

Module 6 - Dietary considerations

Learning objectives

The learning objectives for this module are as follows:

1. Explain the advantages and disadvantages of different dietary approaches to optimise fertility in women
2. List foods that should be avoided to better optimise fertility and outline the evidence supporting these recommendations
3. Recall common side-effects of hormonal treatments for assisted reproductive technologies and understand the role of diet in their management
4. Describe the factors that drive emotional eating and the evidence supporting different strategies for behaviour change

Popular diets and their impact on fertility

The impact of specific diets and their effectiveness in the management of fertility is considered below:

Mediterranean Diet

The Mediterranean diet pattern emphasises minimally processed fruits, vegetables, wholegrains, legumes, nuts and seeds. The primary fat source is olive oil, and dairy, eggs, fish and poultry are consumed in moderate amounts. Alcohol, predominantly red wine, is included in a Mediterranean diet but only consumed at low to moderate amounts with meals. While red meat may also be eaten in very small amounts, the consumption of fish and legumes, and to a lesser extent, poultry, predominate. Mediterranean dietary patterns have been shown to reduce the risk of cardiovascular disease, type 2 diabetes and cancer.¹ They have also been shown to support weight loss and weight maintenance and improve markers of metabolic health.² The benefits of the Mediterranean diet pattern appear to relate to its lipid-lowering properties, its strong antioxidant and anti-inflammatory effects and actions on the gut microbiota.

To date, no randomised control trials or systematic reviews have explored the effectiveness of a Mediterranean diet to improve fertility or reproductive outcomes in women. Three observational studies have been reported in the literature and only two studies have shown beneficial effects of the Mediterranean diet pattern on reproductive outcomes.

In a study by Karayiannis et al. adherence to a Mediterranean diet pattern and the impact on IVF outcomes was explored in 244 non-obese (BMI < 30 kg/m²) Greek women undergoing their first IVF cycle.³ While no association between Mediterranean diet score (MDS) and outcomes such as oocyte yield, fertilization rate and embryo quality measures were observed, 50% of the women in the highest tertile for MDS achieved clinical pregnancy, compared to only 30% of women in the lowest tertile ($p=0.01$). Live births were also significantly higher in women with greater adherence to a Mediterranean diet pattern (48.8% v 26.6%, highest v lowest tertile for MDS, $p = 0.01$). Adherence to

a Mediterranean diet pattern was shown to have the greatest impact on reproductive outcomes in women under the age of 35 years.

Similarly, Gaskins et al. recently demonstrated that greater adherence to a Mediterranean diet pattern was associated with an increased chance of implantation, clinical pregnancy and live birth in their cohort of 357 largely Caucasian women undergoing treatment with ART.⁴ Interestingly, the beneficial effect of the Mediterranean diet on reproductive outcomes plateaued with the highest quartile for MDS in this cohort. The authors hypothesised that this may be due to the less stringent policies governing the use of pesticides on food products in the US when compared to Europe and thus those in the highest quartiles for MDS score may be inadvertently exposed to pesticide residues that have been linked to impaired fertility.

In contrast, Ricci et al. found no relationship between adherence to a Mediterranean diet and any IVF outcomes (oocyte and embryo quality, clinical pregnancy and live birth rates) in a cohort of Italian women (n=474) undergoing their first IVF cycle.⁵ It should be noted that this study used a different method to determine MDS when compared to Karayiannis et al. and Gaskins et al. who used identical methods] thus it is possible that differences in classification in this study mean that women with the lowest scores for MDS obtained some dietary benefit that also plateaued with higher MDS scores.

Recommendations:

In non-obese women under the age of 35 years, following a Mediterranean diet pattern may lead to improved IVF outcomes such as clinical pregnancy and live birth rate. While there is no current evidence supporting this approach in older women or women with a BMI > 30 kg/m², the beneficial effects of the Mediterranean diet on cardiovascular disease risk factors and hormonal profiles may be advantageous if combined with weight reduction and/or used for weight maintenance. Increased Mediterranean diet adherence has also been shown to be associated with higher sperm quality parameters in males thus prescription of a Mediterranean diet pattern for couples with unexplained fertility may also have clinical benefit.⁶ As low to moderate alcohol consumption is a component of the Mediterranean diet pattern, women and couples should be given appropriate counselling regarding the risks of alcohol consumption for fertility and pregnancy.

[Low Carbohydrate Diet](#)

A low carbohydrate diet describes any intervention where the macronutrient intake of carbohydrates is less than 45% of total daily energy intake. There are many terms used to describe low carbohydrate diets including “low carb”, “ketogenic diet”, “ketosis” and “very low energy diet (VLED)”. Low carbohydrate diets have particular utility for obesity as there is a growing body of evidence demonstrating their ability to support weight-loss and improve insulin sensitivity and glycaemic control.⁷

A recent systematic review by McGrice & Porter identified seven studies that examined the effects of low carbohydrate diets on reproductive outcomes in overweight and obese women with diagnosed infertility. The major finding of this review was that reducing carbohydrate intake, in conjunction a moderate caloric deficit, can reduce circulating insulin levels, improve reproductive hormone status and increase menstrual regularity. Three of the seven studies in this review also reported on pregnancy outcomes. Although two studies reported pregnancy rates of at least 40% in their study cohorts, one study was very small (n=5 participants completing the study) and over half the participants withdrew during the 24-week ketogenic diet (20 g CHO per day).⁸ The second study

conducted by Sim et al. involving 27 obese women found that 6 weeks of a VLED, followed by 6 weeks of a hypocaloric diet (2.5 MJ/day deficit) resulted in 44% of the women giving birth within 12 months.⁹ In the same study, control women (n=22) only received dietary counselling (GP or Dietitian) during the 12-week intervention and achieved a significantly lower live birth rate (14%) within 12 months.

Recommendations:

Restriction of carbohydrate intake below 45% of daily energy intake, with a modest caloric deficit, may be one approach to reduce body weight and improve reproductive outcomes in women. In infertile women with a BMI over 30 kg/m², a 6-week VLED followed by at least six weeks of refeeding with a mildly energy restricted diet has been shown to improve the response to fertility treatment. Severely restricted CHO diets < 30 g/day appear to be difficult to sustain in this population and there is limited evidence supporting their efficacy on reproductive outcomes. Any restricted diet, both low carbohydrate and VLED, should be assessed for nutritional adequacy (especially folate and iodine) and supplemented accordingly. Women should be counselled on the importance of healthy eating and managing weight gain during pregnancy and should cease any dietary restriction/weight-loss efforts during fertility treatment or once pregnant.

