mission areas, which has led to significant advances in autoimmune disease research across multiple disease areas. NIH spending across autoimmune disease and women's health totaled \$241 million in Fiscal Year (FY) 2023. The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institute of Allergy and Infectious Diseases (NIAID), and National Institute of Dental and Craniofacial Research supported the largest proportions of women's health funding in autoimmune diseases. NIAID supports the <u>Autoimmunity Centers of Excellence (ACE)</u> to encourage and enable collaborative research to identify improvements in treatments for autoimmune diseases, evaluate the safety and efficacy of treatment strategies for autoimmune diseases, and explore the immune mechanisms underlying the agents evaluated in ACE clinical trials. NIH's recently established Office of Autoimmune Disease Research (OADR) in the Office of Research on Women's Health (ORWH) is focused on identifying emerging areas of innovation and fostering collaboration across NIH ICOs to support high-priority autoimmune disease research. In developing an NIH-wide Strategic Plan for Autoimmune Disease Research, OADR-ORWH will collaborate across ICOs to identify opportunities for synergistic innovation, focused on areas of autoimmune disease research, that will benefit from multi-ICO partnerships and opportunities to catalyze cross-cutting research.

In FY23, OADR-ORWH supported a total of 41 awards across 12 individual ICOs. These awards included 15 extramural co-funding awards, 3 R56 bridge funding awards, 2 Accelerating Medicines Partnership® Autoimmune and Immune-Mediated Diseases (AMP® AIM) awards, 10 intramural co-funding awards, 5 intramural scientific fellowships, and 6 EXposome in Autoimmune Disease Collaborating Teams PLANning (EXACT-PLAN) awards. The EXACT-PLAN program (NOT-OD-23-112) was developed in partnership with NIAMS, the National Institute of Environmental Health Sciences, ORWH, and other ICO collaborators and supports the design, development, and implementation of a future national, interdisciplinary, collaborative, team science research network that will advance the study of the exposome in autoimmune disease.

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### Cancer and Women's Health

**Background:** Cancer develops when cells in the body grow uncontrollably and become capable of spreading to other sites within the body. More than 1.6 million new cancer cases and 600,000 cancer deaths are reported yearly in the U.S.<sup>17</sup>

- A lifetime cancer diagnosis is more common among men than women (42% vs. 40%); higher cancer incidence is seen in men across disease sites, except thyroid and gallbladder.<sup>18,19</sup>
- Breast cancer is the most common malignancy among women; lung cancer is the most common cause of cancer death among women; and breast, lung, and colorectal cancers account for over half of all new cancer diagnoses among women.<sup>18</sup>
- More than 110,000 women per year are diagnosed with a gynecologic cancer, the most common of which are cancers of the uterus, and the most lethal of which is ovarian cancer.<sup>18</sup>
- Recent declines in incidence and mortality have been larger in men compared to women.<sup>18</sup>

Specific considerations relevant to women's health: Sex differences in molecular and genomic alterations have been described across cancer disease sites in specific genes, including actionable mutations such as mismatch repair (MMR) genes, and mutation signatures.<sup>20,21</sup> Gonadal steroid hormones alter cancer risk and outcomes, and hormonal modulation is a common component of cancer therapy.<sup>22</sup> Although the influence of circulating estrogen, progesterone, and androgens is primarily implicated in cancers of reproductive organs, these hormones influence tumor vasculature, stroma, and other aspects of the tumor microenvironment.<sup>23,24</sup> Total body water, lipid composition, and metabolism influence the pharmacodynamic and pharmacokinetics of anticancer agents, potentially altering efficacy and adverse events, which have been demonstrated to be 34% more likely among women compared to men.<sup>25,26</sup> Distinct sex-specific immune features across multiple cancer types as well as differences in response and adverse events with immune-oncology treatments have been demonstrated.<sup>25,27</sup> Significant diagnostic delays for women have been demonstrated in non-sex-specific disease sites.<sup>28</sup> Breast, endometrial, and cervical cancer are three of the five disease

sites with the largest racial disparities in mortality, suggesting overlapping influences of multiple social factors in outcomes for female-specific cancers. As a result of an aging population, obesity epidemic, and decreasing rates of hysterectomy for benign disease, the incidence of endometrial cancer has risen dramatically.<sup>29</sup> Cancers of the uterine corpus are the only cancer disease site for which survival has decreased over the past 4 decades.<sup>30</sup>

Scientific gaps and opportunities: Lung cancer diagnoses have been rising in women, while dropping in men. In fact, when adjusted for smoking, women are more likely to develop lung cancer; although men continue to be more likely to smoke.<sup>31</sup> Specific factors have limited improved outcomes in gynecologic cancers. Federal cancer registry datasets do not adjust for hysterectomy, limiting estimates of the population at risk for gynecologic cancers. Despite the availability of population-wide screening

#### FY23 Women's Health Funding: Cancer



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since the 1950s and a human papillomavirus (HPV) vaccination since 2006, 13,820 patients are expected to be diagnosed with cervical cancer in 2024.<sup>18</sup> Over half of those patients diagnosed will have never been screened. Furthermore, one-quarter of patients with an abnormal cervical cancer screening test do not receive adequate, timely follow-up.<sup>32</sup>

**Current NIH activities:** NIH spending for women's health categorized as cancer research totaled \$1.7 billion in Fiscal Year 2023. The National Cancer Institute (NCI) supported the largest amount of research categorized as women's health and cancer, followed by the National Heart, Lung, and Blood Institute and the National Institute of Environmental Health Sciences. NCI supports research across the cancer continuum, from basic and translational research to clinical and population science studies on all types of cancer, including cancers that are female specific or primarily affecting women. A cornerstone of NCI's translational research program are the <u>Specialized Programs of Research Excellence (SPORE)</u> awards that support the translation of novel scientific discoveries into clinical testing, including early-phase clinical trials. NCI currently supports seven breast cancer, six ovarian cancer, one endometrial cancer, and one cervical cancer SPORE(s). As part of NCI's National Clinical Trials Network, monthly steering committee meetings address the design, prioritization, and evaluation of concepts for Phase II and III clinical trials in adult <u>gynecologic</u> and <u>breast</u> cancers. Women, however, are underenrolled in U.S. cancer clinical trials compared to men (42.9% of participants in oncology clinical trials between 2000 and 2020 despite having 46.5% of the burden).<sup>33</sup> NCI hosted an <u>endometrial cancer clinical trials planning meeting</u> in 2024. Multiple NCI activities support improved implementation and efficacy of cervical cancer screening and prevention. <u>The Last Mile Initiative</u> is a public–private partnership that aims to validate self-sampling-based HPV testing. As part of the Initiative, NCI launched a nationwide, multicenter screening trial, <u>Self-sampling for HPV testing to Improve cervical cancer Prevention (SHIP)</u>.



