



Review article

American Society for Metabolic and Bariatric Surgery position statement on the impact of obesity and obesity treatment on fertility and fertility therapy Endorsed by the American College of Obstetricians and Gynecologists and the Obesity Society

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Preamble

The American Society for Metabolic and Bariatric Surgery issues the following position statement for the purpose of enhancing quality of care in metabolic and bariatric surgery. In this statement, suggestions for management are presented that are derived from available knowledge, peer-reviewed scientific literature, and expert opinion. This was accomplished by performing a review of currently available literature regarding obesity and obesity treatment and fertility and fertility therapy. The intent of issuing such a statement is to provide objective information regarding the impact of obesity and obesity treatment

on fertility and fertility therapy. The statement may be revised in the future should additional evidence become available.

Prevalence of obesity in reproductive-age women

The World Health Organization stratifies body mass index (BMI) into 6 categories to define underweight, normal weight, overweight, and 3 classes of obesity [1]. Based on the 2011–2012 National Health and Nutrition Examination Survey, the prevalence of obesity in women of reproductive age (20–39 years) in the United States is 31.8%, with the highest prevalence (55.8%) in non-Hispanic black women [2]. Furthermore, the prevalence of obesity increased from 28.4% to 34.0% in women ages 20–39 years from 1999–2008, highlighting the escalating role that obesity plays in women's health, including reproductive health [2,3].

Prepregnancy obesity

Obesity during pregnancy is typically defined as a prepregnancy BMI ≥ 30 kg/m² in adult women. If a

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prepregnancy BMI is not available, then the maternal weight at the first prenatal visit is used to determine BMI [4]. Not only does obesity impact the health of every organ system, the combination of obesity and pregnancy introduces additional complications, such as birth defects, preeclampsia, gestational diabetes, stillbirths, and cesarean deliveries [5]. Obese women are also at greater risk for menstrual irregularities, polycystic ovary syndrome (PCOS), and anovulation, all of which contribute to an increased risk of infertility.

Natural fertility and impact of lifestyle factors

The monthly fecundity rate, or the probability of obtaining a clinically recognized pregnancy in a menstrual cycle, is approximately 20–25% in couples not using contraception. Approximately 10–15% of couples experience delays in fertility or subfertility [6]. Fertility declines with age across all populations. Infertility is defined by the failure to achieve a clinical pregnancy after 12 months or more of appropriate, timed, unprotected intercourse. Earlier evaluation and treatment may be justified based on specific medical history and physical findings and is warranted after 6 months for women over the age of 35 years [7].

Fertility rates are decreased in women who are either underweight or overweight, with underweight women demonstrating a 4-fold longer time to pregnancy than normal-weight women. Obesity is also associated with a 2-fold longer time to pregnancy compared with normal-weight women for couples attempting pregnancy without intervention [8].

Several lifestyle factors may be associated with infertility. Although there is no evidence that specific diets are associated with improved fertility, diets that replace animal sources of protein and fat with vegetable sources may be associated with a lower risk of ovulatory infertility [9]. Smoking has a proven detrimental effect on the time to pregnancy, chance for conception, and success of fertility treatments. Smoking is also associated with an earlier age of menopause, suggesting an impact on follicular development [10]. There is no clear link between conception and alcohol consumption [11], although the amount of consumption may matter. In several series, heavy alcohol consumption was associated with decreased fertility [12,13]. Moderate caffeine consumption has not been shown to impair fertility, but increased intake (>500 mg/day) may delay time to pregnancy (Table 1) [14].

