

# Weight Cycling in Women: Adaptation or Risk?

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## Abstract

Obesity, dieting, and weight cycling are common among reproductive-age women. Weight cycling refers to intentional weight loss followed by unintentional weight regain. Weight loss is accompanied by changes in gut peptides, adipose hormones, and energy expenditure that promote weight regain to a tightly regulated set point. While weight loss can improve body composition and surrogate markers of cardiometabolic health, it is hypothesized that the weight regain can result in an overshoot effect, resulting in excess weight gain, altered body composition, and negative effects on surrogate markers of cardiometabolic health. Numerous observational studies have examined the association of weight cycling and health outcomes. There appears to be modest association between weight cycling with type 2 diabetes mellitus and dyslipidemia in women, but no association with hypertension, cardiovascular events, and overall cancer risk. Interestingly, mild weight cycling may be associated with a decreased risk of overall and cardiovascular mortality. Little is known about the effects of weight cycling in the preconception period. Although obesity and weight gain are associated with pregnancy complications, preconception weight loss does not appear to mitigate the risk of most pregnancy complications related to obesity. Research on preconception weight cycling may provide insight into this paradox.

## Keywords

- ▶ weight cycling
- ▶ yo-yo dieting
- ▶ women
- ▶ reproductive outcome
- ▶ diabetes

Weight cycling or “yo-yo dieting” refers to intentional weight loss followed by unintentional weight regain. Weight cycles are measured as a change in weight or percent body weight over an interval of time. The magnitude of a weight cycle varies from the loss and regain of  $\geq 2.25$  to 10 kg or  $\geq 5$  to 10% of body weight over months to years in most studies.<sup>1</sup> While there is no standard definition of a weight cycle, the thresholds cited in studies exceed typical weight fluctuations and exceed changes in percent body weight that are associated with changes in obesity-related outcomes.<sup>2,3</sup>

Dieting is a common experience among reproductive-age women, even while trying to conceive. In the 2013–2016 National Health and Nutrition Examination Survey (NHANES), almost 60% of U.S. reproductive-age women reported trying to lose weight in past year, including more than 70% of women with obesity and 35% of women with normal weight.<sup>4</sup> The most commonly reported approaches were eating less (62%) and exercising more (62%). In a prospective cohort of more

than 600 U.S. women who were trying to conceive, 44% reported trying to lose weight in the past year.<sup>5</sup> Most reported a plan to control food intake (79%), while some resorted to extreme exercising (11%) or shake diets (9%). Another study found that women trying to conceive were more likely to engage in unhealthy weight loss practices, including taking diet pills, supplements, and herbs, compared with women who were not trying to conceive.<sup>6</sup>

While most women can achieve short-term weight loss, few women will maintain long-term weight loss, which has been defined as losing 10% of body weight and maintaining it for at least 1 year.<sup>7</sup> Only approximately 20% of overweight men and women maintain long-term weight loss. The low prevalence of long-term weight loss appears consistent in observational trials that collect self-reported weight change history and in clinical trials that collect weight measurements in clinics. While few studies of long-term weight maintenance are limited to women, analysis that compare gender have found

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that women have more success at long-term weight loss than men (19.2 vs. 15.6%, odds ratio [OR]: 1.2; 95% confidence interval [CI]: 1.1–1.3).<sup>8</sup> Given the high prevalence of dieting and weight regain, it is estimated that 20 to 55% of women weight cycle and that at least 20% of women experience frequent weight cycles, occurring almost yearly.<sup>9</sup>