# Cardiovascular Disease and Women's Health

**Background:** Cardiovascular disease (CVD) is a leading cause of mortality and morbidity in the U.S.<sup>34</sup> CVD mortality rates declined in both men and women between 2000 and 2010, but decreased at a slower pace for women of reproductive age than for other groups.<sup>35,36</sup> Since 2010, a trend of increasing numbers of CVD deaths in both men and women has raised concerns.<sup>37</sup> Disparities in cardiovascular risk indices, prevalence, and mortality by sex, race, ethnicity, education level, socioeconomic status, and geographic location are pervasive.<sup>36</sup>

- Heart disease is the leading cause of death for women in the U.S.
- More than 60 million women (45%) in the U.S. are living with CVD including hypertension.

- Hypertension is often underdiagnosed in women; only 23% of women with high blood pressure have their condition well controlled.<sup>38</sup>
- The symptoms of myocardial infarction are often reported as "atypical" in women—that is, rather than crushing chest pain, symptoms more frequently include back pressure, dizziness, or nausea.

**Specific considerations relevant to women's health:** Unique sex-specific factors influence risk, diagnosis, and progression of CVD among women. Women are more likely to have medical conditions such as anemia that are associated with increased risk of CVD. Even when adjusted for body size, women have smaller coronary artery diameters, which has been postulated to influence increased morbidity and mortality in female

patients undergoing coronary artery bypass graft and percutaneous coronary intervention.<sup>39</sup> Protective effects of estrogen on the vascular system include vasodilation, by activating the transcription of Enos, regulation of remodeling of the extracellular matrix, and promotion of revascularization following ischemic injury.<sup>40</sup> Cardiovascular conditions, including hypertensive disorders of pregnancy (HDP) and peripartum cardiomyopathy (PPCM), are leading causes of pregnancy-related deaths.<sup>41</sup> Treatment of mild chronic hypertension has been demonstrated to improve pregnancy outcomes without negative effects.<sup>42</sup> The CVD risk associated with HDP persists beyond the pregnancy period. Women with HDP have a 3.7-fold increase in the risk of chronic hypertension, a 4.2-fold increase in the risk of heart failure, an 81% increase in the risk of stroke, and

FY23 Women's Health Funding: Cardiovascular Disease



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double the risk of atrial arrhythmias, coronary heart disease, and cardiomyopathy when compared to women without HDP.<sup>43,44</sup> Social and cultural factors such as diet, physical safety, exposure to air pollution, and accessibility of physical exercise also influence the lifetime cardiovascular health of women.<sup>45,46</sup> Racial disparities are pronounced for Black women, for whom worse CVD outcomes have been associated with a higher burden of modifiable risk factors and clinical comorbidities.<sup>47</sup>

**Scientific gaps and opportunities:** Although women have a lower prevalence of CVD than men, they have worse prognoses after experiencing an acute cardiovascular event. Research about the underlying pathophysiology is limited. Certain cardiovascular conditions, such as myocardial infarction with non-obstructive coronary arteries (MINOCA), ischemia and no obstructive coronary arteries (INOCA), heart failure with preserved ejection fraction (HfpEF), and Takotsubo cardiomyopathy disproportionately affect women. Additional research that considers sex and gender differences in CVD risk, diagnosis, treatment, and outcomes is warranted. There are also knowledge gaps on the role of reproductive health conditions, including polycystic ovary syndrome, and factors such as early age of menarche, use of contraceptives, and early onset of menopause in the development of CVD in women across the lifespan.<sup>48</sup> Effective interventions to prevent cardiovascular complications during and after pregnancy and subsequent CVD should be identified. Long-term analyses of the <u>Women's Health Initiative (WHI)</u> suggest that the risk-to-benefit ratio of menopausal hormone therapy (MHT) in preventing cardiovascular disease differs based on the age at which MHT is prescribed, requiring a more nuanced understanding of optimal formulations, doses, and treatment duration.<sup>49</sup> Opportunities exist to interrogate and address the intersections of CVD, mental health, and alcohol and substance use in women across the life course.

**Current NIH activities:** NIH spending for women's health characterized as CVD research totaled \$506 million in Fiscal Year (FY) 2023. The National Heart, Lung, and Blood Institute (NHLBI), National Institute on Aging (NIA), and *Eunice Kennedy Shriver* National Institute of Child Health and Human Development supported the largest amounts of women's health and CVD funding. NHLBI, with co-funding from the National Institute on Minority Health and Health Disparities, National Institute of Diabetes and Digestive and Kidney Diseases, Office of Disease Prevention, Office of Behavioral and Social Sciences Research, and Office of Research on Women's Health, launched the <u>Early Intervention to Promote Cardiovascular Health of Mothers and Children (ENRICH)</u> program in FY22. This multisite clinical trial will test the effectiveness of an implementation-ready intervention delivered within the context of a home visiting program in enhancing cardiovascular health in the maternal–child dyad. NHLBI's <u>REBIRTH</u> trial is evaluating the impact of bromocriptine therapy on myocardial recovery and clinical outcomes in women diagnosed with PPCM. Current observational studies after pregnancy include the <u>CHAP Maternal Follow-up Study</u>, which is assessing whether antihypertensive therapy during pregnancy for mild chronic hypertension reduces the development of subsequent CVD. Investigation into the risks of <u>cardiotoxicity</u> resulting from breast cancer therapies are ongoing. CVD outcomes continue to be assessed in older women in NHLBI's ongoing <u>WHI</u> and NIA's <u>Study of Women's Health Across the Nation (SWAN)</u>.



### Dementia and Women's Health

**Background:** Dementia is the loss of cognitive functioning thinking, remembering, and reasoning—to such an extent that it interferes with a person's daily life and activities and occurs mainly in people aged 65 and older.<sup>50</sup> Alzheimer's disease (AD) is the most common type of dementia.

