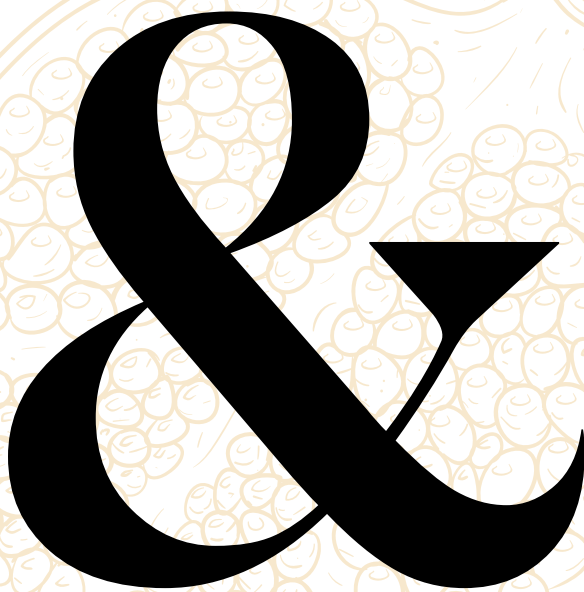


questions
about
fertility



obesity



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Approximately 1/3 of men and 2/3 of women with infertility are either overweight or obese. It is unquestionable that body mass index (BMI), which is a ratio of your weight in kilograms to your height in meters squared, has a very significant impact on fertility. Data indicates that 12% of infertility is the result of abnormal BMI alone, and patients with morbid obesity have a 690% increase in the risk of infertility!

We realize that many patients have battled BMI for much of their lives and that in some instances even aggressive attempts to lose weight have been met with poor or unsatisfying results. For that reason, we want to provide you with some perspective on how an elevated BMI can impact your reproductive journey, and we also want to provide you with guidance on how, together, we can manage this aspect of your care.

We have extensive resources committed to helping you. In particular, if you want more detailed information than what is provided below, we are more than happy to meet with you again and plan your journey forward together.

12%

of infertility is the result of BMI

690%

increase in infertility for morbidly obese patients

How do I know if I am obese?

The World Health Organization has defined obesity and this is a nearly universal standard in use today. BMI is calculated based on your weight divided by your height squared (kg/m^2).

BMI classification (kg/m^2)

| | |
|------------|--------------|
| NORMAL | 18.5 to 24.9 |
| OVERWEIGHT | 25.0 to 29.9 |
| CLASS I | 30.0 to 34.9 |
| CLASS II | 35.0 to 39.9 |
| CLASS III | >40.0 |

Why am I obese?

Obesity is rarely because of simply a bad diet or lack of exercise. Obesity can be caused by hormonal changes such as a thyroid or cortisol condition, by physiological changes from having polycystic ovarian syndrome, or even poor dietary timing, like eating only one meal per day. We are committed to determining the cause of your infertility and will determine if there are any reasons for your non-ideal weight. **If there is a fixable cause we will correct it.**

How does an elevated BMI impact fertility?

Elevated BMI can alter nearly every aspect of fertility care. In women, there is substantial evidence for all of the following adverse effects.



Women

#1 Elevated LH levels

Common in PCOS women this can lead to increased androgen levels, further increases in weight, menstrual irregularity, diminished oocyte (egg) development and maturation

#3 Increased insulin resistance

This leads to significant increases in insulin secretion, increased hyperandrogenemia (elevated levels of androgens in the blood), menstrual and ovulatory disturbances, decreased oocyte development, decreased oocyte retrieval, decreased oocyte maturation and decreased fertilization and implantation because of negative effects on the endometrial lining. Perhaps most importantly this places patients at a significant risk of diabetes.

#2 Elevated androgen levels

Common in PCOS women this can lead to increased androgen levels, further increases in weight, menstrual irregularity, diminished oocyte (egg) development and maturation

#4 Increased Adipokines

Alterations in adipokines including leptin, adiponectin, and others have been directly linked to decreased success in IVF cycles

i. Leptin: Elevated BMI increases leptin levels increase leptin in follicular fluid and studies show that leptin can result in decreased granulosa cell estrogen and production in a dose-dependent manner, with subsequent impact on endometrial receptivity and implantation. Leptin

has been demonstrated to impair follicle development, ovulation and oocyte maturation

ii. Adiponectin: Elevated BMI decreases adiponectin levels, which results in decreased insulin sensitivity. Diminished adiponectin and adiponectin receptors have been associated with recurrent implantation failure

iii. Resistin: BMI is associated with increased resistin and this is associated with decreased insulin sensitivity

iv. Visfatin: Increased in overweight and obese patients, and those with PCOS and type II diabetes mellitus

#5 Increased inflammatory markers

This leads to significant increases in insulin secretion, increased hyperandrogenemia (elevated levels of androgens in the blood), menstrual and ovulatory disturbances, decreased oocyte development, decreased oocyte retrieval, decreased oocyte maturation and decreased fertilization and implantation because of negative effects on the endometrial lining. Perhaps most importantly this places patients at a significant risk of diabetes.