Maintenance of long-term weight loss is a challenge due to homeostatic regulation of body weight. Weight is tightly regulated by hormones produced by the gut and adipocytes that act through the nervous system to alter behavior and metabolism.<sup>10</sup> While most gut peptides increase satiety, ghrelin is the only gut peptide that increases hunger. Ghrelin is secreted by the gastric fundus and body when the stomach is empty. Ghrelin secretion stimulates the orexigenic neuron system, the weight gain pathway in the central nervous system (CNS), which is mediated by neuropeptide Y (NPY)/agouti-related peptide (AgRP) neurons. As the stomach is stretched by food, ghrelin secretion is inhibited and hunger declines. All other gut peptides suppress hunger through short acting effects on the CNS and vagal afferents to trigger meal termination. Examples of these gut peptides include cholecystokinin (CCK), which is secreted by the small intestine, and glucagon-like peptide-1 (GLP-1), oxyntomodulin (OXM), and peptide YY (PYY), which are secreted by the small intestine and the colon. Macronutrients, such as carbohydrates, fats, and proteins, stimulate the secretion of these gut peptides. Weight loss leads to gut peptide secretion changes that promote hunger and weight regain to restore the energy deficit. Sumithran et al observed that ghrelin levels increased and CCK and PYY levels decreased over the first 10 weeks of weight loss in overweight and obese men and postmenopausal women who lost more than 10% of their body weight.<sup>11</sup> Ghrelin levels increased between 10 and 62 weeks after weight loss, despite weight regain, and remained significantly higher than pre-weight loss levels. CCK and PYY levels also remained significantly lower than pre-weight loss levels. Increased ghrelin levels also occur among normal-weight women who lose weight.<sup>12</sup>

Weight change alters insulin and leptin levels, which regulate long-term energy storage. Insulin is secreted by the pancreas and converts glucose to glycogen in muscle and the liver and also promotes triglyceride storage in adipose tissue.<sup>13</sup> Leptin is produced by adipocytes and promotes lipolysis and inhibits lipogenesis by reducing adipocyte sensitivity to insulin.<sup>14</sup> Both insulin and leptin circulate in levels that correlate with adiposity. As adiposity increases, insulin and leptin levels increase. Increased insulin and leptin levels act centrally to reduce food intake and increase energy expenditure. Both insulin and leptin inhibit the NPY/AgRP neuron system, or weight gain pathway in the CNS. Leptin also stimulates the proopiomelanocortin neuron system, or weight loss pathway in the CNS. Resistance to insulin and leptin appears to contribute to obesity in some individuals who exhibit high circulating levels of these hormones without the anticipated weight loss effects. While leptin resistance may be induced by chronically elevated levels of circulating leptin due to obesity, low levels of leptin appear to persistently increase appetite and reduce energy expenditure to promote weight gain. Leptin levels

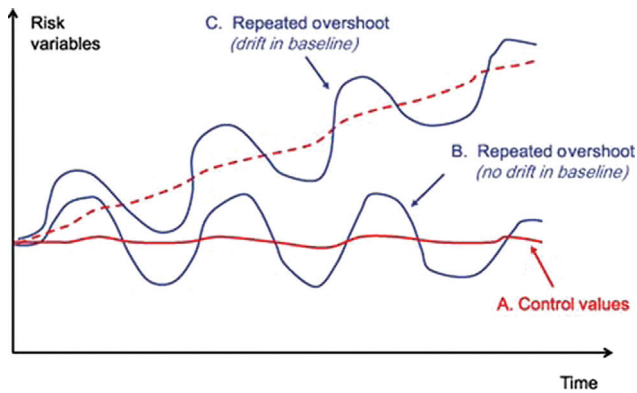
decline by 65% by 10 weeks of weight loss.<sup>11</sup> Sumithran et al found that leptin levels increase between 10 and 62 weeks after weight loss but remain 35% lower than pre-weight loss levels despite weight regain.

Weight loss also triggers a reduction in energy expenditure which enables metabolism and physical activity at lower caloric cost. Energy expenditure is expected to decline with weight loss as less energy is needed to support a lower weight; yet, the observed reduction in energy expenditure often exceeds the predicted reduction in energy expenditure after weight loss.<sup>15</sup> Participants in a reality weight loss show called “The Biggest Loser” were found to have mean resting metabolic rates that were 300 to 500 kcal/day lower than expected at 6 and 30 weeks after significant weight loss that exceeded 30% of their body weight. The reduction in resting energy expenditure appeared to persist for up to 6 years after significant weight loss, even despite weight regain.<sup>16</sup> Nonresting energy expenditure is also reduced after weight loss. Skeletal muscle efficiency improves by 20% following weight loss, resulting in a reduction in the caloric demand to perform an activity compared with the caloric demand to perform the same activity prior to weight loss.<sup>17</sup> As a result, long-term weight loss often requires  $\geq 1$  hour per day of moderate physical activity for years after weight loss.<sup>7</sup>