Intermittent Fasting

Over the past five years there has been a steady increase in interest in intermittent fasting (IF) as a method for weight loss. IF does not describe a specific diet approach, instead it is a broad term for a range of different approaches that involve alternating between periods of fasting (low or no energy intake) and normal (or high) energy intake.¹⁰ Example of IF regimens include alternate day fasting, the “5:2 diet” and time restricted feeding. Alternate day fasting is a day on, day off approach while the “5:2” method involves two non-consecutive fasting days in a week. Time restricted feeding is a daily method whereby food is consumed within an 8h window, followed by a 16h fast. Another example of time restricted feeding is the dawn to sunset fasting that occurs during the month of Ramadan.¹¹ The popularity of IF seems to be related to the flexibility that it offers for individuals trying to achieve weight loss. This is reportedly in contrast to continuous energy restriction methods that are more rigid and difficult to maintain.¹²

To date, no studies have explored the effects of IF approaches on fertility outcomes in men and women. However, two recent systematic reviews and meta-analyses have shown positive effects of IF on weight-loss and varying effects on cardiometabolic risk factors. Schwingshackl et al. included 17 RCTs with 1328 participants that compared IF to a normal diet or continuous energy restriction for interventions ≥ 12 weeks duration. IF was found to significantly reduce body weight, waist circumference, fat mass, triglycerides and systolic blood pressure when compared to a normal diet. Importantly, no difference between the effects of IF and continuous energy restriction were observed. Cho et al. included 12 studies involving 545 participants that also compared IF to a normal diet or continuous energy restriction.¹³ Their review focussed on studies between 4 and 24 weeks in duration and found that compared to the control IF led to significant reductions in BMI, fasting glucose levels and insulin resistance (measured using the homeostatic model assessment of insulin resistance). Trends for reduction in body weight and fat mass were also observed but they did not reach significance. Differences in findings between the two studies may related to the length of interventions included in these studies and the different methods used to analyse the data.

Recommendations:

While there is no evidence to support this dietary approach to improve fertility outcomes in men and women, IF appears to have positive effects on weight reduction and may also improve insulin sensitivity. Although IF does not appear to perform better than continuous energy restriction regarding weight loss, there is evidence suggesting that IF regimens may have improved adherence when compared to other forms of weight loss, which may ultimately be beneficial for weight control.

Vegan Diets

Over the past five years we have seen a rapid increase in the interest in vegan diets relative to other popular movements such as gluten-free diets and vegetarianism (Figure 1). There are several reasons why people choose to adopt a vegan dietary approach including increased health consciousness, ethical grounds, environmental concerns, or religious/spiritual beliefs.¹⁴

Vegans follow a plant-based diet that typically does not include any meat, eggs, dairy products and honey. Food additives that are derived from animal products such as gelatine, lysozyme and lactitol are also avoided. Although well planned vegan diets are likely to be nutritionally adequate, individuals adopting this dietary approach are susceptible to deficiencies in protein, iron, vitamin B12, calcium, vitamin D, iodine, choline and omega-3 fatty acids.^{14 15} This is of particular concern for women and men who are planning a pregnancy as many of these nutrients are important for oocyte and sperm maturation, conception, embryogenesis and fetal development. There is also evidence that inadequate nutrition can impact on offspring health and development but also their risk of developing chronic diseases later in life.¹⁶

To date, no studies have examined whether a vegan diet can improve hormonal imbalances and/or reproductive outcomes in women with fertility issues. While there is evidence that following a vegan diet can lead to significant reductions in body weight, visceral fat content and improvements insulin sensitivity, this study involved a population of older women (mean age 53.2 ± 12.6 years) who were highly motivated based on an attrition rate of 4%.¹⁷ In contrast, Turner-McGrievy et al. only observed modest reductions in body weight in their population of obese women with PCOS who followed a vegan diet for 6 months.¹⁸ Furthermore, attrition rate in this study was 67% at the end of the study period raising questions about the suitability of this dietary approach for women experiencing fertility issues.

Google Trends - Web Search

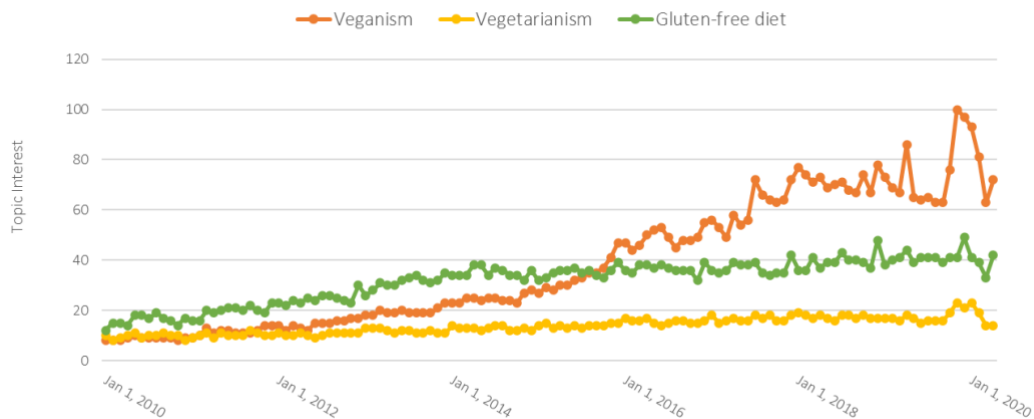


Figure 1: Google search interest for the topics of veganism, vegetarianism and gluten-free diet in Australia from January, 2010 to April, 2020. A significant spike in veganism interest was observed in September 2019 which coincided with the international release of the Gamechangers documentary which focused on plant-based diets. Data derived from Google Trends. The Y axis represents search interest relative to the highest point on the chart for the given region and time. A value of 100 represents peak popularity for the term. A value of 50 means that the term is half as popular.

