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## Obesity Management in Women of Reproductive Age

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The prevalence of obesity has continued to increase among women of reproductive age in the US and has serious implications for pregnancy health.<sup>1,2</sup> Nearly 25% of women in the US who become pregnant have obesity, with the highest prevalence among underrepresented racial and ethnic groups.<sup>2</sup> Women with obesity-related adverse pregnancy outcomes (APOs), such as gestational diabetes (GD) and hypertensive disorders of pregnancy (HDP), from prior pregnancies may benefit from aggressive weight management during the postpartum and interpregnancy period. However, current US obesity guidelines do not consider pregnancy history or intention or account for obesity-related APOs in the decision to escalate obesity therapies. This omission represents a potentially missed opportunity to initiate aggressive weight loss intervention and reduce postpartum weight retention, which is strongly associated with incident and persistent obesity, as well as prepregnancy obesity for future pregnancies.

Obesity guidelines should specifically consider women of reproductive age and their pregnancy history because (1) this life stage is often the time of greatest weight gain, (2) aggressive weight loss interventions among women with obesity may reduce incident and recurrent APOs, and (3) in utero exposure to obesity is associated with altered gene expression and metabolic abnormalities in offspring.<sup>3</sup> Accordingly, reducing obesity among women before they become pregnant could have an intergenerational effect, potentially contributing to lower incidence of childhood obesity.<sup>3</sup>

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## Obesity Treatment Escalation

The 2014 guidelines on the management of overweight and obesity in adults from the American College of Cardiology, the American Heart Association, and The Obesity Society (the most recent guidelines on this topic from these organizations) call for therapy escalation when lifestyle interventions fail to produce significant weight loss among patients with obesity.<sup>4</sup> Antiobesity medication is typically recommended for individuals with a body mass index (BMI) of 30 or greater or among those with a BMI of 27 or greater and an obesity-related comorbidity. Surgical options are recommended for individuals with a BMI of 40 or greater or among those with a BMI of 35 or greater and an obesity-related comorbidity. These guidelines are for the general population of adults with overweight and obesity and there is no specific mention of the need for obesity-related APO assessment or specific consideration for women of reproductive age.

## Obesity-Related APOs and Comorbidities

For the general population, obesity-related comorbidities typically include conditions such as hypertension, diabetes, dyslipidemia, obstructive sleep apnea, and cardiovascular disease.<sup>4</sup> In general, an obesity-related comorbidity assessment is based on whether obesity is a major modifiable risk factor for the condition and whether the condition is associated with increased morbidity or mortality. For an APO to qualify as an obesity-related comorbidity based on this rationale, obesity must be a modifiable risk factor for the APO (meaning weight loss should result in a reduction of the APO risk or recurrence) and the APO must be associated with morbidity or mortality.

Several pregnancy complications either have obesity as an associated modifiable risk factor (eg, cesarean delivery and large for gestational age infant)<sup>1</sup> or are associated with cardiovascular disease (eg, intrauterine growth restriction, preterm birth, and small for gestational age infant) (eTable in the Supplement).<sup>5</sup> Conversely, GD and HDP meet both criteria and are subsequently classified as obesity-related comorbidities. The incidence of GD, which affects 6% to 7% of pregnancies in the US, increases with higher prepregnancy BMI. An analysis of National Vital Statistics System birth data<sup>6</sup> showed that 3.6% of 1 699 751 women with a normal prepregnancy BMI (range, 18.5–24.9) developed GD vs 6.1% of 997 977 women with an overweight prepregnancy BMI (range, 25.0–29.9), 8.8% of 548 092 women with class I obesity (BMI range, 30.0–34.9), 11.2% of 266 105 women with class II obesity (BMI range, 35.0–39.9), and 13.9% of 187 689 women with class III obesity (BMI 40.0).

In a systematic review and meta-analysis<sup>7</sup> of 675 455 women, investigators found that those with GD (n = 31 867) were more likely to develop type 2 diabetes postpartum than those without GD (n = 643 588) (absolute risk, 12.5% [3997 of 31 867] vs 1.1% [6862 of 643 588], respectively; pooled weighted relative risk [RR], 7.43 [95% CI, 4.79–11.51]). A pooled analysis<sup>8</sup> of 5 390 591 women showed that those with GD (n = 258 646) had an increased risk of major cardiovascular events vs those without GD (n = 5 131 945) (absolute risk, 3.1% [8003 of 258 646] vs 1.8% [93 421 of 5 131 945], respectively; pooled weighted

RR, 1.98 [95% CI, 1.57–2.50]), and that this risk was independent of the development of type 2 diabetes.