Weight loss leads to prolonged changes in leptin levels, gut peptide secretion, and energy expenditure that promote hunger and weight regain, supporting the notion that the low rate of long-term weight loss is driven by physiology more so than a lack of discipline among dieters. Collectively, these adaptations can promote excess weight regain and altered body composition in some.<sup>18</sup> In cross-sectional studies, women who are obese and weight cycle had increased subcutaneous adipose tissue, visceral adipose tissue, and waist circumference compared with women who are obese and weight stable.<sup>19,20</sup> A reanalysis of the Minnesota Starvation Experiment, where 12 healthy men were starved and refed, provides additional insight into the magnitude and nature of excess weight gain.<sup>21</sup> Participants gained an excess of 4 kg on average (range: 0–9 kg) with refeeding and experienced restoration of adipose tissue before lean muscle. Overshooting weight gain induces changes in blood glucose, insulin, lipids, blood pressure, and sympathetic tone that favor insulin resistance, dyslipidemia, and hypertension.<sup>22</sup> It has been hypothesized that repetitive overshooting through weight cycling may cause fluctuations in the risk of metabolic and cardiovascular disease (**► Fig. 1**).<sup>9</sup> It is debated if weight cycling leads to reproductive, metabolic, and cardiovascular disorders in women with obesity. This article will review the impact of weight change on pregnancy and pregnancy outcomes as well as the impact of weight cycling on the risk of diabetes, hypertension, cardiovascular disease, cancer, and mortality among women.

## Weight Change and Pregnancy

Over 40% of reproductive-age women in the United States are obese, defined as a body mass index (BMI) of 30 kg/m<sup>2</sup> or greater.<sup>4</sup> Epidemiologic studies have consistently associated obesity with infertility and a reduction in live birth due to



**Fig. 1** Concept of repeated overshooting. Weight cycling may lead to fluctuations in cardiometabolic surrogate markers with improved parameters observed with weight loss and worsening parameters observed with weight gain. Repeated weight cycles may lead to cardiometabolic disease if the baseline drifts with weight cycling (C). (Reprinted with permission from Montani et al.<sup>9</sup>)

delayed conception and higher rates of miscarriage and stillbirth. However, randomized controlled trials of preconception weight loss prior to fertility treatment have not consistently shown increased live birth.<sup>23–25</sup>

Despite a lack of high-quality evidence that supports benefits of weight loss prior to pregnancy, many women attempt to do so. In a prospective cohort of over 600 women trying to conceive, 44% of women reported a desire to lose weight in the preceding 12 months.<sup>5</sup> While 12% of women achieved weight loss, 58% experienced weight gain. Though few studies have considered preconception weight cycling as a variable, we will review the data regarding preconception and interpregnancy weight change with pregnancy outcomes and argue that weight cycling should be considered in future studies.

Weight change in the weeks, months, and years that precedes pregnancy appears to influence the risk of miscarriage. In the preliminary report of a randomized control trial, the risk of early pregnancy loss was 6.1-fold higher (Relative Risk: 6.1, 95% CI 1.4–25.8,  $P = 0.005$ ) in women with obesity and unexplained infertility who underwent a 16-week intensive lifestyle intervention prior to fertility treatment compared with women who received a standard lifestyle intervention.<sup>26</sup> Data regarding weight loss maintenance and weight regain were not available in the abstract. In a prospective cohort, weight loss of  $\geq 5\%$  of body weight in the 12 to 18 months preceding a spontaneously conceived pregnancy was not consistently associated with miscarriage, though the cohort included women with normal, overweight, and obese BMIs.<sup>5</sup> Weight cycling was not associated with the risk of miscarriage, though the magnitude and frequency of weight cycling was not reported and the stratified data did not categorize women with a BMI of  $\geq 30 \text{ kg/m}^2$  as a subgroup. Weight gain of  $\geq 5\%$  was associated with an increased risk of early pregnancy loss (RR: 1.65, 95% CI: 1.09–2.49) compared with the weight stable group, though the association was no longer significant once the data were stratified by women with a BMI of 18.5 to 24.9 and a BMI of  $\geq 25 \text{ kg/m}^2$ . In a different prospective cohort, weight gain of  $\geq 20 \text{ lb}$  from the