Recommendations:

Given the potential for nutrient deficiencies on a vegan diet, and the lack of available evidence, adoption of a vegan diet for the purpose of improving reproductive outcomes is not recommended. However, the different reasons people follow a vegan lifestyle needs to be acknowledged and this should be supported by a thorough dietary assessment if planning to become pregnant. The focus of any assessment and management plan should be to ensure sufficient intake of protein, folic acid, vitamin B12, iron, zinc, calcium, vitamin D, iodine, choline and omega-3 fatty acids. Supplementation of these nutrients should be encouraged as they are unlikely to be met by diet alone.

Gluten-free diets

Gluten-free diets are essential for individuals who suffer from coeliac disease. Non-coeliac gluten sensitivity is another condition where gastrointestinal symptoms can be significantly improved by following a gluten-free diet.¹⁹ However, many individuals follow a gluten-free diet under the perception that it is healthier or that it will support weight loss. Others may self-restrict gluten containing products due to unexplained gastrointestinal symptoms that have not been investigated by a health professional.

Restriction of gluten from the diet typically results in a substantial reduction in the intake of cereals and grains which are important sources of carbohydrate, dietary fibre, B-group vitamins and vitamin E. In addition, Australian law does not require gluten-free breads to be fortified with folic acid (unlike wheat-based breads), thus women of childbearing age who follow a gluten-free diet have an increased risk of folate deficiency which is an established risk factor the development of neural tube defects in their offspring.²⁰

Conflicting evidence exists as to whether coeliac disease affects reproductive outcomes such fertility and miscarriage risk.²¹ Interestingly, a recent meta-analysis demonstrated that while diagnosed

coeliac disease did not increase the risk of fertility issues in women, undiagnosed coeliac disease was associated with a 3-fold greater risk of experiencing infertility.²²

Recommendations:

In otherwise healthy individuals, there is no evidence that a gluten-free diet is beneficial for fertility. Reasons for following a gluten-free diet, in the absence of diagnosed coeliac disease or non-coeliac gluten sensitivity, should be explored especially in clients who also report gastrointestinal symptoms. If undiagnosed coeliac disease is suspected, referral to their doctor for further testing is necessary. Individuals who follow a gluten-free diet should be encouraged to take a folic acid supplement in line with current recommendations and considering their risk of giving birth to a baby with a neural tube defect.

Controversial foods

Increasingly the pre-natal period is identified as a critical time whereby the development and health of offspring can be affected by parental exposures. For women and couples experiencing infertility, it is an opportune time to address nutritional concerns as they are more likely to be motivated to adapt existing behaviours.²³

A growing body of evidence has identified several foods that should be avoided in men and women who are trying to conceive. These include alcohol, caffeine, trans fats, refined carbohydrates and artificial sweeteners. In addition, exposures to toxins such as mercury in fish and bisphenol A (from plastic containers) should also be determined so clients can be appropriately counselled regarding the risks. Evidence demonstrating links between these foods and exposures and their impact on fertility outcomes are explored in the following sections.

Alcohol

Current public health guidelines in Australia recommend that women who are planning to become pregnant or are pregnant or breastfeeding should avoid alcohol (NHMRC, 2009). Despite this, a recent study demonstrated that 60% of Australian women consumed alcohol in the period from conception until pregnancy was recognised.²⁴ Furthermore, 30% of women in this cohort continued to consume alcohol once learning they were pregnant. Regular alcohol consumption, especially in the first trimester of pregnancy, has been linked to a range of adverse outcomes including miscarriage, birth defects, still birth and impaired fetal brain development.²⁵ However, it is less clear whether alcohol consumption impacts on fertility and IVF outcomes.

A systematic review and meta-analysis involving over ninety thousand reproductive age women found that moderate to heavy drinking (greater than one standard drink per day) was associated with a 25% decrease in the ability to fall pregnant within one menstrual cycle (also known as fecundability).²⁶ Importantly, this study demonstrated that any alcohol consumption, regardless of intake, reduced fecundability by 13%.

More recently, a study of 1708 women undergoing treatment at a public fertility clinic in Denmark found no relationship between low-to-moderate weekly alcohol intake and outcomes such as achieving clinical pregnancy or live birth following IUI, IVF or ICSI when adjusted for confounding factors such as age, BMI, cigarette smoking, daily coffee consumption, chronic diseases, education and cycle number.²⁷ Similar findings were also observed at even higher levels of intake (> 7 drinks/week) however this group was relatively small (when compared to abstainers) so the results may underestimate the true effect of alcohol at higher intakes.

Studies in men suggest that long-term heavy alcohol consumption can reduce fertility via decreased gonadotropin release, reduced testosterone production and impaired spermatogenesis.²⁸ Similarly, a recent systematic review of 15 studies involving 16 395 men found that alcohol intake does have a small but significant effect on sperm volume and morphology. However, when these results were stratified by the level of alcohol consumption, moderate consumption (defined as occasional versus daily use) was not shown to have any impact on sperm quality.²⁹

Recommendations:

From the studies presented above, the extent to which alcohol affects fertility in men and women is not clear. Given that fertility treatment can be both lengthy and stressful, couples should be advised to avoid alcohol if possible or limit their intake to 1 – 2 standard drinks per week. Women should also be educated about the risks of alcohol consumption on fetal development and be advised to avoid alcohol following IUI and embryo transfer procedures and for the duration of pregnancy to minimise harm to their developing baby.

Caffeine

Studies that have explored the effects of caffeine on reproductive outcomes in women are not extensive and have yielded inconsistent findings. For example, a recent systematic review and meta-analysis found that the risk of miscarriage was nearly 40% higher with caffeine intakes of 300mg/day and this continued in a dose-dependent manner such that the risk doubled with intakes in the order of 600mg/day.³⁰ These same authors found no association between caffeine intake and other reproductive outcomes such as fertility, fertility treatment outcomes and waiting time to pregnancy. Oostingh et al. also found that the risk of miscarriage in the first trimester of pregnancy was increased in a dose-dependent manner in two out of four studies.³¹ The only other outcome linked to elevated caffeine intake (>540 mg/day) was embryonic development (reduced crown-rump length) observed in one study.