Similarly, HDP affects approximately 6% of pregnancies in the US, and the risk of HDP increases with increasing BMI.<sup>1</sup> In an analysis of 48 113 postmenopausal participants from the Women’s Health Initiative study,<sup>5</sup> those with prior HDP (n = 2936) vs those without a prior APO (n = 30 522) had a higher prevalence of chronic hypertension (49.6% [1457 of 2936] vs 21.5% [6551 of 30 522], respectively). In the same study of women,<sup>5</sup> prior HDP (n = 2936) vs no prior APO (n = 30 522) was associated with a higher prevalence of atherosclerotic cardiovascular disease (9.3% [273 of 2936] vs 5.8% [1758 of 30 522], respectively) and the adjusted risk of atherosclerotic disease was higher among those with prior HDP vs those without a prior APO (odds ratio, 1.27 [95% CI, 1.15–1.40]).

There is also evidence suggesting that prepregnancy and interpregnancy weight loss (with both medical and surgical treatments) can significantly reduce the risk of incident and recurrent APOs. A meta-analysis<sup>9</sup> of 12 observational studies (representing 415 605 women; mean follow-up, 10.6 years [range, 2–22 years]), showed that interpregnancy weight loss was associated with a reduced risk of HDP (RR reduction of 10% for gestational hypertension and 7% for preeclampsia). Bariatric surgery also has been associated with a reduced risk of GD, gestational hypertension, and cesarean delivery in a meta-analysis<sup>10</sup> of 20 cohort studies representing approximately 2.8 million women. Recurrent APOs are associated with higher long-term cardiovascular risk than single APO events, further underscoring the need for interpregnancy interventions among women with incident APOs.

In addition, because several APOs are associated with cardiovascular risk factors (eg, chronic hypertension and chronic diabetes) as well as overt cardiovascular disease, interpregnancy weight loss could reduce the direct and indirect risk of cardiovascular disease regardless of the decision to attempt future pregnancies.

## Important Considerations for Clinical Management

Lifestyle interventions remain the mainstay of therapy for all people with obesity and should always continue in combination with measures aimed at achieving a healthy weight.<sup>4</sup> However, in the absence of significant weight loss with the initiation of comprehensive lifestyle interventions, escalation of therapy should be considered. The medications for the treatment of obesity approved by the US Food and Drug Administration have not been studied or are contraindicated during pregnancy and breastfeeding. As such, women of reproductive age should be closely monitored for pregnancy if they use pharmacotherapy for the treatment of obesity and should be counseled about options to prevent pregnancy, including long-acting reversible contraceptives. Medication for the treatment of obesity should be stopped if pregnancy occurs to prevent adverse outcomes in offspring. Patients should notify their clinician if they plan to pursue pregnancy so that the antiobesity medication may be discontinued prior to conception.

With an appropriate contraceptive plan and following completion of breastfeeding, escalation of therapy to treat obesity is appropriate in women of reproductive age. Even

though data are lacking on the specific degree of obesity reduction needed to reduce APOs, a pre-pregnancy weight loss goal of 5% to 7% is a reasonable target and approximates the additional total body weight loss of adjunct antiobesity medications.

Bariatric surgery has the highest efficacy for achieving sustained long-term weight loss. Nonetheless, the potential benefits of bariatric surgery for reducing obesity-related APOs must be balanced against short-term and long-term risks associated with the procedure, which vary for adjustable gastric banding, sleeve gastrectomy, and Roux-en-Y gastric bypass, and include complications such as postoperative deep venous thrombosis, gastric leak, dysphagia, gastroesophageal reflux, small bowel obstruction, dumping syndrome, hypoglycemia, nutritional deficiencies, and weight regain. Although malabsorptive methods (eg, gastric bypass) are associated with greater nutrient deficiencies that could potentially affect the growing fetus, there is no agreement or sufficient evidence to recommend restrictive bariatric surgical methods (eg, gastric banding or sleeve gastrectomy) as the preferred strategy for women of reproductive age. There is also no consensus on the ideal time to conceive following bariatric surgery, but the general recommendation is to wait 12 months in an attempt to avoid conceiving during the period of rapid weight loss that occurs during the early months after bariatric surgery.

For women of reproductive age, clinicians should assess their intention to become pregnant to identify women at risk for poor outcomes. Pregnancy history (with special attention to those with APOs that could be associated with obesity) should be considered in the management of women with obesity. A history of HDP or GD reflects an important obesity-related APO and should be considered in the decision to escalate therapy for women with obesity. Updated guidelines for obesity management in adults should include topics that are unique to women of reproductive age. More rigorous research is needed to better understand the comparative effectiveness of different lifestyle interventions, including tailoring treatment for historically marginalized populations, assessing the long-term effects of antiobesity medications, and determining the specific degree of weight loss that would improve obesity-related APOs.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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