Impact of obesity, polycystic ovary syndrome, and insulin resistance on natural fertility

Obesity is independently associated with a longer time to pregnancy even in eumenorrheic women, despite similar coital frequency noted among normal-weight and overweight/obese women participating in studies of couples trying to conceive [15–17]. This delay may be due, in part,

Table 1
Lifestyle factors and fertility [9–14]

Factor	Impact
Smoking	Associated with longer time to pregnancy, reduction in per-cycle pregnancy, and earlier age of menopause
Caffeine	Possible reduction in fecundity with >500 mg/d
Alcohol	Contradictory evidence, but increased consumption may be associated with longer time to pregnancy
Diet	Possible reduced rate of ovulatory dysfunction with lower animal fat consumption.

to abnormalities in oocytes or ovulation arising from decreased luteinizing hormone amplitude in the hypothalamic-pituitary-ovarian axis of eumenorrheic obese women, a gonadotropin defect that is distinct from that noted in women with PCOS [18].

PCOS is a well-recognized and common endocrinopathy that affects 5–10% of women of reproductive age. It is defined by the presence of at least 2 of 3 conditions: irregular menses, hyperandrogenism, and the finding of polycystic ovary morphology on ultrasound [19]. PCOS has been associated with obesity since the original description of the condition; however, the disorder itself is independent of obesity, and many women with PCOS are not overweight or obese [20]. The prevalence of obesity in PCOS is highly variable, with rates ranging from 30–70%, and this variation is likely related to both genetic and environmental factors [21]. There is some evidence that the diagnosis of PCOS is associated with an increased risk of obesity [22], although not all studies support this [23]. The relative risk of obesity in women with PCOS in one meta-analysis was 2.77 (95% confidence interval [CI] 1.80–4.10), with obesity prevalence highest in Caucasian women and lowest in Asian women [20]. PCOS is associated with infertility due to oligo-anovulation even in normal-weight patients; however, increased weight is known to exacerbate the symptoms of PCOS and is associated with significantly more reproductive dysfunction and abnormal bleeding and increased androgenic symptoms [15]. The symptoms of PCOS are remarkably sensitive to weight changes, and weight loss of as little as 5% can improve ovulatory dysfunction and restore fertility [16].

Obesity and excess adiposity are also associated with insulin resistance (IR) and significant metabolic perturbation. Specifically, increased abdominal fat mass may worsen the metabolic consequences of obesity and is associated with an increased risk of metabolic syndrome (hypertension, elevated fasting glucose, increased waist circumference, elevated triglycerides, and low HDL cholesterol) [17,18,24]. The metabolic disturbance associated with excess adiposity is likely due to lipotoxicity and increased production of excess free fatty acids, resulting in tissue inflammation and increased IR [25]. Women with PCOS have a high predisposition to IR, seen in both normal-weight and obese individuals [26]. Abnormalities in the production of adipokines might play a main role in the development and progression of PCOS. In particular,

reduced secretion of adiponectin has a critical role in IR. A systematic review demonstrated that adiponectin is lower in women with PCOS compared with non-PCOS controls with similar BMI. Lower adiponectin levels are associated with IR observed in women with PCOS compared with controls [27]. As such, it is possible that IR is specific to the pathophysiology of PCOS, although it is not a universal feature. Improvement in IR is associated with an increase in ovulation in women with PCOS [28].

Abnormal adipokine balance might also mediate the disturbance of sympathetic nervous system activity, postulated as one of the mechanisms of ovulatory dysfunction in PCOS [29]. Leptin, an adipokine mediator of long-term energy balance, plays a role in suppressing food intake. Obesity is paradoxically associated with increases in leptin, suggesting that obesity is associated with leptin resistance. Women with PCOS demonstrate increased leptin resistance and have been shown in many, though not all, studies to have increased leptin levels, which may in turn impact reproductive features. Increased leptin secretion may lead to increased sympathetic nervous system activity [30]. Disturbance of leptin secretion may act at central levels to modulate luteinizing hormone secretion, whose activity is altered in PCOS, but also directly at the ovarian level, where leptin has been shown to be expressed in ovaries of women with PCOS [31], and where direct leptin effects might contribute to dysfunction of follicular maturation and ovulation. Furthermore, it has been suggested that leptin contributes to the state of IR and hyperandrogenism seen in the majority of women with PCOS [32].