Several mechanisms have been proposed to explain how caffeine may affect reproductive function and embryonic development. It has been suggested that caffeine might increase oestrogen levels, leading to effects on ovulation and corpus luteal function which is important for establishing and supporting pregnancy in the first trimester. Caffeine can also cross the placental barrier, and its effects on the uteroplacental circulation may cause vasoconstriction and restriction of embryonic and placental growth.³² Furthermore, the rate of caffeine metabolism is halved during pregnancy which will expose the embryo to higher concentrations of caffeine.

There are a number of challenges for research into the effects of caffeine that may account for inconsistency in the evidence regarding female reproductive outcomes. Firstly, the speed at which caffeine is metabolised by the body varies widely amongst individuals due to differences in CYP1A2 enzyme activity that is in part mediated by a person's genes. Secondly, estimates of caffeine intakes from coffee can be difficult to quantify due to differences in caffeine content depending on the type of brewing method used (Table 1).

Recommendations:

Current recommendations in Australia, which were published in 2009, suggest that women should limit their caffeine consumption to 300mg per day which is equivalent to 3 cups of coffee or 6 cups of tea per day. Given that more recent studies have found that intakes from 200 mg/day are associated with a higher risk of miscarriage, it would seem sensible to recommend women to restrict

their intake to 200 mg of caffeine per day and not exceed 300 mg/day. As seen in Table 1, this would be equivalent to 1.5 to 2 servings of espresso (30ml) or 4 cups of black tea. Women should also be counselled about caffeine in energy drinks, cola soft drinks and foods such as chocolate which also contain significant amounts of caffeine (Table 1).

	Caffeine per 100 ml [mg]	Serving size [ml]	Caffeine per serving [mg]
Brewed coffee	60–100	150	90–150
Espresso	100–150	30	30–50
Instant Coffee	27–72	150	40–108
Decaffeinated	1–3	150	2–5
Tea	6–22	250	15–55
Iced tea	6–10	250	15–25
Coca cola	10	250	25
Diet coke	13	250	33
Decaffeinated coke	0	250	0
Energy drinks monster	34	250	85
Red bull	34	250	85
Energy Shots e.g., 5-h-energy	333	60	200
Chocolate Milk beverage	1–3	250	2–7

Table 1: Beverages containing caffeine with data about caffeine content.³³

Trans fatty acids

Industrial processing of vegetable oils to produce hardened fats such as margarine and shortening creates artificial *trans* fatty acids. Dietary exposure to these artificial *trans* fats occurs with the consumption of margarine and foods such as baked goods and fried foods that are produced or cooked in these partially hydrogenated oils. Artificially produced *trans* fats have a poor health profile with higher intakes strongly linked to increased levels of systemic inflammation, insulin resistance, cardiovascular disease and type 2 diabetes. The WHO recommends that the intake of *trans* fats should not exceed 1% of total energy intake.³⁴

The intake of *trans* fatty acids has been linked to infertility in both men and women. In men, *trans* fat intake has consistently been shown to be negatively associated with total sperm count and sperm concentration.²⁹ Other studies have shown links between increased *trans* fatty acid intake and defects in sperm motility.³⁵ High intakes of *trans* fatty acids were associated with a greater risk of endometriosis and ovulatory infertility in women from the Nurses' Health Study II.^{36 37} Wise et al. found *trans* fatty acid intake to reduce fecundability in a population of North American women, but not in Danish women.³⁸ While a recent study involving 60 women undergoing IVF treatment found that increasing erythrocyte *trans* fatty acid content (a surrogate measure of fatty acid content in follicular fluid) was associated with reduced IVF fertilisation rate, blastocyst conversion rate and the

number of usable embryos.³⁹ Although the number of studies is limited, and all have reported on different fertility endpoints, the collective findings suggest that *trans* fatty acid intake may influence reproductive health in women.

Recommendations:

Trans fatty acid intake has been linked to a number of adverse health outcomes and in line with this, current public health recommendations suggest that both men and women should limit their intake to less than 1% of daily energy intake. Foods high in *trans* fatty acids include baked goods, biscuits, chips, pies and pastries and deep-fried foods. Clients should be educated about the sources of *trans* fats in the diet to assist with minimising their intake.

Sugar-sweetened beverages

Consumption of sugar-sweetened beverages may have adverse effects on fertility. Sugar-sweetened beverages have been associated with poor semen quality in cross-sectional studies, and female soda intake has been associated with lower fecundability in some, but not all, studies. A prospective cohort study of 3828 women and 1045 of their partners found both female and male intakes of sugar-sweetened beverages were associated with reduced fecundability (FR= 0.81; 95% CI: 0.70, 0.94 and 0.78; 95% CI: 0.63, 0.95 for ≥ 7 sugar-sweetened beverages (juice, sports drinks) per week compared with none, for females and males, respectively).⁴⁰ Fecundability was further reduced among those who drank ≥ 7 servings per week of sugar-sweetened sodas (FR= 0.75, 95% CI: 0.59, 0.95 for females and 0.67, 95% CI: 0.51, 0.89 for males).

A prospective study of 340 women who were undergoing IVF found that women who consumed soda had on average 1.1 fewer oocytes retrieved, 1.2 fewer mature oocytes retrieved, 0.6 fewer fertilized oocytes, and 0.6 fewer top-quality embryos compared with women who did not consume sugared soda.⁴¹

Recommendations:

Clients planning to conceive should avoid sugar-sweetened beverages for three months prior to egg and sperm collection.

Fish and seafood high in methyl mercury

Fish, in their natural environment, eat plants and other organisms that contain mercury. This leads to the accumulation of methyl mercury (MeHg), a highly toxic organic form of mercury, in their muscular tissue. Some fish, particularly larger predatory species, accumulate more MeHg in their tissues because they eat smaller fish that contain mercury in their system. Eating mercury contaminated fish and other seafood is the most common source of MeHg exposure in humans.⁴² This occurs because MeHg is lipid soluble and it rapidly enters the blood stream. Once in the bloodstream it is rapidly distributed around the body and because of its lipid solubility it can cross all lipophilic barriers such as the blood-brain barrier, the blood-testis barrier and the placental barrier.