#6 Decreased oocyte quality

Obese women have reduced egg quality because of hormonal alterations, adipokine alterations, and inflammatory marker changes. This is related to the multiple biochemical alterations noted above. Eggs are smaller, have



more molecular alterations, more meiotic spindle alterations, and are programmed to die more often, a process referred to as apoptosis. Poor egg quality means lower chances of fertilization, embryo development, blastulation, and implantation, with an increased risk of miscarriage and early pregnancy loss

#8 Reduced Ovulation Potential

Chances of ovulation are substantially reduced in obese women. Depending on your weight there is up to a 310% increase in the chances of ovulatory dysfunction – in other words, not releasing an egg

#10 Response to Stimulatory Medications

Patients with elevated BMI have a significant decrease in response to letrozole and clomid, medications used to induce ovulation in particular in women with PCOS, while those using injectable medications will require significantly higher doses, drastically increasing treatment costs.

#7 Decreased oocyte number at egg retrieval

Obesity causes women to have fewer eggs in response to stimulation. This is true even in obese PCOS women compared to PCOS women without obesity. Fewer oocytes are retrieved at IVF egg retrieval, and of the eggs that are retrieved fewer are mature (metaphase II) eggs. Despite the increased number of eggs usually associated with PCOS, obese PCOS women have fewer eggs develop than normal weight PCOS patients.

#9 Reduced Fertilization

Although controversial, some studies have demonstrated up to a 45% reduction in egg fertilization at IVF

#1 Hormonal changes (hypogonadism)

Obesity is related to increased estrogen and leptin levels in men. This causes decreased testosterone, follicle-stimulating hormone, and sex hormone binding globulin, ghrelin and inhibin B levels. All of these result in hormonal imbalances that increase estrogen production and decrease testosterone production and subsequently sperm production. As a result, you will feel lethargic, have decreased muscle mass, have a reduced sex drive, increased erectile dysfunction and in some instances develop breast tissue, a condition referred to as gynecomastia.

#2 Adipokines and Inflammatory markers

In men as well as inflammatory markers increase a loss of male hormones (androgens). In the testis, these inflammatory markers directly cause the seminiferous tubules where sperm are produced to become dysfunctional. These same changes also cause damage to the storage site of sperm, the epididymis, where it leads to a failure of sperm maturation and fertilization potential.

#3 Oxidative Damage

Obesity in men increases the presence of oxygen free radicals. This can create an environment that has excessive oxidative stress. This results in an increased risk in sperm DNA fragmentation, which has been associated with failed



intrauterine insemination, failed fertilization in IVF, decreased blastulation, and a significant increase in miscarriage risk.

#5 Actual Sperm Performance Parameters

In regards to the actual semen analysis, numerous studies have demonstrated significant reductions in every category, including sperm count, sperm motility. In one of the most recent studies, the following results for overweight men demonstrated:

Semen volume

Decreased by 4.2%

Sperm Count

Decreased by 3.9%

Total Motile Count

Decreased by 3.6%

Two large studies demonstrated increased risks of low sperm count or even azoospermia (the absence of any sperm). (sermondale HRU 2013, Sermondale Arch Int Med 2012)

#4 Scrotal and Testicular Temperature

Obese males have higher scrotal temperatures. When the scrotal temperature is elevated, sperm motility, sperm count, sperm DNA damage and sperm oxidative stress are all increased.

#6 Sperm DNA Fragmentation

Damage to the Sperm DNA and Epigenetic Changes (changes to the DNA that can be passed on to offspring)

Obese men have changes increased sperm DNA fragmentation. In a recent study that controlled for factors such as smoking and age, men who were obese (BMI > 30 kg/m²) had a 150% increase in the risk of moving from a normal sperm DNA fragmentation category to a moderate, or from the moderate category to severe DNA fragmentation. As previously mentioned, elevated sperm DNA

fragmentation can increase risks of fertilization failure, poor blastocyst development, failed implantation and increased risks of miscarriage.