- AD is the fifth leading cause of death for women in the U.S.<sup>51</sup>
- Over two-thirds of the 6 million people aged 65 and older with AD are women.<sup>52</sup>
- One in five women are at risk for AD, compared to 1 in 10 men.<sup>52</sup>
- Approximately two-thirds of caregivers of people with AD and AD Related Dementias (AD/ADRD) are women.<sup>52</sup>

**Specific considerations relevant to women's health:** The higher lifetime risk of dementia for women is primarily attributable to women having a greater life expectancy compared to men.<sup>53</sup> Several sex-specific factors have been implicated in the risk, progression, and outcomes of AD in women.<sup>53,54</sup> Premenopausal surgical menopause and the resultant abrupt decline in

estrogen have been associated with accelerated aging including an increased risk of dementia.<sup>55</sup> Interactions of estrogen with APOE4, the strongest genetic risk factor for AD, are associated with the development of dementia.<sup>54</sup> Recent evidence of the "timing hypothesis" of menopausal hormone replacement suggests that estrogen therapy initiated during the menopausal (as opposed to the postmenopausal) transition may reduce the risk of dementia.<sup>56,57</sup> Social and structural factors also influence dementia risk and outcomes for women. For example, women are more likely than men to live in poverty and experience wage gaps and limited availability of caregiving supports—chronic stressors that increase the susceptibility of the aging brain to cognitive decline and other neuropathologic insults.<sup>53,58</sup>

Scientific gaps and opportunities: Although women are enrolled at equal rates to men in dementia-related clinical trials, their representation remains proportionately low compared to the number of women with a dementia diagnosis. The <u>Alzheimer's</u> <u>Disease Preclinical Efficacy Database (AlzPed)</u> includes sex as a biological variable as one of nine core design elements to promote rigor for preclinical AD research. Sex-disaggregated

efficacy and safety outcomes have been infrequently reported. Needed is additional research on sex differences and female-specific etiologies, prevention, and treatment strategies for AD specific to women, and on the intersection of AD with age-related health conditions, to which older women are vulnerable.<sup>59</sup> A better understanding of how gender, as a social and structural construct, contributes to AD/ADRD risk and outcomes, particularly in sexual and gender minority populations and in different ethnic and racial populations, is needed. Women have significantly different caregiving needs compared to men, and novel approaches to the delivery of AD care also are warranted.

**Current NIH activities:** NIH spending for AD/ADRD specific to women's health totaled \$196 million in Fiscal Year (FY) 2023. AD/ADRD research activities are primarily led by the National Institute on Aging (NIA), National Institute of Neurological Disorders and Stroke, and National Heart, Lung, and Blood Institute (NHLBI). Women represent 53–60% of

FY23 Women's Health Funding: Dementia



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participants included in AD-related research, lower than the percentage of women in the underlying dementia population.<sup>59</sup> NIA and NHLBI support the <u>WHI Memory Study (WHIMS</u>), an ancillary study to the <u>WHI Hormone Trials</u>, which is enrolling women aged 65 and older and investigating the effects of menopausal hormone therapy on age-related changes in cognition. Measures of cognitive function have been obtained annually from participants enrolled in the <u>Study of Women's Health Across the Nation (SWAN</u>). As women within the <u>Women's Interagency HIV Study (WIHS</u>) have aged, NIH-supported research is investigating the unique risks of dementia in this population. The Office of Research on Women's Health and NIA have recently <u>co-funded research</u> on sex-specific effects of sex hormones on aging and AD. Since the mid-1980s, 33 <u>Alzheimer's Disease Research Centers</u> have received NIH funding.



# HIV and Women's Health

**Background:** An estimated 39 million people are living with human immunodeficiency virus (HIV) globally.<sup>60</sup> Approximately 1.7 million new HIV diagnoses are reported globally each year, with two-thirds in southern and eastern Africa. In the U.S., an estimated 1.1 million adults are currently living with HIV, with more than 30,000 new HIV diagnoses each year.<sup>61</sup>

- Globally, 54% of people living with HIV are women.
- In 2020, more than 250,000 women in the U.S. were living with HIV and more than 5,000 women with newly acquired HIV.<sup>61</sup>
- An estimated 44% of Black and 26% of Latinx transgender women in the U.S. are living with HIV.<sup>62,63</sup>
- Black women accounted for 54% of new diagnoses among women in the U.S.<sup>61</sup>

**Specific considerations relevant to women's health:** Women—particularly women from racial and ethnic groups underrepresented in research, transgender women, and young women—remain disproportionately affected by HIV.<sup>64</sup> Biological and social factors affect HIV risk, progression, and outcomes. Sex-specific anatomic vulnerabilities to HIV acquisition are linked to unique characteristics of the female genital tract, the vaginal microbiome, and sex differences in inflammation.<sup>65,66</sup> Significant differences in pretreatment viral loads exist between cisgender men and women, with women having lower HIV viral loads early in infection.<sup>67</sup> Estrogen may suppress HIV transcription, leading to lower HIV expression in premenopausal female patients as compared to postmenopausal female and male affected individuals.<sup>68</sup> Social and structural determinants of health influence vulnerability of women to HIV. Stigma, exclusion from economic opportunities, lack of access to secondary school, and gender-based violence all disproportionately affect women living with HIV. For example, researchers have shown that 36-55% of women with HIV experience intimate partner violence (IPV).69 Women with a lifetime history of IPV have been found to have a 1.5 times higher incidence of HIV infection compared with women who have not experienced IPV.<sup>70</sup> Perinatal viral transmission is a unique consideration for pregnant and lactating individuals living with HIV. Prevention

of maternal-to-child transmission of HIV with antiretroviral therapy is a seminal example of NIH-supported science impacting public health.<sup>71,72</sup>

### Scientific gaps and opportunities:

Despite sex and gender influences on HIV pathogenesis, immunology, and disease management, women comprise only 17% of HIV cure-related trial participants.73 Intentional efforts to increase accrual of women to HIV cure-related clinical trials are warranted. Women living with HIV are aging, and aging women remain at risk for HIV. Approximately 54% of women living with HIV in the U.S. are over age 50, and Centers for Disease Control and Prevention analyses reveal that acquisition HIV is increasing among women aged 55 and older.<sup>74</sup> Women aging with HIV have unique risks for multimorbidity, highlighting a need for research addressing the impact of HIV in women across the lifespan, including those who are postmenopausal. Social and behavioral research to understand





and address weathering, social isolation, stigma, elder mistreatment, and loneliness in the context of HIV and aging is also needed.