Obesity is associated with an increased risk of failure to achieve clinical pregnancy after in vitro fertilization (IVF). This risk increases with increasing BMI. A 2011 study investigating 45,163 IVF cycles from data collected by the Society for Assisted Reproductive Technology demonstrated that this risk increased with increasing BMI. The relationship was stronger among women <35 years than older women, suggesting that after 35 years, age becomes a more important factor than obesity in infertility (Table 2) [33]. The underlying pathophysiology is poorly understood, but obese women undergoing IVF require more gonadotropin than normal-weight women and have fewer normally fertilized oocytes (fewer 2 pronuclei embryos and more 1 pronuclei and 3 pronuclei embryos) [34]. Overall, evidence from clinical practice suggests that obesity negatively affects both the oocyte and the endometrium, as indicated by studies of women receiving donor oocytes, where a normal-weight woman receives oocytes from an obese woman or an obese woman receives oocytes from a normal-weight donor. In either case, obesity is associated with decreased chance of pregnancy and live birth [35,36].

Impact of medical and surgical weight loss on female fertility

Normal ovulation is critical in achieving pregnancy, and for obese women with abnormal or absent ovulatory cycles,

Table 2
Risk of failure after IVF [33]

Age group, years	BMI category	Adjusted OR	95% CI
<35	Underweight	1.00	0.84–1.19
	Normal weight	1.00	Reference
	Overweight	1.07	1.00–1.16
	Obese Class I	1.21	1.10–1.34
	Obese Class II	1.38	1.20–1.60
	Obese Class III	1.80	1.46–2.23
≥35	Underweight	1.00	0.82–1.21
	Normal weight	1.00	Reference
	Overweight	1.00	0.93–1.08
	Obese Class I	1.07	0.97–1.18
	Obese Class II	1.25	1.08–1.45
	Obese Class III	1.31	1.05–1.64

BMI = body mass index; CI = confidence interval; IVF = in vitro fertilization; OR = odds ratio.

weight loss frequently improves ovulatory dysfunction. Obesity has long been recognized as a risk factor for infertility, in large part due to changes in the insulin growth factor system, the opioid system, estrogens, and cytokines such as leptin, as mentioned earlier [37]. Such hormonal effects are understood to disrupt the normal ovulatory cycle. Regarding infertility in the setting of PCOS, the presentation of PCOS differs depending on whether or not the patient is obese. In obese patients with PCOS, androgen abnormalities can be more pronounced, particularly in those with central or abdominal obesity (measured by increased waist circumference). Even in patients with normal BMI, central obesity is seen in >60% of women with PCOS. For women with PCOS, weight loss is the first-line treatment. Second-line treatment includes clomiphene or letrozole to promote ovulation. Gonadotropin therapy may be added to (or substituted for) clomiphene/letrozole if those agents fail to achieve ovulation and, finally, possible surgical intervention with ovarian drilling [38]. As many as 70% of women with PCOS also have IR, and about 10% have diabetes [39]. Smoking cessation, exercise, and acupuncture have all been studied as therapies to reduce IR, but weight loss remains the most effective modality.

Guidelines from the American College of Obstetricians and Gynecologists and the American Society for Reproductive Medicine recommend addressing obesity and weight loss in obese women who are planning to conceive, even in those who have not experienced infertility [4,39–41]. Dietary and behavioral weight-loss interventions have been shown to improve oocyte parameters and increase the likelihood of spontaneous conception and decrease the number of cycles of fertility treatment needed to conceive. However, there is little evidence that this leads to improved fecundity [42,43]. These specific weight-loss interventions are of minimal intensity and include limited use of proven medical weight-loss strategies, thereby leading to a relatively small likelihood and magnitude of weight loss. Further study is needed to evaluate fertility

outcomes using comprehensive, coordinated intervention, including intensive behavioral therapy, pharmacotherapy, and other medical weight-loss strategies. Of note, only orlistat, a lipase inhibitor that is not absorbed from the gastrointestinal tract, has been studied in the context of infertility [44–47]. Studies that evaluate fertility outcomes consider fetal and maternal morbidity in addition to successful conception endpoints. Therefore, although pregnancy complications are not the focus of this position statement, there is evidence for improved gestational age at delivery and reduced overall maternal morbidity when weight loss is achieved before pregnancy [48–51].