Equally concerning is the fact that obesity can cause changes in the actual sperm

DNA that can result in higher risks of disease in their offspring, including obesity, diabetes, hypertension and heart disease.

#7 Erectile Dysfunction

Men with obesity have an increased risk of erectile dysfunction. While the overall risk of erectile dysfunction is 17% in infertile men, it was increased to 45% in men with a BMI > 30 kg/m²

How does elevated BMI affect IVF success rates?

Clinical Pregnancy Rate

Patients with an overweight BMI have a **18% decrease in seeing a fetal heartbeat** following IVF treatment.

| | CLASS II | CLASS III |
|--------------------------------|----------|-----------|
| Cycle Cancellation Rate | 17% ▲ | 50% ▲ |
| Egg Retrieval Rate | 2% ▼ | 7% ▼ |
| Usable Embryos | 3% ▼ | 5% ▼ |



Clinical Pregnancy Rate

Patients with an overweight BMI have a **19% decrease in delivering a live-born child** compared to patients with a normal BMI. For every unit increase in BMI over 25 kg/m² the odds for pregnancy are reduced by 0.84.

Miscarriage

One study demonstrated that the risk of miscarriage in obese women was as high as 40% compared to less than 15% in normal BMI patients. To put this into perspective, this is the equivalent of making a 25 year old woman have the same miscarriage risk as a 40 year old woman.

Even more concerning is the fact that patients with obesity have a **350% increase in the risk of recurrent pregnancy loss**, meaning 3 or more spontaneous miscarriages consecutively.

Does BMI increase the risks of birth defects?

Both congenital heart malformations and neural tube defects are increased in women who are obese or severely obese. For women with obesity there is a **70% increase in the risk** of neural tube defects, while for those with a Class II BMI there is a **211% increase in risk**. In one American study they demonstrated increased risks of anencephaly (OR 2.3, 95% CI 1.2 - 4.3), spina bifida (OR 2.8,

95% CI 1.7 - 4.5) and isolated hydrocephaly (OR 2.7, 95% CI 1.5 - 5.0). Risks of congenital heart disease in obese women ranges from **20% - 100% higher** than normal weight women.

Does elevated BMI increase the risk of gestational diabetes?

Gestational diabetes risk is directly correlated to maternal obesity. Compared to women with a normal BMI, overweight women have a **3.42 fold** increase in risk, obese

women have a **7.54 fold** increase in risk, an severely obese women have a **10.83 fold** increase, or almost 1000% higher risk. In actual numbers, less than 1% of women with normal weight will develop gestational diabetes, 3.1% of overweight women, 6.7% of obese women, and 9.3% of severely obese women. Women who develop gestational diabetes have nearly a 50% increase in risk of type II diabetes mellitus, a **potentially life-threatening disease**.

Importantly, mothers with gestational diabetes have increased risks of caesarean section, extensive vaginal tearing, shoulder dystocia and intrapartum fetal asphyxia, a condition that frequently can result in cerebral palsy.

obese women have

10x

the risk of gestational diabetes



Does an elevated BMI increase the risks of hypertensive disorders of pregnancy?

In a study examining results of nearly 1.4 million women, **pre-eclampsia risk doubled** with every 5-7 kg/m² increase. In an Australian study, risk of pre-eclampsia was 2.4% in normal weight women, and as high as 14.5% in women with a Class III BMI, representing a nearly **5 fold increase** in risk.

Does obesity increase the risk of stillbirth?

Unfortunately, all fetal and neonatal/newborn risks are increased for women with an elevated BMI. Specifically, for

| | BMI | 20-25 | 25-30 | 30+ |
|------------------------|-----|-------|-------|-----|
| Fetal Death | | 76 | 82 | 102 |
| Stillbirth | | 40 | 48 | 59 |
| Perinatal Death | | 66 | 73 | 86 |
| Neonatal Death | | 20 | 21 | 24 |
| Infant Death | | 33 | 37 | 43 |

every 5 unit increase in BMI there was a 21% increase in risk of fetal death, a 24% increase in risk of stillbirth, a 24% increase in risk for perinatal death, a 16% increase in neonatal death, and a 15% increase in infant death. If you have an Obese BMI your overall risk of an unexpected infant death before, near or even after delivery is 3.14%

Does elevated BMI increase the risk of delivering a premature infant?