Current NIH activities: NIH funding on HIV and women's health totaled \$472 million in Fiscal Year 2023. The National Institute of Allergy and Infectious Diseases (NIAID), Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), and the National Cancer Institute supported the largest amounts of HIV and women's health funding. Nineteen NIAID-supported Centers for AIDS Research are located at academic and research institutions throughout the U.S. The Women's Interagency HIV Study (WIHS) was established in 1993 as a multi-center, prospective, observational cohort study of cisgender women living in the U.S. The study was merged in 2019 with the Multicenter AIDS Cohort Study (MACS) under a unified study of men and women, the MACS-WIHS Combined Cohort Study (MACS-WIHS CCS), in which research to define the clinical outcomes for women with HIV across their full lifespan remains a critical focus. In May 2022, NIAID reissued the program Transgender People: Immunity, Prevention, and Treatment of HIV and STIs that supports hypothesis-generating research of transgender people, including women, and will characterize the biological and immunological impacts of gender affirming interventions on HIV susceptibility. In 2023, NIAID and NICHD supported three projects under the American Women: Assessing Risk Epidemiologically (AWARE) program, which aim to better understand HIV prevention, transmission, and early care-cascade points for cisgender, transgender, and gender nonconforming women living in the U.S. In December 2023, NIAID reissued the Next Generation Multipurpose Prevention Technologies (NGM) program, which supports development of new and innovative multipurpose prevention technologies that prevent HIV infection and pregnancy and/or other sexually transmitted infections. The NIH Office of Research on Women's Health and Office of AIDS Research launched the joint HIV and Women Signature Program in February 2023 as an intersectional, equity-informed, data-driven approach to research on HIV and women. Strategies to accomplish programmatic goals include an NIH-wide working group with representation from 19 NIH institutes, centers, and offices, ongoing NIH funding portfolio analyses, information dissemination (website, blog posts), Requests for Information, and workshops.



## Maternal Morbidity and Mortality

**Background:** Maternal morbidity and mortality (MMM) refers to any health condition attributed to and/or aggravated by pregnancy and childbirth that has a negative impact on the woman's wellbeing.<sup>75</sup> Maternal mortality is defined as any pregnancy-related death as a death while pregnant or within 1 year of the end of pregnancy from any cause related to or aggravated by the pregnancy.<sup>41</sup> Severe maternal morbidity (SMM) includes unexpected outcomes of labor and delivery that result in significant short- or long-term consequences to a woman's health.<sup>76</sup> Rates of SMM have nearly doubled during the past decade.<sup>77,78</sup>

- In 2021, 1,205 women died in the U.S. as a result of pregnancy or delivery complications,<sup>79</sup> representing a maternal mortality rate of 32.9 deaths per 100,000 live births.
- An estimated 80% of maternal deaths are preventable.<sup>80</sup>
- Each year, more than 60,000 women in the U.S. are affected by SMM.<sup>81,82</sup>

 Among pregnancy-related deaths with information on timing, 22% occurred during pregnancy, 25% occurred on the day of delivery or within 7 days after, and 53% occurred between 7 days to 1 year after pregnancy.<sup>83</sup>

Specific considerations relevant to women's health: The leading underlying causes of pregnancy-related death include mental health conditions (including deaths to suicide and overdose/poisoning related to substance use disorder; 23%), hemorrhage (14%), cardiac and coronary conditions (13%), infection (9%), thrombotic embolism (9%), cardiomyopathy (9%), and hypertensive disorders of pregnancy (7%).<sup>83</sup> For every pregnancy-related death in the U.S., 100 women experience a "near miss" (i.e., SMM).<sup>81</sup> Illnesses and complications occurring before or after the birth hospitalization affect 14-22% of pregnancies in the U.S., and few therapies for these conditions have been studied in pregnancy.<sup>84</sup> Pregnancy can be viewed as a stress test for the health of women later in life because health before pregnancy influences the experience of MMM and because several conditions that occur during pregnancy are associated with the development of chronic conditions after

pregnancy. For example, a diagnosis of preeclampsia is associated with future hypertension and cardiovascular disease; the risk for type 2 diabetes is almost 10 times higher in women with gestational diabetes.85,86 Structural disparities related to geography exist, with half of rural counties in the U.S. lacking an obstetrician or delivering facility. Further, rural counties with primarily Black or Indigenous residents are experiencing closures of maternity care facilities at a greater rate than primarily White communities.<sup>87</sup> Access to reproductive health care, including access to contraception and abortion services, to optimize maternal health prior, during, and after pregnancy is critical to the long-term health of women and their families.

#### FY23 Women's Health Funding: Maternal Morbidity and Mortality



#### Scientific gaps and opportunities: High

MMM in the U.S.<sup>88</sup> is complicated by the multifactorial nature and causes of pregnancy-related illnesses and

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complications, and the broad potential timing of incidence—whether during pregnancy, at birth, or postpartum. To gain a richer understanding of maternal health, researchers should consider women's interactions with the maternity care system. MMM is characterized by marked racial and ethnic disparities.<sup>81,89</sup> It is crucial to develop a richer understanding of how structural factors, such as racism and bias, manifest within patient engagements with maternity care systems, because they have significant implications for maternal experience. Two-thirds of pregnancy-related deaths occur outside of the time of delivery; development of stronger evidentiary foundations, regarding maternal care services before and after pregnancy, is needed to ensure uninterrupted, safe, and more effective approaches to maternal care and postpartum health.<sup>90</sup>

#### **Current NIH activities:**

NIH spending related to maternal health totaled \$384 million in Fiscal Year (FY) 2023. The Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), National Heart, Lung, and Blood Institute (NHLBI), and National Institute on Minority Health and Health Disparities (NIMHD) supported the largest amounts of maternal health funding. The NIH Coordinating Committee for Maternal Morbidity and Mortality oversees the Implementing a Maternal health and PRegnancy Outcomes Vision for Everyone (IMPROVE) Initiative and engages NIH-wide expertise on how to mitigate preventable maternal mortality, decrease severe maternal morbidity, and promote health equity. Through this initiative Maternal Health Research Centers of Excellence were established in FY23. NICHD supports the Maternal-Fetal Medicine Units (MFMU) Network to reduce maternal, fetal, and infant morbidity related to preterm birth, fetal growth anomalies, and maternal complications and to provide the rationale for evidence-based, costeffective obstetric practice. The Early Intervention to Promote Cardiovascular Health of Mothers and Children (ENRICH) program, led by NHLBI, examines the effectiveness of implementation-ready interventions within the context of a home visiting program to enhance cardiovascular health. In 2022, the National Institute of Nursing Research launched Advancing Integrated Models (AIM) of Care to Improve Maternal Health Outcomes among Women Who Experience Persistent Disparities. In 2021, the National Institute of Diabetes and Digestive and Kidney Diseases established the Glycemic Observation and Metabolic Outcomes in Mothers and Offspring (GO MOMS) study to improve gestational diabetes care throughout pregnancy. The Pathways to Prevention (P2P) Program Identifying Risks and Interventions to Optimize Postpartum Health was launched by the Office of Disease Prevention and sponsoring organizations (Office of Research on Women's Health [ORWH], NHLBI, NIMHD, and NICHD) to address the growing maternal health crisis. In June 2023, the National Institute of Allergy and Infectious Diseases and ORWH reissued the Immune Mechanisms at the Maternal-Fetal Interface program that supports research improving the understanding of how the maternal and fetal immune and non-immune cells interact to support normal pregnancy, as well as the contribution of immune dysregulation to adverse pregnancy outcomes. ORWH also supports the Maternal Morbidity & Mortality (MMM) Web Portal, designed to serve as a central hub and resource to view information about the scope of relevant research at NIH, specific funding opportunities, programs, and events.



