

# Understanding Sex Differences in Obesity

Obesity, defined as abnormal or excessive accumulation of body fat, is a chronic disease resulting from internal and external factors that impact metabolic, physiologic, structural, psychological, and social health. Obesity can be caused by a combination of factors including biological sex, genetics, psychology, medical conditions, medications, environment, and socioeconomics.

In the United States, **two in five women are living with obesity**.<sup>1</sup> While the prevalence of obesity among U.S. men and women is almost equivalent, the prevalence of severe (Class III) obesity is higher in women (12.1%) than men (6.7%).<sup>1</sup> Further, there are reported **sex differences in the biological, physiological, behavioral, sociocultural, and psychological mechanisms of obesity**. There are also differences in comorbidities, treatment responses, and health outcomes.

## Sex-specific differences that influence weight, obesity risk, and treatment outcomes:

- Body composition and adipose tissue distribution
- Metabolism and insulin resistance<sup>6</sup>
- Treatment seeking, engagement, and responses<sup>19,20,21</sup>
- Structural, chemical, and functional changes in the brain influencing food intake and food choices<sup>22</sup>

It is well studied that there are sex differences in adipose tissue (body fat) distribution and function.<sup>2,3</sup> **Women have a higher percentage of adipose tissue**, more subcutaneous adipose tissue (SAT) (fat under the skin), and more SAT in the abdominal and thigh areas.<sup>4</sup> These differences are in part due to sex hormones and sex chromosomes, which influence metabolism, inflammatory response, and potentially, gene expression.<sup>5,6</sup>



Obesity is associated with over 220 diseases and conditions and there are also sex differences in obesity-related comorbidities including type 2 diabetes, cardiovascular disease, and cancer.<sup>7,8,9,10</sup> **Women living with obesity are also at unique risk of specific medical conditions** including ovarian cancer, polycystic ovary syndrome, and vasomotor symptoms of menopause.<sup>11,12,13</sup> While consistently understudied, race and ethnicity also influence the risk of obesity, effectiveness of treatments, and related health outcomes.<sup>14,15</sup> There are also sex and gender differences in obesity prevalence due to behavioral, sociocultural, and psychological factors including stress, socioeconomics, and weight stigma and bias.<sup>16,17,18</sup>



**Explore the SWHR Obesity Policy Agenda!** “Enacting Change to Improve Outcomes for Women Living with Obesity Across the Lifespan”



# Illuminating Gaps in Sex Differences Research in Obesity



While there have been significant scientific advancements in metabolism and obesity research in recent decades, gaps remains particularly in sex differences research.

Further research is needed to understand the underlying biological mechanisms driving sex differences in incidence, prevalence, treatment responses, and comorbidities as well as the external factors impacting women living with and at risk for obesity. The Society for Women's Health Research emphasizes the following areas to close gaps in obesity research and care and to improve health outcomes for women living with obesity:

- **Incorporate sex-specific lifespan considerations** (pregnancy, menopause, older age) for women in both preclinical and clinical obesity research.
- **Investigate sex differences in treatment responses and complications**, particularly pharmacological interventions, and consider potential sex-specific recommendations. Consider sex differences in responses including medications' impact on bone health, muscle mass, and muscle function.
- **Ensure sufficient representation of individuals living with obesity in research**, including in clinical trials for new drugs intended for use by people with obesity, to ensure obesity-specific prescribing guidance.
- **Ensure sufficient representation of diverse populations in obesity research** to investigate racial and ethnic differences in diagnosis, care, and treatment.
- **Explore the impact of pregnancy** on short- and long-term obesity and cardiometabolic risk for women.

- **Research the role of weight stigma** in obesity prevalence and the direct impact of stigma on obesity-related health outcomes and treatment responses.
- **Further investigate the impact of adverse social conditions** on sex differences in obesity and cardiometabolic risk.
- **Reconsider how body mass index (BMI) is used as a diagnostic tool** in clinical settings and consider potential precision metrics or biomarkers for diagnosing obesity, particularly as a means to predict cardiometabolic risk.
- **Consider the impact of chronic disease medication** initiation and discontinuation on obesity and cardiometabolic risk.
- **Ensure there is intentional and accurate sex-stratified analysis** of research data from preclinical and clinical studies.

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