As the most durable and effective route to significant weight loss, weight-loss surgery has been studied in regard to female fertility outcomes. Case-control studies have demonstrated improved fertility after weight-loss surgery [52]. Purely restrictive procedures such as vertical banded gastroplasty (no longer performed) and adjustable gastric band (less commonly performed) can improve fertility when weight loss is achieved. Some matched cohort studies have shown that adverse maternal outcomes in pregnancy are generally lower in women who have undergone any of a variety of bariatric procedures, and may approach the rates in normal weight pregnant women [53].

Contraception and bariatric surgery

The Centers for Disease Control identifies bariatric surgery in the past 2 years as a condition associated with an increased risk for adverse complications as a result of unintended pregnancy [54]. As a result, contraception education, counseling, and follow-up should be considered at the time of bariatric surgery for all women with the potential to conceive. The evidence regarding use of contraception after bariatric surgery, however, is very limited in terms of both overall utilization and optimal method. Based mainly on evidence from surveys, condoms and oral contraceptive pills (OCPs) appear to be the most commonly utilized contraception methods in the United States, whereas intrauterine devices are the predominant method for women in the Scandinavian Obesity Surgery Registry. Gaps in communication regarding contraception education and level of postoperative compliance were reported in all surveys [55–57]. Another survey of 574 bariatric surgeons, most of whom were men (89%), reported that the majority provided a consistent message to patients to delay pregnancy after bariatric surgery (87%); 52% of respondents required postoperative contraception and 64% provided referral to an obstetrician-gynecologist or primary care physician, but 35% were unaware of how or whether patients obtained contraception. This supports the need for better communication between bariatric surgeons and women's healthcare providers [58]. A 2010 systematic review that evaluated contraception after bariatric surgery identified only 5 relevant studies, 2 of which were on jejunioileal

bypass, a procedure no longer performed. No randomized controlled trials or large prospective longitudinal studies were identified [59]. They included a small case series of 40 patients who had undergone biliopancreatic diversion and were advised to avoid pregnancy for at least 2 years. They reported 2 OCP failures at 9 months and 24 months postoperatively. Based on the 5% failure rate, which is higher than the 4% rate in the general population, the authors advised using contraception methods other than OCP and called for a large randomized controlled trial to determine the best method of contraception after bariatric surgery [60]. A single case series evaluated etonorgestrel-releasing implant (Implanon, Merck Sharp & Dohme Corp., a subsidiary of MERCK & Co., INC., Whitehouse Station, NJ 08889, USA) after Roux-en-Y gastric bypass (RYGB). Three women received the implant 1–2 months before RYGB. Serum etonorgestrel levels decreased with weight loss but remained above the minimum concentration for effectiveness for at least 6 months after the surgery without resulting in unintended pregnancy [61]. Although there are conflicting data regarding the efficacy of OCPs in obese women, the failures attributable to OCPs are generally no higher than those of normal-weight women. The risk of certain complications such as venous thromboembolism or deep vein thrombosis, however, may be higher in obese women and should be considered during counseling on contraceptive methods, given that women can remain obese for some period after bariatric surgery or despite bariatric surgery [62]. Given the available evidence, it is unclear whether there is a difference in the efficacy of OCPs after bariatric procedures that involve some degree of malabsorption and/or the optimal method of contraception.