### Menopause

**Background:** Menopause is defined as the normal, irreversible cessation of menstrual cycling due to an aging-related decline in female reproductive hormones and affects more than 1 million women and other individuals born with ovaries in the U.S. every year, at an average age of 51.<sup>91</sup>

- More than 1 million women in the U.S. experience menopause each year.<sup>49</sup>
- An estimated one in eight women enters surgical menopause before reaching natural menopause.
- Vasomotor symptoms (VMS) are the most commonly experienced symptoms during the menopausal transition (MT) with up to 80% of women affected. Additional menopausal symptoms include sleep disturbances, genitourinary symptoms, joint pain, urinary tract infection, mental health changes, and decreased sexual function.<sup>92,93</sup>
- Only 15% of women receive evidence-based interventions for menopause symptoms.<sup>91</sup>

#### Specific considerations relevant to women's health:

Menopause is a female-specific life course transition and a public health issue because of the degree and range of morbidities associated with menopause as well as the associated influence on the health of women as they age. Surgical menopause has been associated with increased risk of the development of chronic conditions and overall mortality.<sup>55</sup> For patients with VMS, the cost to address this symptom is estimated to range from \$248 to \$770 per woman per year due to decreased productivity at work.<sup>94,95</sup> Lifestyle factors, environmental exposures, and social determinants of health influence the timing of onset of menopause as well as the severity and duration of menopausal symptoms. Earlier onset and increased severity of symptoms of menopause are reported by Black women; separately, lower educational attainment, lower socioeconomic status, less physical activity, and higher rates of anxiety are associated with increased symptom severity.<sup>96,97</sup> Following menopause, diagnoses of chronic conditions begin to accumulate, making the MT and midlife a critical window for understanding the impact of sex-specific effects on morbidity and multimorbidity.<sup>55</sup> The decline in estrogen associated with menopause contributes to osteoporosis because estrogen is critical to maintaining bone health by preventing bone breakdown.<sup>98</sup> Greater than 50 percent of postmenopausal White women will have an osteoporotic-related fracture in their lifetime.99 Without treatment, the risk for a second fracture increases significantly.<sup>100</sup> Measures are needed to ensure that proven protocols to treat postmenopausal women who suffer their first fracture are routinely initiated to prevent additional fractures.

Scientific gaps and opportunities: The basic mechanisms underlying the timing of menopause and the development of menopausal symptoms and the effect of sex-specific factors and conditions on menopause are not yet fully understood. Animal model systems are needed because hormone levels stay constant or increase even into older age for most female mammals.<sup>94</sup> The Women's Health Initiative (WHI) was the largest set of randomized, controlled trials that were designed to study whether menopausal hormone therapy (MHT) could prevent the onset of chronic disease (specifically cardiovascular disease [CVD] and breast cancer) in postmenopausal women; investigators also studied osteoporosis. The trials were designed to assess the efficacy of MHT to prevent CVD, not to assess the efficacy or outcomes associated with the use of MHT to reduce menopausal symptoms. The trials were stopped early following the

FY23 Women's Health Funding: Menopause



The women's health funding figures included in these Fact Sheets were derived with assistance from the Office of Extramural Research using draft RCDC data.

observation that use of conjugated equine estrogen (CEE) plus medroxyprogesterone acetate (MPA) was associated with statistically increased rates of breast cancer and the global index statistic supported risks exceeding benefits,<sup>101</sup> as well as an association with CEE alone and an excess number of strokes.<sup>102</sup> Subsequent, long-term analyses by WHI revealed that the risks associated with MHT and the subsequent development of cancer, stroke, and other chronic diseases differs by type, age at which MHT was prescribed, and various other risk factors.<sup>49,103,104</sup> These data suggest the safety of MHT for many women experiencing symptoms of menopause when prescribed during or shortly after the MT. Evidence regarding the efficacy and safety of new and different formulations (e.g., micronized progesterone), doses, and modes of delivery (e.g., transdermal, or vaginal) of MHT is currently insufficient. The risks and benefits of the long-term use of many osteoporosis drugs remain underexplored. The role and timing of the treatment of symptoms to best prevent the accumulation of chronic conditions and multimorbidity in postmenopausal women remains inadequately understood.

**Current NIH activities:** NIH women's health spending on menopause totaled \$53 million in Fiscal Year 2023. The National Institute on Aging (NIA), National Institute of Mental Health (NIMH), and National Heart, Lung, and Blood Institute (NHLBI) supported the largest amounts of menopause research. The Office of Research on Women's Health's <u>7th Annual Vivian W. Pinn Symposium</u> in May 2023 focused on menopause and optimizing midlife health of women. Ongoing work supported by NIA and others includes the <u>Study of Women's Health Across the Nation</u> that helps scientists, health care providers, and patients understand the relationship between women's midlife experiences, such as menopause, and their health and quality of life in later years in an ethnically and racially diverse sample of women. NHLBI's <u>WHI</u> continues to follow enrolled patients. NIA's <u>Menopause Strategies: Finding Lasting Answers for Symptoms and Health</u> trials and <u>Menopausal Vasomotor Symptoms and Brain Aging in Women</u> studies explore treatment of physical symptoms of menopause and the MT's effects on brain health, respectively. The NIMH <u>Behavioral Endocrinology Branch</u> conducts research on the relationship between sex steroids, stress, and mood such as perimenopausal-related depressions. Researchers supported by NIA and NIAMS are leveraging existing databases and newly collected and validated data to determine the best ways to improve bone mineral density and reduce fracture risk in postmenopausal women. The National Library of Medicine's <u>MedlinePlus</u> produces content specific to women's health issues, including <u>menopause</u>.