A limited number of studies have examined the effects of MeHg exposure on fertility in women and results have been conflicting. A recent case-control study involving 98 infertile women and 43 healthy controls found no difference in blood mercury levels between two groups of women.⁴³ However, after adjustment for blood selenium levels and age, a statistically significant association between elevated mercury levels and infertility was found. Mercury binds to selenium with very high affinity, and it has been suggested that this interferes with selenium's antioxidant activities in human tissues.⁴⁴ In this study, it is possible that the high levels of selenium in control subjects are

protective and in the infertile participants, low selenium levels contribute to increased mercury toxicity.⁴³ It should be noted that fish are an excellent dietary source of selenium and studies in men have shown that fish intake offsets any negative effect of MeHg on reproductive health.⁴⁵

Recommendations:

Fish consumption is particularly important for men and women experiencing infertility as it is an excellent source of long-chain, omega-3 fatty acids, particularly DHA. Individuals should be encouraged to consume fish at least 2 – 3 times a week (300 – 350g) and where possible, at least three months prior to fertility treatments or conception as this the time it takes for both oocyte and sperm maturation. Education should identify the types of fish to avoid such as orange roughy (sea perch), catfish, shark (flake), swordfish and marlin due to their higher levels of mercury.⁴⁶ Suitable fish that should be encouraged due to their low mercury levels and high long-chain, omega-3 fatty acid content include salmon, mackerel, herring and sardines. Tinned tuna and salmon are also recommended.

Bisphenol A (BPA) in plastic containers

Bisphenol A is a synthetic compound that is used in the manufacture of a range of products including re-usable polycarbonate plastic food containers.⁴⁷ It has received considerable attention in health literature because it can be absorbed via the skin, airways and digestive tract then accumulate in tissues. BPA has weak oestrogenic properties and at high doses in animal studies, has been shown to have adverse effects on kidney, liver and reproductive function.⁴⁸

In humans, studies that have examined BPA exposures and effects on fertility and other reproductive outcomes have yielded conflicting findings. For example, one study from India involving 79 women found that 77% of infertile women (n=34) had detectable levels of BPA in their plasma compared to only 29% of fertile women.⁴⁹ A larger study involving 700 Chinese women found that fecundability was reduced by 30% in women with the highest concentrations of urinary BPA. In addition, when compared to women with low levels of BPA in their urine, those with high urinary BPA had a 64% increase in the odds of infertility (defined as a time to pregnancy > 12 months).⁵⁰

In men, Pollard et al. recently demonstrated that higher urinary BPA concentrations are associated with a significant increase in the number of sperm with abnormal tail morphology but no other measures of sperm quality.⁵¹ Another study of 315 men found that increasing urinary BPA concentrations were associated with an increase sperm aneuploidy and an increased percentage of immature sperm. Increased BPA exposure was also associated with reduced sperm motility.⁵²

In contrast, Yeum et al. found no association between BPA exposure and time to pregnancy in their cohort of 164 heterosexual couples.⁵³ Similarly, a study involving 256 women who were undergoing IVF treatment found no relationship between urinary BPA and range of IVF outcomes such as embryo quality, fertilisation rate, implantation, clinical pregnancy and live birth rates.⁵⁴

Recommendations:

Although BPA exposure has been associated with adverse reproductive outcomes in some studies, the current level of exposure in Australian and other developed populations is considered too low to pose a health risk.⁵⁵ However, the European Food Safety Authority is currently awaiting the outcomes of a long-term study involving pre- and post-natal exposures to BPA in rats. It is anticipated that the results of this study will help to determine whether current exposure limits are sufficient to prevent adverse reproductive outcomes.⁴⁸ In the absence of this data, it seems prudent

to recommend that women and men reduce potential exposures to BPA prior to conception. Strategies to reduce BPA exposure include avoiding plastic containers labelled with the resin code symbol 7 (Figure 2) or listed as containing polycarbonate. Stainless steel, glass or plastic containers labelled BPA-free should be used for storing food and water. Foods should not be heated in plastic containers unless it is certain that they do not contain BPA. Most canned foods now contain liners that are BPA-free, so these foods do not need to be avoided.⁵⁶ Cling wraps such as Glad® Wrap do not contain BPA and are also safe to use.



Figure 2: Plastics made from polycarbonate that contain BPA are labelled with the symbol resin code 7. Not all plastic containers that contain BPA will be labelled with the resin code symbol as it is not a legal requirement. Plastics labelled with resin codes 1 through 6 do not contain BPA.

IVF and weight gain

Anecdotal reports suggest that weight gain is a common side effect of ART. However, research suggests that whilst many women gain weight during ART, not all do.⁵⁷ A study of 66 women undertaking IVF found that although they may have experienced some cursory weight gain during their cycle, there was no significant weight gain at the end of the cycle. The following may affect weight during ART.

Fluid retention

Some women may put on weight due to fluid retention during the superovulation phase of the IVF cycle. Fertility stimulating hormones dramatically increase oestrogen levels resulting in enlarged ovaries, bloating and fluid retention. Once the superovulation stops, the hormones get excreted into the urine and the bloating subsides. This means that most women will quickly lose the fluid they accumulated and will go back to their normal body weight.

Hormonal changes

IVF medications have the capacity to induce weight gain indirectly as a result of their hormonal responses.⁵⁸ Increased progesterone and estrogen levels have been associated with small, but significant increases in body fat.^{59 60} Furthermore, emerging research suggests that FSH (used for ovulation induction) may be linked to body fat.⁶¹ During menopause, levels of FSH surge. In studies of mice, it was found that blocking FSH increased the calories burned and reduced abdominal fat. Human studies are yet to be undertaken.

Restricted activity

Many women limit physical activity before and after an embryo transfer due to unsubstantiated beliefs that bed rest may increase embryo implantation. Research suggests that immediate mobilisation after an embryo transfer does not have a negative influence over IVF success rates so bed rest should not be recommended.⁶² Furthermore, restricted activity may contribute to weight gain in some women.