Impact of medical and surgical weight loss on the effectiveness of infertility treatment

Although obesity is associated with several aspects of infertility, including oligo- and anovulation, follicular development and oocyte maturation, endometrial development and implantation, and response to assisted conception treatments, there are limited data regarding the effects of nonsurgical weight loss on outcomes of infertility treatment [63]. Several studies suggest that weight loss may improve reproductive function [64], decrease the number of cycles of fertility treatment needed to conceive [65], and improve outcomes of fertility treatment in women both with and without PCOS [66–68]. However, the effects of these improvements on fecundity have been mixed [65–68]. Moreover, very-low-calorie diets, utilized in adult obesity treatment with variable success, have been shown to worsen infertility treatment outcomes [69].

Overall, there is also a paucity of literature regarding the specific impact of bariatric surgery on the responsiveness to subsequent treatments for infertility. The general findings on female fertility and PCOS after bariatric surgery have

been very positive. The latest position statement on PCOS from the European Society for Endocrinology recommended including bariatric surgery as a treatment for PCOS in women with morbid obesity, particularly when metabolic syndrome is also present [70]. A recent systematic review and meta-analysis evaluated the impact of bariatric surgery on PCOS and identified 13 studies involving 2,130 patients. The preoperative incidence of PCOS was 45.6%, which decreased to 6.8% ($P < .001$) at 12 months postoperatively. Infertility decreased from 18.2% to 4.3% ($P = .0009$) between preoperative states and the end of the study. Similar significant improvements were found for hirsutism and menstrual irregularity [71].

There is only 1 published study that evaluated results of IVF cycle characteristics both before and after bariatric surgery. In this retrospective study, 18 out of 9,869 patients treated with IVF had bariatric surgery, 7 patients had IVF both before and after bariatric surgery (5 laparoscopic sleeve gastrectomy, 2 laparoscopic adjustable gastric banding), allowing for direct comparison. Despite a significant reduction in BMI (43.1 ± 3.3 versus 29.6 ± 7.33 kg/m², $P = .018$), 3 of the 7 patients remained obese or morbidly obese. There was a significant decrease in the total number of gonadotropin ampules required during the IVF cycle following bariatric surgery (which was associated with reduced treatment cost and improved patient comfort from fewer injections), with no adverse effects on the number of follicles or oocytes retrieved [72]. IVF after bariatric surgery has also been reported in 5 patients (4 RYGB and 1 laparoscopic adjustable gastric banding) who conceived after their first or second IVF cycle without IVF complications, resulting in 4 term live births [73].

Impact of male partner's obesity and surgical weight loss on fertility and infertility treatment

As with women, men of reproductive age have a high prevalence of obesity [2]. Obesity in men is associated with decreased reproductive function and needs to be considered in the evaluation of the infertile couple. Obesity impacts sexual function because it is associated with erectile dysfunction and decreased quality of life [74]. Obesity impacts the endocrinology of reproduction in men by suppressing sex hormone-binding globulin and increasing aromatization of androgens to estrogen. This may reduce gonadotropin secretion [75].

In one meta-analysis, most studies indicated that obesity in men was associated with an increased incidence of abnormal semen parameters [76], but another study had contradictory findings [72–83]. Independent of sperm parameters, there is evidence to suggest that there may be some impact of obesity on sperm function, such as DNA damage, decreased mitochondrial activity, or oxidative stress [84–89]. In one study, paternal obesity was associated with decreased blastocyst formation and decreased

pregnancy in couples undergoing IVF [90]. In another study of couples undergoing intracytoplasmic sperm injection during IVF, increased BMI of the male partner was associated with significantly lower odds of pregnancy in the female partner than for normal-weight men. This relationship was not seen in couples using IVF alone [91]. Both of these studies suggest that there is an increased miscarriage rate with male partner obesity.