## Mental Health and Women's Health

**Background:** Mental health is an overarching term that describes emotional, psychological, and social wellbeing.<sup>105</sup>Greater than 20% of adults in the U.S. currently live with a mental health disorder, and estimates suggest that half of the population will be diagnosed with a mental health disorder at some point during their lifetime.<sup>106,107,108</sup>

- The prevalence of any mental health disorder is higher among women (27.2%) than men (18.1%).<sup>106</sup>
- The prevalence of serious mental illness is higher among females (7%) than males (4%).<sup>106</sup>
- Women are more likely than men to experience depression, post-traumatic stress disorder, anxiety, and eating disorders.<sup>109</sup>
- Women may experience psychiatric conditions specific to their reproductive life cycle.<sup>109</sup>
- One in eight women experience perinatal depressive symptoms.<sup>110</sup>

Specific considerations relevant to women's health: Biological factors play a role in the differences in risk, prevalence, and outcomes of mental health disorders in women. Steroid sex hormones have important regulatory functions in relation to neurotransmitter systems-modifying neurotransmitters and thereby influencing cognition and behavioral processes. Estrogens are widely believed to provide neuro-protection against schizophrenic psychoses, a disorder significantly less common in women.<sup>111</sup> Estrogens stimulate neuronal growth and boost neuro-reparative processes such as remyelination, and also play a role in protecting against the effects of ischemia, inflammation, injury, and apoptosis.<sup>112</sup> Changes in symptoms of mental health disorders across the menstrual cycle are commonly reported.<sup>113</sup> Mental health conditions commonly complicate pregnancy and are reported as the underlying cause for approximately 23% of pregnancy-related deaths.<sup>83</sup> Despite recommendations for routine screening, perinatal depression remains underdiagnosed and undertreated.<sup>114</sup> Similarly, the physiologic changes associated with menopause can increase risk for developing depressive symptoms and anxiety, which

may compound symptoms of menopause such as vasomotor symptoms and insomnia.115 Together, these time periods related to female reproductionthe menstrual cycle, pregnancy, postpartum, and menopause are each often associated with aggravation or emergence of psychiatric symptoms.<sup>112</sup> Further, exposure to psychosocial and environmental stressors arising in the context of gender-based structural disparities and gender socialization, roles, and identity may contribute to the 1.5 and 1.7 times increased prevalence of anxiety or depression, respectively, and may increase the risk of contemplated and attempted suicide in women.116,117 Although women are more likely to attempt suicide, men are nearly four times more likely to die by suicide.<sup>109</sup> Gender differences in help-seeking may contribute to gender differences in mental health disorders.<sup>118</sup>



FY23 Women's Health Funding: Mental Health

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Scientific gaps and opportunities: To distinguish sex-based differences in mental health conditions, sex-based differences in the brain anatomy, the hypothalamic-pituitary-adrenal axis, immune system, and hormones merit study.<sup>112</sup> Differences in treatment and outcomes may also be related to gender differences, social norms, and power dynamics experienced by women and warrant further investigation.<sup>118</sup> A higher proportion of women than men (25.6% vs. 14.6%) received mental health treatment in the past year, with women more likely to receive medication (21.2% vs. 11.5%) and counseling (12.1% vs. 7.9%) than men.<sup>119</sup> Implementation and longterm outcomes from the recently Food and Drug Administration-approved agent zuranolone, an oral version of brexanolone, to treat postpartum depression, requires research.

Current NIH activities: NIH spending on women's mental health totaled \$711 million in Fiscal Year 2023. The National Institute of Mental Health (NIMH), National Heart, Lung, and Blood Institute, National Institute on Drug Abuse, and Eunice Kennedy Shriver National Institute of Child Health and Human Development supported the largest amounts of research on women's mental health. The NIMH Women's Mental Health Program promotes the emotional well-being of women throughout the lifespan, with a particular focus on sex- and gender-related research that explores the pivotal life stages for brain health, such as birth, puberty, pregnancy, reproductive years, menopause, and aging. New NIMH-funded research tracked population-level rates of postpartum depression among new mothers before, during, and after pregnancy. Study findings support the idea that pregnancy and postpartum are risk periods for maternal mental health.



# Substance Misuse, Substance Use Disorder, and Women's Health

**Background:** The misuse of alcohol and drug use can progress to substance use disorders (SUDs), which are defined by an impaired ability to stop or control substance use even after experiencing negative consequences.<sup>120</sup> An estimated 17.3% of the population over age 12 reported having an SUD in the past year, with 29.5 million people reporting alcohol use disorder, 27.2 million people reporting a drug use disorder, and 8 million reporting both an alcohol and drug use disorder.<sup>121</sup> SUDs can be mild, moderate, or severe, with addiction as the most severe.<sup>122</sup>

- Nearly half (47.2%) of people reporting lifetime illicit drug use are women.<sup>123</sup>
- Alcohol use, binge drinking, and prescription misuse are more commonly reported by female than male high school students.<sup>124</sup>

- The age-adjusted rate of drug overdose deaths for women increased over 3-fold during the past 3 decades.<sup>125</sup>
- Ten percent of pregnant people reported use of an illicit substance (including cannabis) within the past month, while 11% of pregnant people reported using alcohol.<sup>123</sup>
- The majority of women with an SUD have a co-occurring mental illness that may impact the course of disease.<sup>126</sup>

**Specific considerations relevant to women's health:** Research on substance misuse and SUDs has been historically focused on men; however, sex and gender influence risk, severity, and outcomes for women.<sup>120,127</sup> Although women who use substances typically initiate use later in life than do men, following initiation of use, women tend to progress more rapidly from use or misuse to SUD more rapidly than men—a

phenomenon known as "telescoping."128 Among women with an SUD, susceptibility to craving and relapse has been demonstrated as higher than in men.<sup>129,130</sup> Sex differences such as body size and composition influence the effect of substances on an individual.<sup>120</sup> For example, the metabolism of alcohol in females is on average less rapid than in males because of differences in total body water.<sup>127</sup> Hormonal variations across the menstrual cycle may affect addictive behaviors.<sup>131</sup> Women's reproductive health is also impacted by substance use, with an increased likelihood of infertility and early menopause.<sup>120</sup> Women experience stress and trauma more frequently than men, and alcohol can be used to cope with psychological distress.<sup>132</sup> Many women who begin to use injection drugs do so with the influence of a male partner.<sup>133</sup> Women often face unique barriers to accessing treatment. Women are less likely to be screened for substance use during emergency room visits and less likely to be referred to treatment following identification of an SUD.134 Caregiving responsibilities, availability of

FY23 Women's Health Funding: Substance Misuse



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childcare, and stigma also contribute to lower SUD treatment utilization among women.<sup>135</sup> As a result of these multiple factors, women tend to enter SUD treatment with more severe medical, behavioral, and psycho-social problems.<sup>136</sup> Pregnancy provides a unique window of opportunity for many women with SUD, because most people reduce or cease using drugs or alcohol during this time.<sup>127</sup> However, availability of treatment during pregnancy is limited, and women frequently lose access to treatment during the postpartum period, placing them at risk of relapse, suicide, and overdose, and compromising their treatment of co-occurring mental health and chronic physical health conditions.<sup>137</sup> SUD and overdose are significant contributors to maternal mortality, especially for pregnant and postpartum women aged 35–44, with the rate of overdose deaths tripling between 2018 and 2021.<sup>138</sup>