age of 18 years to the age at conception was associated with a 11% increased risk of miscarriage (95% CI: 1–23%) and women who lost  $\geq 4 \text{ kg}$  between the age of 18 years and the time of conception had a 20% lower risk of miscarriage (95% CI: –29% to –9%), particularly when women were overweight at the age of 18 years.<sup>27</sup> Data regarding weight cycling were not provided in the analysis.

Weight gain as an adult is associated with the risk of preeclampsia; on the contrary, weight cycling was not. In a prospective cohort of U.S. women, weight gain of  $\geq 10 \text{ kg}$  from the age of 18 years to their age at conception was associated with a 5.1-fold (RR: 5.1, 95% CI: 2.2–12.2) increased risk of preeclampsia compared with women who maintained their adult weight.<sup>28</sup> A history of weight cycling was associated with a 1.5-fold increased risk of preeclampsia, though the association was attenuated (adjusted RR: 1.1, 95% CI: 0.6–1.8) after adjusting for maternal age, race, parity, BMI at the age of 18 years, and weight change since the age of 18 years. There was no evidence of a linear relation between the number of intentional weight cycles and increasing risk of preeclampsia ( $p$  for linear trend = 0.831), although only 1.9% of the cohort was obese based on BMI prior to pregnancy. Data regarding weight loss and preeclampsia risk were not available.

Weight change between pregnancies is associated with pregnancy outcomes even though timing between pregnancies is highly variable. In a prospective cohort of Swedish women, a BMI increase of  $\geq 3$  units over approximately 2 years between pregnancies was associated with an increased risk of preeclampsia (RR: 1.78, 95% CI: 1.52–2.08); gestational hypertension (RR: 1.76, 95% CI: 1.39–2.23); gestational diabetes (RR: 2.09, 95% CI: 1.68–2.61); caesarean delivery (RR: 1.32, 95% CI: 1.22–1.44); stillbirth (RR: 1.63, 95% CI: 1.20–2.21); and large-for-gestational-age (LGA) infant (RR: 1.87, 95% CI: 1.72–2.04) compared with women who are weight stable between pregnancies. The increased risks were observed for women with normal and obese pre-pregnancy BMIs.<sup>29</sup> Several meta-analyses have confirmed the association of modest interpregnancy weight gain and increased risk of perinatal complications, particularly when normal weight women gain weight.<sup>30–32</sup> Weight loss between pregnancies was not associated with a protective effect on perinatal complications, except for a reduction in risk of LGA infant and gestational diabetes among women who were overweight or obese before their first pregnancy. Weight loss between pregnancies was associated with increased risks of small-for-gestational-age infant and preterm birth.<sup>32</sup>

Overall, preconception and interpregnancy weight gain are associated with increased risks of miscarriage, still birth, preeclampsia, gestational diabetes, and caesarean delivery; yet, weight loss is not associated with a reduced risk of most perinatal outcomes and may increase the risk of some. Weight maintenance, or preventing weight gain, during the preconception period and between pregnancies should be encouraged to avoid the risks associated with weight gain and loss. Only two studies have analyzed the association of weight cycling and pregnancy outcomes and both studies were based on women who were normal weight and overweight, with few women with obesity.<sup>5,28</sup> Weight cycling is common,

particularly among women with obesity, and should be considered as a variable in future studies of weight and pregnancy outcomes. Investigators should consider the timing of pregnancy and fertility treatment relative to the weight cycle—loss, plateau, and regain.