Emotional eating

Emotional eating is a term used to describe a potentially maladaptive behaviour whereby food is consumed in response to events that incite negative mood or emotions.^{63 64} It has been associated with overweight and obesity, in both women and men, and is suggested to be a significant barrier to maintaining weight management goals.^{65 66 67} Emotional eating is different to binge-eating disorder (BED) despite both involving the consumption of food in response to negative emotions. In BED, very large amounts of food are consumed in a limited time (2h period) with individuals feeling a loss of control over their behaviour.⁶⁸ These eating episodes also occur on a regular basis ranging from 1 episode per week (mild BED) to 14 or more (severe BED) and are associated with marked post-binge shame and distress. While emotional eating can be a precursor to BED, it differs in that the eating behaviour seeks to provide comfort and/or divert attention from negative affect without the perception of a loss of control.⁶⁹

To date, no studies have explored the impact of infertility and ART on emotional eating behaviour. Instead, most studies have been conducted in university students and examined responses to exam stress or used simulations designed to evoke different moods such as joy, shame, guilt and sadness. Devonport et al. recently reviewed 29 studies that examined the association between emotions and eating behaviour in normal and overweight adults.⁶⁴ A consistent finding across several studies was that participants ate more in response to positive emotions and those who identified themselves as high emotional eaters were more likely to eat more in response to negative emotions such as sadness and stress. The type of food consumed in response to emotional stress was typically highly palatable and less healthy including crisps, biscuits and chocolate. Other factors that were found to contribute to high emotional eating behaviour included a lack of sleep (≤ 7 hours per night), low cortisol responsiveness and high dietary restraint.

A number of individual determinants have been suggested to contribute to emotional eating behaviour. These include psychological factors such as increased reward sensitivity, high dietary restraint, reduced cognitive reappraisal and impulsiveness, situational factors such as stress and hunger and biological determinants such as weight status, cortisol responsiveness and gender. Mantau et al. recently investigated these factors simultaneously in 179 university-based participants and found that high dietary restraint and stress were the only factors that explained unhealthy food choices in response to negative mood.⁶³ They concluded that individuals with high dietary restraint are more likely to choose unhealthy foods in response to negative emotions. Similarly, high stress situations that evoke negative mood can also lead to increased seeking of unhealthy foods. Interestingly, other psychological factors and biological determinants such as weight status did have a significant impact on emotional eating.

Several different approaches for managing emotional eating are recommended. Mindful eating falls under the umbrella of mindfulness which is an approach used to increase awareness and develop affirmative responses to emotional pain and/or negative behaviours.⁷⁰ When an individual engages in mindful eating the focus is on making conscious food choices, developing an awareness of physical



hunger versus emotional 'wanting' and responding to the cue by eating healthfully. Mindful eating encourages individuals to be in the present moment, to acknowledge the effect of food on the senses (e.g. seeing, smelling, hearing, tasting, feeling) and be aware of one's emotional and physical responses to eating. Cognitive behavioural therapy (CBT) is a goal-oriented treatment that encourages the individual to take a hands-on approach to addressing real or perceived problems.⁷¹ In this approach, the individual is encouraged to change patterns of thinking or behaviours that are associated with problems or emotional challenges with the goal of changing their response to a situation.

Women experiencing fertility issues, undergoing fertility treatments or who have suffered miscarriage are likely to feel a range of emotions including stress, fear, guilt, loss and frustration. These negative emotions are likely to increase comfort seeking behaviours and emotional eating may be an outlet for many women. Individuals with a history of constant dieting or other restrained eating behaviours (e.g. carbohydrate counting for diabetes, eating disorders) should be encouraged to develop strategies to manage emotional eating, especially to avoid unnecessary weight gain. Approaches for managing emotional eating include cognitive behavioural therapy and mindful eating. Good sleep quality, greater than 7 hours per night should also be encouraged.

References

- ¹ Tosti, V., B. Bertozzi, and L. Fontana, *Health Benefits of the Mediterranean Diet: Metabolic and Molecular Mechanisms*. J Gerontol A Biol Sci Med Sci, 2018. **73**(3): p. 318-326
- ² Shai, I., et al., *Weight loss with a low-carbohydrate, Mediterranean, or low-fat diet*. 2008. **359**(3): p. 229-241.
- ³ Karayiannis, D., et al., *Adherence to the Mediterranean diet and IVF success rate among non-obese women attempting fertility*. Hum Reprod, 2018. **33**(3): p. 494-502.
- ⁴ Gaskins, A.J., et al., *Dietary patterns and outcomes of assisted reproduction*. Am J Obstet Gynecol, 2019. **220**(6): e1-567.e18.
- ⁵ Ricci, E., et al., *Mediterranean diet and outcomes of assisted reproduction: an Italian cohort study*. Am J Obstet Gynecol, 2019. **221**(6): e1-627 e14.
- ⁶ Karayiannis, D., et al., *Association between adherence to the Mediterranean diet and semen quality parameters in male partners of couples attempting fertility*. Hum Reprod, 2017. **32**(1): p. 215-222.
- ⁷ McGrice, M. and J. Porter, *The Effect of Low Carbohydrate Diets on Fertility Hormones and Outcomes in Overweight and Obese Women: A Systematic Review*. Nutrients, 2017. **9**(3).
- ⁸ Mavropoulos, J.C., et al., *The effects of a low-carbohydrate, ketogenic diet on the polycystic ovary syndrome: a pilot study*. Nutr Metab (Lond), 2005. **2**: p. 35.
- ⁹ Sim, K.A., et al., *Weight loss improves reproductive outcomes in obese women undergoing fertility treatment: a randomized controlled trial*. Clin Obes, 2014. **4**(2): p. 61-68.
- ¹⁰ Schwingshackl, L., et al., *Impact of intermittent energy restriction on anthropometric outcomes and intermediate disease markers in patients with overweight and obesity: systematic review and meta-analyses*. Critical Reviews in Food Science and Nutrition, 2020: p. 1-12.
- ¹¹ Mindikoglu, A.L., et al., *Impact of Time-Restricted Feeding and Dawn-to-Sunset Fasting on Circadian Rhythm, Obesity, Metabolic Syndrome, and Nonalcoholic Fatty Liver Disease*. Gastroenterology Research and Practice, 2017. **2017**: p. 3932491.
- ¹² Del Corral, P., et al., *Effect of dietary adherence with or without exercise on weight loss: a mechanistic approach to a global problem*. J Clin Endocrinol Metab, 2009. **94**(5): p. 1602-1607.
- ¹³ Cho, Y., et al., *The Effectiveness of Intermittent Fasting to Reduce Body Mass Index and Glucose Metabolism: A Systematic Review and Meta-Analysis*. Journal of Clinical Medicine, 2019. **8**(10).
- ¹⁴ Sebastiani, G., et al., *The Effects of Vegetarian and Vegan Diet during Pregnancy on the Health of Mothers and Offspring*. Nutrients, 2019. **11**(3).
- ¹⁵ Rizzo, N.S., et al., *Nutrient profiles of vegetarian and nonvegetarian dietary patterns*. J Acad Nutr Diet, 2013. **113**(12): p. 1610-1619.
- ¹⁶ Mandy, M. and M. Nyirenda, *Developmental Origins of Health and Disease: the relevance to developing nations*. International health, 2018. **10**(2): p. 66-70.
- ¹⁷ Kahleova, H., et al., *A plant-based diet in overweight individuals in a 16-week randomized clinical trial: metabolic benefits of plant protein*. Nutr Diabetes, 2018. **8**(1): p. 58.
- ¹⁸ Turner-McGrievy, G.M., et al., *Low glycemic index vegan or low-calorie weight loss diets for women with polycystic ovary syndrome: a randomized controlled feasibility study*. Nutr Res, 2014. **34**(6): p. 552-8.
- ¹⁹ Czaja-Bulsa, G., *Non coeliac gluten sensitivity – A new disease with gluten intolerance*. Clinical Nutrition, 2015. **34**(2): p. 189-194.
- ²⁰ FSANZ. *Folic acid fortification*. 2016 [cited 2020 April 1st, 2020]; Available at: <https://www.foodstandards.gov.au/consumer/nutrition/folicmandatory/Pages/default.aspx>.
- ²¹ Butler, M.M., L.C. Kenny, and F.P. McCarthy, *Coeliac disease and pregnancy outcomes*. Obstetric medicine, 2011. **4**(3): p. 95-98.
- ²² Lasa, J.S., I. Zubiaurre, and L.O. Soifer, *Risk of infertility in patients with celiac disease: a meta-analysis of observational studies*. Arq Gastroenterol, 2014. **51**(2): p. 144-150.
- ²³ Swajcer, E.M., et al., *Nutrition-related information-seeking behaviours of women trying to conceive and pregnant women: evidence for the life course perspective*. Fam Pract, 2008. **25 Suppl 1**: p. 99-104.
- ²⁴ Practice Committee of the American Society for Reproductive Medicine, *Ovarian hyperstimulation syndrome*. Fertility and Sterility, 2008. **90**(5): S188-S193.
- ²⁵ NHMRC, *Australian guidelines to reduce health risks from drinking alcohol*. 2009, Australian Government: Canberra.