Scientific gaps and opportunities: Research supported by the National Institute on Alcohol Abuse and Alcoholism (NIAAA) and the National Institute on Drug Abuse (NIDA) has led to the development of effective interventions for treating SUDs and overdose, including medications (such as those for opioid use disorder or tobacco dependence), behavioral interventions, and digital therapeutics. Adoption and implementation of evidence-based practices in SUD treatment have been slow despite evidence of efficacy in overdose prevention and reduction in communicable disease (e.g., HIV transmission).<sup>139</sup> Women have remained underrepresented in modern addiction treatment trials, and an improved understanding of the unique pharmacodynamics of opioid agonist therapies is needed.<sup>140</sup> Specifically, the distribution of substances in the placenta and breast milk remains underexplored. Interventions to reduce the incidence of neonatal abstinence syndrome and fetal alcohol spectrum disorders are needed. Novel and integrated care delivery models could overcome sex and gender–specific barriers to substance use treatment including stigma, and in particular stigma faced by women with substance use, substance misuse, or SUD during pregnancy and in motherhood. Research on the effects of punitive policies on pregnant women who use substances and their families is needed to optimize interventions to promote health and prevent family separation.<sup>140,141</sup> Research priorities should address these nuanced needs of women to advance the health of women who misuse alcohol or other substance use continues to rise among women.

**Current NIH activities:** NIH spending on substance misuse specific to women's health totaled \$398 million in Fiscal Year 2023. NIDA, NIAAA, and the National Institute on Allergy and Infectious Diseases supported the largest amounts of substance misuse and women's health funding. The NIH-wide <u>Helping to End Addiction Long-term® (HEAL) Initiative</u> was launched as a response to the opioid use, addiction, and overdose public health crisis. Currently, the initiative funds more than <u>1,800 research projects</u> nationwide. In 2021, NIDA released its <u>Substance Use in Women Research Report</u>, which details the implications of sex and gender differences on substance use. NIAAA recently launched a new initiative titled the <u>Model Continuums of Care Initiative (MCCI)</u> to advance health equity and end health disparities among women and girls in racial and ethnic minority communities. MCCI will apply the latest dissemination and implementation science approaches to significantly reduce the prevalence and impact of multimorbidity among racial and ethnic minority women and girls of reproductive age at risk and living with mental health disorders, SUDs, chronic stress, cardiopulmonary diseases, common metabolic disorders (e.g., diabetes), cancer, and HIV/AIDS.



## Violence Against Women and Trauma

**Background:** Violence against women (VAW) refers to "any act of gender-based violence that results in, or is likely to result in, physical, sexual, or psychological harm or suffering to women, including threats of such acts, coercion or arbitrary deprivation of liberty, whether occurring in public or in private life."<sup>142</sup> Violent acts go beyond just physical or sexual violations; they are also emotional, economic, and psychological in nature.<sup>143</sup> In addition to physical injury and death, women who experience violence have higher risk of experiencing many other conditions that affect their physical and mental health, including new onset of chronic diseases, depression, poorer pregnancy outcomes, and substance use.<sup>144,145,146,147,148</sup>

- Women are more likely than men to experience violence perpetrated by intimate partners.<sup>149</sup>
- About 41% of women have experienced sexual violence, physical violence, and/or stalking by an intimate partner and have reported an intimate partner violence (IPV)-related impact.<sup>150</sup>

 More than 61 million women and 53 million men have experienced psychological aggression by an intimate partner in their lifetime.<sup>150</sup>

Specific considerations relevant to women's health: The type, severity, and nature of violence experienced differ by gender. Women are three times more likely to experience rape or sexual assault than men.<sup>149</sup> Women are more likely to experience injuries from violence that are more severe, compared to men.<sup>151</sup> IPV, defined as "abuse or aggression that occurs in a romantic relationship," includes physical and sexual violence, stalking, and psychological aggression.<sup>150</sup> Although both men and women experience IPV, studies consistently show that the frequency and severity of IPV perpetrated against women is higher and that men are more likely to be perpetrators than are women. For three-quarters of women affected by IPV, violence occurs before age 25.149 Approximately 6% of women experience some form of IPV during pregnancy, which evidence suggests is associated with unintended pregnancy.<sup>152</sup> Primary prevention of VAW requires addressing its root causes through

a holistic approach that includes promoting gender equality, challenging harmful cultural norms, dismantling systemic racial and ethnic inequalities, and strengthening legal and policy frameworks to protect women's rights.<sup>153,154</sup> It is also crucial to invest in and provide appropriate support services for survivors, such as health care, counseling, and legal aid, to help them process trauma and rebuild their lives, especially because 75% of women IPV survivors experience some form of injury related to IPV.150

#### Scientific gaps and

**opportunities:** Although violence significantly impacts the health of women, there are no nationally representative data sources that estimate the prevalence or incidence of trauma, and national surveys and crime statistics

#### FY23 Women's Health Funding: Violence Against Women



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typically track only physical and sexual violence. As a social driver of health, VAW impacts the individual survivors, their autonomy when parenting, and social interactions when working, as well as society as a whole.<sup>155,156</sup> Stigma, lack of trust in the legal system, and fear of repercussions prevent reporting of the violence, which complicates efforts to accurately assess the true magnitude of VAW and its impact on the health and well-being of women. Currently, the causes and consequences of gender-based violence in older adults have been underexamined, particularly with respect to the continuation of abuse that was initiated in earlier adulthood. More comprehensive data are needed to develop targeted interventions and policies to prevent and address VAW. Effective violence prevention and response requires consideration of social and structural barriers that prevent help seeking.<sup>154</sup> Concerted efforts that address the underlying causes of VAW offer the greatest opportunity to realize sustained improvements in the prevention and ultimate elimination of VAW.

**Current NIH activities:** NIH spending related to violence against women and trauma (VAWT) totaled \$56 million in Fiscal Year 2023. The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, National Institute on Alcohol Abuse and Alcoholism, and National Institute of Mental Health supported the largest amounts of women's health and VAWT funding. In May 2023, <u>the White House</u> released its first-ever <u>U.S. National Plan to End Gender-Based Violence: Strategies for Action</u> to align government-wide initiatives to prevent and address sexual violence, IPV, stalking, and other forms of gender-based violence. The NIH Office of Research on Women's Health, the National Institute of Nursing Research, and five other institutes, centers, and offices from across NIH released a <u>Request for Information</u> in 2023 to gather public input on priority scientific directions in VAW. Their findings were published in a recent <u>report</u>. This request was intended to complement ongoing NIH <u>Violence Research Initiatives</u> to understand, prevent, and address VAWT and its health impacts.