Numerous studies have demonstrated that overweight and obese women are at increased risk of being forced to deliver prematurely secondary to pregnancy related complications. In a large Scottish study, the authors demonstrated that BMI linearly increased the risks of premature delivery. If your BMI is overweight risks is 15% elevated, for Class I - 52% higher, and for **Class II it is 113% higher**.

I made it through the pregnancy with no complications! Am I at risk during delivery if my BMI is elevated?

Patients who are overweight have a 46% increase in risk of caesarean section, obese women have a 105% increase in risk of caesarean section, and **severely obese women have an almost 300% increase** in caesarean section risk.

Equally concerning is that in cases requiring emergent caesarean section, time from decision to delivery is longer in obese women, blood loss is greater, post partum



hemorrhage is greater, and risk of infection is increased 124%. For women with a Class III BMI the risk of wound infection is 4 fold normal, and if BMI is greater than 50 kg/m² wound infection occurs in 66% of women and wound dehiscence (the wound coming apart) occurs in up to 14% of cases.

Intensive care admission is increased in women with a BMI > 50 kg/m², and prolonged hospital stay is more common.

Am I or my infant at risk during the delivery if I have an elevated BMI?

Labour is less likely to occur spontaneously, more likely to be induced, is prolonged and is less likely to result in a vaginal delivery in obese compared to normal BMI women. Rates of operative vaginal delivery and caesarean section are higher as well.

Infants of obese mothers have considerably higher risks of being macrosomic (odds 2.1 fold increase),

| RISK | INCREASE |
|----------------------------|----------|
| Bone injury | 2x |
| Respiratory Distress | 2x |
| Bacterial Sepsis | 3x |
| Seizures | 3x |
| Intrapartum Fetal Asphyxia | 3x |
| Feeding Difficulties | 3x |
| Peripheral nerve injury | 4x |
| Hypoglycemia | 4x |

Risks to infants when mother's BMI is greater than 40 kg/m²

having shoulder dystocia which can permanently damage fetal arm and hand function (odds 2.9 fold increase), and birth trauma including fractures, bruises, skin damage, muscle and scalp bruising/bleeds (odds 1.5 fold increase).

Can I still use any kind of obstetrical anaesthesia?

Obese women have increased risks of needing a general anaesthetic, failed intubation and aspiration, failed epidural and multiple epidural attempts are often necessary.

What if I have no complications right through the pregnancy and the delivery?

Risks of developing a life threatening blood clot in the calves or lungs increases from 0.6% to 2.5% in obese women after delivery. Some authorities recommend prophylactic blood thinning after delivery for these women to prevent the formation of blood clots.

Breast feeding is also reduced in women suffering from obesity. And while many feel that bottle feeding is adequate, it is important to note that breastfeeding is protective against the child developing obesity, while formula feeding **increases the risk of childhood obesity.**



Is my child at risk, if my BMI is elevated?

Infants born to obese mothers have a **3.5 fold increase in admission to NICU** primarily because of gestational diabetes. When babies are born to mother's with elevated circulating blood sugars, the infant's insulin level increases significantly. Once they are born and there is a drop in sugar supply, these babies become low in sugar (hypoglycemic) necessitating IV therapy in some cases and close monitoring. Insulin also acts as a fetal growth factor causing many infants to become large (macrosomic). This can then increase risks of birth trauma such as shoulder dystocia, need for operative vaginal delivery, caesarean section and again need for NICU admission.

Infants born to mothers who are obese are significantly more likely to become obese themselves. This is true of childhood obesity, adolescent obesity and adult obesity.

Other studies have demonstrated a reduction in childhood intelligence, and reduced IQ scores.

There are numerous other outcomes that have also been associated, including intellectual outcomes, future outcomes for the children including heart disease, diabetes and hypertension.

We fully respect the emotional burden these terrifying statistics carry and feel strongly that patients who struggle with an elevated BMI should work closely with us and our allied health care professionals to ensure a successful and safe pregnancy. We recognize that in many instances, **weight loss can be extremely difficult** for some patients either because of health conditions, access to appropriate resources, or even simply a lack of time. We are always happy to work closely together with you to develop a diet and exercise plan that anyone can employ. We have numerous resources available to help you including physicians, our incredible naturopath, Dr. Jennifer Strong, nutritionists, a fertility specialized social worker, and associations with local gyms to facilitate your weight loss goals.

As you can see, the risks of infertility are increased, success rates are substantially decreased, pregnancy complications are drastically increased, and chances of pregnancy or newborn loss are absolutely unacceptable.