- ²⁶ Fan, D., et al., *Female alcohol consumption and fecundability: a systematic review and dose-response meta-analysis*. Sci Rep, 2017. **7**(1): p. 13815.
- ²⁷ Lyngso, J., et al., *Low-to-moderate alcohol consumption and success in fertility treatment: a Danish cohort study*. Hum Reprod, 2019. **34**(7): p. 1334-1344.
- ²⁸ Van Heertum, K. and B. Rossi, *Alcohol and fertility: how much is too much?* Fertility research and practice, 2017. **3**: p. 10-19.
- ²⁹ Ricci, E., et al., *Semen quality and alcohol intake: a systematic review and meta-analysis*. Reproductive BioMedicine Online, 2017. **34**(1): p. 38-47.
- ³⁰ Lyngsø, J., et al., *Association between coffee or caffeine consumption and fecundity and fertility: a systematic review and dose-response meta-analysis*. Clin Epidemiol, 2017. **9**: p. 699-719.
- ³¹ Oostingh, E.C., et al., *The impact of maternal lifestyle factors on periconception outcomes: a systematic review of observational studies*. Reprod Biomed Online, 2019. **38**(1): p. 77-94.
- ³² Chen, L.-W., et al., *Maternal caffeine intake during pregnancy and risk of pregnancy loss: a categorical and dose-response meta-analysis of prospective studies*. Public Health Nutrition, 2016. **19**(7): p. 1233-1244.
- ³³ Herden, L. and R. Weissert, *The Impact of Coffee and Caffeine on Multiple Sclerosis Compared to Other Neurodegenerative Diseases*. Frontiers in Nutrition, 2018. **5**: p. 133.
- ³⁴ FSANZ. *Trans fatty acids*. 2017 [cited 2020 April 1st, 2020]; Available at: <https://www.foodstandards.gov.au/consumer/nutrition/transfat/Pages/default.aspx>.
- ³⁵ Eslamian, G., et al., *Dietary fatty acid intakes and asthenozoospermia: a case-control study*. Fertility and Sterility, 2015. **103**(1): p. 190-198.
- ³⁶ Missmer, S.A., et al., *A prospective study of dietary fat consumption and endometriosis risk*. Human reproduction (Oxford, England), 2010. **25**(6): p. 1528-1535.
- ³⁷ Chavarro, J.E., et al., *Dietary fatty acid intakes and the risk of ovulatory infertility*. Am J Clin Nutr, 2007. **85**(1): p. 231-237.
- ³⁸ Wise, L.A., et al., *Dietary Fat Intake and Fecundability in 2 Preconception Cohort Studies*. American journal of epidemiology, 2018. **187**(1): p. 60-74.
- ³⁹ Eskew, A.M., et al., *The association between fatty acid index and in vitro fertilization outcomes*. J Assist Reprod Genet, 2017. **34**(12): p. 1627-1632.
- ⁴⁰ Hatch, E.E., et al., *Intake of sugar-sweetened beverages and fecundability in a North American Preconception cohort*. Epidemiology, 2018. **29**(3): p. 369-379.
- ⁴¹ Machtinger, R., et al., *Association between preconception maternal beverage intake and in Vitro fertilization outcomes*. Fertil Steril, 2017. **108**(6): p. 1026-1033.
- ⁴² Hong, Y.-S., Y.-M. Kim, and K.-E. Lee, *Methylmercury exposure and health effects*. Journal of preventive medicine and public health = Yebang Uihakhoe chi, 2012. **45**(6): p. 353-363.
- ⁴³ Maeda, E., et al., *Associations of environmental exposures to methylmercury and selenium with female infertility: A case-control study*. Environmental Research, 2019. **168**: p. 357-363.
- ⁴⁴ Berry, M.J. and N.V. Ralston, *Mercury toxicity and the mitigating role of selenium*. Ecohealth, 2008. **5**(4): p. 456-459.
- ⁴⁵ Mínguez-Alarcón, L., et al., *Hair mercury (Hg) levels, fish consumption and semen parameters among men attending a fertility center*. International journal of hygiene and environmental health, 2018. **221**(2): p. 174-182.
- ⁴⁶ Better Health Channel. *Mercury in fish 2013*; Available at: <https://www.betterhealth.vic.gov.au/health/healthyliving/mercury-in-fish>.
- ⁴⁷ Matuszczak, E., et al., *The Impact of Bisphenol A on Fertility, Reproductive System, and Development: A Review of the Literature*. Int J Endocrinol, 2019. **2019**: p. 4068717.
- ⁴⁸ Matuszczak, E., et al., *The Impact of Bisphenol A on Fertility, Reproductive System, and Development: A Review of the Literature*. Int J Endocrinol, 2019. **2019**: p. 4068717.
- ⁴⁹ Pednekar, P.P., et al., *Estimation of plasma levels of bisphenol-A & phthalates in fertile & infertile women by gas chromatography-mass spectrometry*. Indian J Med Res, 2018. **148**(6): p. 734-742.
- ⁵⁰ Wang, B., et al., *Associations of female exposure to bisphenol A with fecundability: Evidence from a preconception cohort study*. Environ Int, 2018. **117**: p. 139-145.
- ⁵¹ Pollard, S.H., et al., *Male exposure to bisphenol A (BPA) and semen quality in the Home Observation of Periconceptional Exposures (HOPE) cohort*. Reprod Toxicol, 2019. **90**: p. 82-87.