Whether obesity treatment in male partners improves fertility in the couple is not entirely clear. Studies of low-calorie diets and bariatric surgery have demonstrated improvements in quality of life and erectile dysfunction as well as reproductive hormones [92]. In contrast, one case series on male fertility after RYGB surgery reported on 6 men with a mean age of 38.3 ± 2.4 years, all with a history of 1 child with their partner before surgery. They presented for infertility evaluation after a minimum of 8 months of trying to conceive >12 months from the time of RYGB surgery. All men had secondary azoospermia with complete spermatogenic arrest. It was unclear whether these results were permanent or temporary, and although nutritional depletion was considered as a possible etiology, the study did not evaluate or discuss whether these men had any nutrient deficiencies [93]. Two additional case series reported on 5 men with similar declines in sperm parameters 3–18 months after RYGB. One patient had reversible effects after 24 months [76,94]. Although more data with longer follow-up are necessary to determine the true impact of bariatric surgery on sperm parameters, these findings highlight the role that male infertility can have on assisted reproduction outcomes [76,93,94]. More investigation is needed to fully understand the impact of surgical weight loss on fertility and infertility treatment in men.

Conclusion and summary recommendations

There is a very high prevalence of obesity among women of childbearing age. Obesity in women is associated with an increased risk of infertility and an increased rate of complications during every stage of pregnancy. Obesity is associated with PCOS and IR, which also negatively impact fertility. Overall, however, there is a paucity of high-level evidence regarding the impact of obesity and obesity treatment on fertility and infertility treatment. Ongoing investigation and randomized controlled trials are necessary to fully understand the role of obesity and the impact of medical and surgical treatments for obesity on male and female fertility and infertility treatment outcomes.

1. Obesity is associated with a significant delay in conception that is partly, but not entirely, due to an impact on normal ovulation.
2. Obesity reduces male fertility parameters and should be considered in the evaluation of a couple presenting with infertility.

3. The symptoms of PCOS, particularly with respect to fertility and metabolic disturbance, are exacerbated in the presence of obesity.
4. Weight loss can improve weight-associated causes for infertility such as PCOS and IR.
5. For some overweight and obese women, particularly with PCOS, weight loss may improve ovulatory function, leading to improved fertility.
6. Obese women have a lower probability of achieving live birth after in vitro fertilization.
7. Bariatric surgery is effective in achieving significant and sustained weight loss in morbidly obese women and has been shown in case-control studies to improve fertility.
8. Pregnancy is not recommended during the rapid weight-loss phase after bariatric surgery; therefore, counseling and follow-up regarding contraception during this period is important.
9. The specific impact of either medical weight-loss treatments or bariatric surgery on the responsiveness to subsequent treatments for infertility in both men and women is not clearly understood at this time.

This position statement is not intended to provide inflexible rules or requirements of practice and is not intended, nor should it be used, to state or establish a local, regional, or national legal standard of care. Ultimately, there are various appropriate treatment modalities for each patient, and surgeons must use their judgment in selecting from among the feasible options. The American Society for Metabolic and Bariatric Surgery cautions against using this position statement in litigation in which the clinical decisions of a physician are called into question. The physician, in light of all the circumstances presented, must make the ultimate judgment regarding the appropriateness of any specific procedure or course of action. Thus, an approach that differs from the position statement, standing alone, does not necessarily imply that the approach was below the standard of care. To the contrary, a conscientious physician may responsibly adopt a course of action different from that set forth in the position statement when, in the reasonable judgment of the physician, such course of action is indicated by the condition of the patient, limitations on available resources, or advances in knowledge or technology. All that should be expected is that the physician will follow a reasonable course of action based on current knowledge, available resources, and the needs of the patient to deliver effective and safe medical care. The sole purpose of this position statement is to assist practitioners in achieving this objective.

This position statement has been endorsed by the American College of Obstetricians and Gynecologists, May 2017, and should be construed as its clinical guidance.



Disclosure

The authors have no commercial associations that might be a conflict of interest in relation to this article.

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