As a result of these complications, we feel strongly that while each patient's care must be individualized, as a general rule, **patients with a Class III BMI should not attempt to conceive** until they have achieved weight loss. Exceptions include women with advanced age (> 40 years old) where the duration needed for adequate weight loss can compromise outcomes.



Does Weight loss improve fertility and pregnancy outcomes?

In women who undergo physical activity interventions for weight reduction, there was a **110% increase in pregnancy rates**, a 111% increase in live birth rates!

In a meta-analysis of several studies, physical activity was as effective as treatments for conception, including clomiphene, injectable medications, and even IVF.

In the same study, patients with PCOS who engaged in physical activity had higher success rates than those that underwent fertility treatments alone! Obviously, combination therapy with diet, weight loss, and fertility treatments yields the best overall results.

Numerous studies have demonstrated that even a small amount of weight loss can significantly reduce the risks described above. **Even a loss of 5 lbs** has been shown to improve outcomes!

I've tried everything! How can I lose weight?

Weight loss can be daunting and always involves significant lifestyle changes. But **it is always possible**. Weight loss when it is really examined in its simplest form is a matter of making your input (calories from your diet)

be less than your output (calories you burn from activities of daily living +/- exercise). If you take in less than you burn off, it is impossible to not lose weight.

However, there are several important factors to consider:

1. Your caloric intake needs to be between **1200 – 1500 calories/day**. There are many food guides available including the Canada Food Guide which can help you develop a safe meal plan that fits these criteria. Atkins, Paleo, Mediterranean, Whole Food diets can also be useful weight loss diet approaches.
2. You need to **spread out your calorie intake**. Many patients think it is better to only eat one meal per day. This drives up your insulin levels and makes your body store the majority of excess calories. Simply eating small meals frequently throughout the day can significantly decrease your weight. A good general approach is breakfast – snack – lunch – snack – dinner. You still need to stay in the calorie limit though! So your meals need to be small and your snacks should be very low calorie choices, like celery, some apple slices, a few nuts etc.
3. **Drink water**. Patients should have at least two liters or 8 cups of water per day. This helps to cleanse the body, but also keeps your stomach slightly full, which can make you feel less hungry.

4. Maintain good eating habits. Eat slowly and without distraction, and chew your food at least 20 times before swallowing. This provides you with enough time to recognize that you're becoming full.

5. If you don't exercise it is almost impossible to keep the weight off. Exercise must be an active component of any healthy lifestyle. In particular, developing lean muscle mass significantly assists with consuming calories and contributes to loss of unnecessary adipose tissue. Many people say they walk, and while walking is better than no activity, it is generally insufficient for weight loss. For weight loss, you need to remember to burn more calories than you're taking in, so walking is usually not sufficient. But not everyone needs to or can afford to join a gym. Running, elliptical machines, treadmills, weight training, plyometrics, or high intensity interval training (HIIT) can be done at home and in some instances even without any equipment. To burn adequate calories you need to increase your heart rate, generate sweat, and try to build muscle mass. Make sure you engage in exercise only after speaking with a physician as some people can injure themselves or endanger their health with certain types of exercise.

6. Finally, the type of diet is important. Diets rich in protein, and low carbohydrate vegetables will contribute

to weight loss. High carbohydrate foods are generally detrimental and particularly detrimental to patients with PCOS. It is critical to eat a healthy balanced diet and minimize items that are high in fat or carbohydrates including chips, cookies, cakes, donuts, ice cream, chocolate, pies, breads, pastas, pizza, french fries.

7. Set reasonable goals. Diet plans that aim to have you lose 20 lbs in one month are not reasonable and cannot be sustained, in general. A safe and reasonable goal to set is a weight loss of 1 – 2 lbs per week. While some individuals can manage more, this should exclusively be done with the advice and guidance of an expert.

8. Address emotional eating. Recognize why you're eating and only eat when you're actually hungry. Use meditation, mindfulness, yoga and journaling to keep track of your habits.

Remember: if you eat at appropriate intervals, have a diet low in carbohydrates and exercise regularly, and can keep your calorie burn higher than your calorie intake, **it is impossible to not lose weight.** Aside from commitment, simple tasks like a dietary diary can be helpful, as can apps that track your work outs and steps, heart rate, etc.

We trust that you have found this information helpful. As always, we are here to assist you with your journey and will guide you through whatever process you chose. If you have questions, need more information, or want assistance with your fertility journey please don't hesitate to meet with one of our specialists!

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