### Weight Cycling and Type 2 Diabetes

Women who weight cycle appear to have a higher risk of diabetes than men who weight cycle, though few studies have focused on women.<sup>33</sup> In an analysis of over 3 million participants in the National Health Insurance Service in South Korea, weight fluctuation was assessed over three weights recorded over a 5-year period and new-onset diabetes was recorded over a 5-year follow-up period. Weight fluctuation was associated with a higher risk of new-onset diabetes (hazard ratio [HR]: 1.10, 95% CI: 1.07–1.12) after adjusting for baseline BMI. The risk was highest among participants with a BMI of 25 kg/m<sup>2</sup> or more, which is considered obese in Asian populations. The risk was also higher among women (HR: 1.14, 95% CI: 1.1–1.17) compared with men (HR: 1.08, 95% CI: 1.06–1.10;  $p = 0.001$ ). The association of weight cycling and type 2 diabetes risk has also been observed among U.S. women. In a population-based sample of over 33,000 postmenopausal women enrolled in the Iowa Women's Health Study, self-reported body weights were recorded at ages 18, 30, 40, and 50 years and were used to calculate weight change.<sup>34</sup> Weight cycling was associated with a 1.4-fold increased risk of diabetes after adjusting for age and BMI. Other studies have observed an association of weight cycling and type 2 diabetes in middle-aged women, but the association is no longer significant once adjusted for BMI. In a nested cohort of over 2,000 young and middle-aged U.S. women enrolled in the Nurses' Health Study II, 20% experienced mild self-reported weight cycling, defined as  $\geq 10$  lb weight loss and regain three or more times, and 1.6% experienced severe weight cycling defined as  $\geq 20$  lb weight loss and regain three or more times.<sup>35</sup> Weight cycling was associated with higher BMI, but was not associated with risk for diabetes among mild weight cyclers (OR: 1.1, 95% CI: 0.89–1.37) or severe weight cyclers (OR: 1.39, 95% CI: 0.9–2.13) after adjusting for BMI. Similarly, self-reported weight cycling was no longer associated with type 2 diabetes after adjusting for BMI (HR: 1.2, 95% CI: 0.8–1.5) in a nested cohort of more than 1,000 middle-aged men and women in the Framingham Heart Study.<sup>36</sup> The association between weight cycling and type 2 diabetes appears to be small, which may contribute to the inconsistent findings between studies of different size.

### Weight Cycling and Cardiovascular Disease

While weight gain is associated with an increased risk of hypertension in women, weight cycling does not appear to be an independent risk factor. In over 46,000 young and middle-aged women enrolled in the Nurses' Health Study II, for every 10 lb of self-reported weight gain, the risk of hypertension increased by 20% (OR: 1.20, 95% CI: 1.15–1.24).<sup>37</sup> Neither mild weight cycling (OR: 1.15, 95% CI: 1.00–1.33) or severe

weight cycling (OR: 1.13, 95% CI: 0.79–1.61) was associated with hypertension after adjusting for BMI and weight gain. In a prospective 30-month study of over 150 overweight men and women who achieved weight loss through an 18-month lifestyle program, blood pressure decreased with weight loss and returned to baseline levels after one weight cycle and did not appear to overshoot.<sup>38</sup>