### Selected Women's Health NIH Activities—FY22 and FY23

### **Autoimmune Disease**

- NIAMS: <u>New Awardees Aim to Develop National Research Network That Will Explore the Role of the Exposome in Autoimmune Diseases</u>
- NIAMS: NIAMS-funded Study Offers Clues to Why Women Are Disproportionately Affected by Autoimmune Disease
- NIAMS: Study Identifies Subtypes of Inflammation in People with Rheumatoid Arthritis
- NIH-OD: Connecting the Dots: Oral Infection to Rheumatoid Arthritis
- NIAMS: Exercise Energizes Patients with Autoimmune Disease
- NICHD: Preservation of Beta Cell Function in Type 1 Diabetes
- NIEHS: Dietary Risk Factors of Type 1 Diabetes
- NIEHS: When Normal Isn't Normal: Understanding the Skin of Lupus Patients

#### Cancer

- NCI: Targeting Adipose Inflammation to Improve Breast Cancer Outcomes
- NCI and NICHD: OCS Director's Series: Fertility Preservation for Cancer Survivors
- NIH-OIR: <u>Heterogeneity of Breast Cancer Genomes: Going Beyond Therapy to Risk Assessment and Precision Healthcare</u>
- NCI: The Influence of African Ancestry in Tumor Biology and Disparities in Breast Cancer
- NCI: Considerations for Body Composition in Ovarian Cancer Interventions and Analysis
- NCI: Cancer Moonshot Seminar: The Role of Epithelium Derived Alarmins in Breast Cancer Immunoprevention
- NIDDK: The More You Know ... About HPV and Cervical Cancer in Native American Communities
- NCI: <u>Associations Between Aging Biomarkers and Cancer Risk and Outcomes: Findings from the Women's Health Initiative and the</u> <u>St. Jude Lifetime Cohort</u>
- NIH: Mitochondria Driven Chromatin Remodeling Via Histone H3.1 Oxidation. Implications for EMT and Breast Cancer Metastasis
- NCI: Genetics of Breast Cancer in Women of Latin American Heritage Cardiovascular Disease and Women's Health
- NCI: The Estrogen Receptor Signaling in Female Reproductive Health: The Good, the Bad and the Deadly
- NCI: <u>CURE Shining Stars Seminar: Expression of the Adipokines and Their Receptors in the Breast Tumor Microenvironment: The Link Between Adiposity and Poorer Breast Cancer Outcomes?</u>
- NCI: <u>Hereditary Cancer Series: Genotype Phenotype Associations and Lifetime Risks in Hereditary Diffuse Gastric Cancer and</u>
   Lobular Breast Cancer Syndrome
- NIH: Cancer Genomics in Kenya: A Focus on Breast Cancer
- ORWH: Diverse Voices: Cancer Disparities: Methods and Measurement of Racial and Ethnic Diversity

### **Cardiovascular Disease**

- NHLBI: <u>Sex/gender Specific COVID 19 Outcomes and Management Relevant for Heart, Lung, Blood, and Sleep Disorders: From</u> <u>Bench to Bedside</u>
- NIH: <u>A Biomedical Engineering Talk! Sex Specific in Vitro Models of Aortic Valve Stenosis</u>

### Dementia

- NIA: National Research Summit on Care, Services, and Supports for Persons with Dementia and Their Caregivers
- NIA, ORWH: <u>Women's Health and Aging Q&A</u>

### HIV

- ORWH: Diverse Voices: Intersectionality and the Health of Women Social Determinants and Uptake of Infectious Disease Control
   Measures
- NIH: Viral Reservoirs and Rebound in a Model of Perinatal HIV Infection

### **Maternal Morbidity and Mortality**

- NIBIB: Technology to Improve Maternal Health Workshop
- NICHD: <u>Connecting the Community for Maternal Health Challenge</u>
- NICHD: IMPROVE Centers of Excellence
- NICHD: Maternal Fetal Medicine Units (MFMU)
- NICHD, NIBIB, OD and ORWH: NIH Radx Tech for Maternal Health Challenge
- NICHD: <u>Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC) Implementation Working Group of</u>
   <u>Council</u>
- NICHD: <u>Maternal and Pediatric Precision in Therapeutics (MPRINT) Hub</u>
- NHLBI: Trans NIH Workshop: Innovative Approaches to Improve Maternal Health
- NIAID: <u>Measuring and Predicting Reproductive Health: Advancing Technology and Fundamental Understanding in Maternal Fetal</u>
   <u>Immunity Workshop</u>
- ODP: Addressing Maternal Mortality: Unveiling Racial Disparities and Charting a Path to Change
- NHLBI: Improving Maternal Health: Allies Sharing Promising Strategies
- NICHD, ORWH, OBSSR, OD: <u>Reproductive Life Planning and Pregnancy for Sexual and Gender Minority (SGM) Communities</u>
- NHLBI: Innovative Approaches to Improve Maternal Health Hybrid Workshop

#### Menopause

- NIAAA: Clinical Center Grand Rounds: Depression During Perimenopause: Clinical, Endocrine, and Cellular Characteristics
- NIA and NIAMS: Leveraging Existing Large Databases and Cohorts to Better Understand the Risks and Benefits of Long-Term
   Osteoporosis Therapy and Drug Holiday
- NIDDK: Premenopausal Osteoporosis and Pregnancy and Lactation Associated Osteoporosis
- NIA: Midlife Stress and the Hallmarks of Aging
- NIA: <u>The Long-Term Effects of Pregnancy on Aging</u>

#### Substance Use Disorder

- NIAAA: <u>2022 National Conference on Alcohol and Other Substance Use in Women and Girls: Advances in Prevention, Treatment,</u> and Recovery
- NCCIH: From the Mouths of Babes: What Can Research on Babies, Moms, Stress, and Substance Use Tell Us About Resilience?
- NIDA: Impact of Comorbid COVID 19 and Substance Use During Pregnancy on Fetal and Infant Development
- NIAAA: <u>NIAAA IWG on Drinking and Drug Use in Women and Girls: Achieving Equity in Women's Addiction Prevention and</u>
  <u>Treatment: Accent on Promising Programs</u>
- ORWH: <u>Diverse Voices: Intersectional Approaches to Substance Use and Misuse</u>

### **Violence Against Women and Trauma**

- NINR and ORWH: <u>Violence Against Women RFI Report</u>
- OBSSR: <u>Violence Research Initiatives</u>
- ORWH: Diverse Voices Virtual Talk: Violence and Women: Trauma and Addiction Impacts on Pregnant/postpartum Women

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