- ⁵² Radwan, M., et al., *Urinary Bisphenol A Levels and Male Fertility*. Am J Mens Health, 2018. **12**(6): p. 2144-2151.
- ⁵³ Yeum, D., et al., *Association between peri-conceptional bisphenol A exposure in women and men and time to pregnancy-The HOPE study*. Paediatr Perinat Epidemiol, 2019. **33**(6): p. 397-404.
- ⁵⁴ Minguez-Alarcon, L., et al., *Urinary bisphenol A concentrations and association with in vitro fertilization outcomes among women from a fertility clinic*. Hum Reprod, 2015. **30**(9): p. 2120-2128.
- ⁵⁵ FSANZ. *Bisphenol A (BPA)*. 2018 [cited 2020 April 1st, 2020]; Available at: <https://www.foodstandards.gov.au/consumer/chemicals/bpa/Pages/default.aspx>.
- ⁵⁶ McTigue, L., *Most food cans no longer use BPA in their linings*, in *Packaging Digest*. 2018, Informa Markets: Oakbrook, IL.
- ⁵⁷ Sutherson, D., et al., *The impact of long down regulation in Vitro fertilisation cycles on patients' weigh*. Hum Feril (Camb), 2011. **14**(1): p. 23-28.
- ⁵⁸ Leener, B., et al., *Ovarian hormones and obesity*. Hum Reprod Update, 2017. **23**(3): p. 300-321. Doi: [10.1093/humupd/dmw045](https://doi.org/10.1093/humupd/dmw045)
- ⁵⁹ Lopez, L.M., et al., *Progestin-only contraceptives: effects on weight*. Cochrane Database Syst Rev, 2013. Doi: [10.1002/14651858.CD008815.pub3](https://doi.org/10.1002/14651858.CD008815.pub3)
- ⁶⁰ Frank, A., et al., *The role of hypothalamic estrogen receptors in metabolic regulation*. Front Neuroendocrinol, 2014. **35**(4): p. 550-557. Doi: [10.1016/j.yfrne.2014.05.002](https://doi.org/10.1016/j.yfrne.2014.05.002)
- ⁶¹ Liu, P., et al., *Blocking FSH induces thermogenic adipose tissue and reduces body fat*. Nature, 2017. **546**(7656): p. 107-112. Doi: [10.1038/nature22342](https://doi.org/10.1038/nature22342)
- ⁶² Cozzolino, M., et al., *Bed rest after an embryo transfer: A systematic review and meta-analysis*. Archives of Gynecology and Obstetrics, 2019. **300**: p. 1121-1130.
- ⁶³ Mantau, A., S. Hattula, and T. Bornemann, *Individual determinants of emotional eating: A simultaneous investigation*. Appetite, 2018. **130**: p. 93-103.
- ⁶⁴ Devonport, T.J., W. Nicholls, and C. Fullerton, *A systematic review of the association between emotions and eating behaviour in normal and overweight adult populations*. J Health Psychol, 2019. **24**(1): p. 3-24.
- ⁶⁵ Jayne, J.M., et al., *Body weight status, perceived stress, and emotional eating among US Army Soldiers: A mediator model*. Eat Behav, 2020. **36**: p. 101367.
- ⁶⁶ Wong, L., et al., *Emotional eating in patients attending a specialist obesity treatment service*. Appetite, 2020. **151**: p. 104708.
- ⁶⁷ Elfhag, K. and S. Rössner, *Who succeeds in maintaining weight loss? A conceptual review of factors associated with weight loss maintenance and weight regain*. Obes Rev, 2005. **6**(1): p. 67-85.
- ⁶⁸ American Psychiatric Association, DSM-5 Task Force, *Diagnostic and statistical manual of mental disorders : DSM-5*. 5th ed. 2013, Washington, D.C.: American Psychiatric Association. xlv, 947 p.
- ⁶⁹ Pollert, G.A., et al., *The role of eating and emotion in binge eating disorder and loss of control eating*. Int J Eat Disord, 2013. **46**(3): p. 233-238.
- ⁷⁰ Warren, J.M., N. Smith, and M. Ashwell, *A structured literature review on the role of mindfulness, mindful eating and intuitive eating in changing eating behaviours: effectiveness and associated potential mechanisms*. Nutrition Research Reviews, 2017. **30**(2): p. 272-283.
- ⁷¹ Martin, B. *In Depth: Cognitive Behavioural Therapy*. PsychCentral 2019 May 8th, 2020. Available at: <https://psychcentral.com/lib/in-depth-cognitive-behavioral-therapy/>.