It is unclear if weight cycling is associated with dyslipidemia and cardiovascular events in women. In a cross-sectional study of over 450 Italian participants with obesity, of which 340 were women, self-reported weight cycling of varying degrees was not correlated with cholesterol, high-density lipoprotein (HDL), or triglycerides in women after controlling for BMI and age.<sup>39</sup> In a different cross-sectional study of over 480 U.S. women undergoing coronary angiography for suspected ischemia, self-reported  $\geq 3$  weight cycles of  $\geq 10$  lb was associated with 7% lower HDL levels in women.<sup>40</sup> Weight cycles that exceeded 50 lb were associated with a 27% lower HDL level after controlling for BMI and additional confounders. This cohort was followed up prospectively for a median of 6 years and despite exhibiting lower HDL values, higher BMI, larger waist circumferences, and higher values for fasting blood sugar, women who weight cycled experienced less adverse cardiac outcomes, including cardiovascular mortality, nonfatal myocardial infarction, nonfatal stroke, and hospitalization for heart failure, as compared with women who were weight stable (21 vs. 29%, respectively,  $p = 0.03$ ).<sup>41</sup> In the Iowa Women's Health cohort, self-reported weight cycling of  $\geq 10\%$  body weight between the ages of 18 and 50 years was associated with an increased risk myocardial infarction (RR: 1.89, 95% CI: 1.42–2.53) after adjusting for BMI and age.<sup>42</sup> Differences in the definition of weight cycling may contribute to the conflicting observations.

### Weight Cycling and Long-Term Risks

Weight cycling has been associated with an increased risk in cancer and mortality, though the association does not persist when controlled for covariates, such as BMI. In a case-control study of over 740 U.S. women, self-reported weight cycling, defined as losing  $\geq 20$  lb and gaining  $\geq 10$  lb within a year, was associated with an increased odds of endometrial cancer (OR: 1.72, 95% CI: 1.37–2.15), though adjustment for BMI attenuated the increased odds (OR: 1.27, 95% CI: 1.00–1.61).<sup>43</sup> In a prospective cohort of over 69,000 U.S. women enrolled in the Cancer Prevention Study II Nutrition Cohort, women who experienced weight cycles of  $\geq 10$  lb did not appear to have an increased overall risk of cancer, including endometrial cancer, after controlling for BMI as a continuous variable and other covariates.<sup>44</sup> In over 62,000 women enrolled in the Cancer Prevention Study II Nutrition Cohort, women who experienced one to four weight cycles had a 7% reduction in the risk of overall mortality (RR: 0.93, 95% CI: 0.89–98) and an 11% reduction in the risk of cardiovascular mortality (RR: 0.91, 95% CI: 0.79–1.04) in a multivariate model stratified by age that adjusted for alcohol consumption, race, smoking status, educational level, physical activity level, BMI in 1982, weight

**Table 1** Summary of selected studies on weight cycling and associated risk of adverse reproductive and cardiometabolic health outcomes in women

Outcome	Decreased risk	Not associated	Increased risk	Notes
Miscarriage		5		
Preeclampsia		28		
Type 2 diabetes		35,36	33,34	Association appears to be small, which may contribute to the inconsistent findings between larger and smaller studies
Hypertension		37,38		
Dyslipidemia		39	40	
Cardiovascular events		41	42	Differences in the definition of weight cycling may contribute to the conflicting observations
Cancer		44	43	Largest prospective study does not show an association
Mortality	45			

change from 18 years of age to 1982, history of high blood pressure, history of diabetes, and total energy intake. No association was observed between higher numbers of weight cycles, classified as 5 to 9, 10 to 19, and  $\geq 20$ , and overall and cardiovascular mortality.<sup>45</sup>

## Conclusion

While claims that diets make some “fatter” may be valid, the available evidence suggests that there are few detrimental effects of weight cycling in women (– **Table 1**). There appears to be a modest association between weight cycling with both type 2 diabetes mellitus and dyslipidemia, but no association with hypertension, cardiovascular events, and overall cancer risk. Interestingly, mild weight cycling may be associated with a decreased risk of overall and cardiovascular mortality. It appears that the benefits of reduced weight, even for a short amount of time, outweigh the risk of weight regain and overshooting.

Little is known about the effects of weight cycling during the preconception period and pregnancy outcomes. Available evidence suggests that among obese and infertile patients, weight loss in this period fails to improve live birth and most perinatal outcomes and may introduce some risks. Given the high prevalence of obesity, dieting, and weight cycling among reproductive-age women, more evidence is needed. Future studies should consider weight cycling as a variable and determine if pregnancy outcomes differ when conception occurs during periods of weight loss or weight stability.

### Conflict of Interest

None declared.

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