

MANAGING FEMALE OBESITY

Obesity in women extends beyond CVD risks to contraception, conception, pregnancy, neonatal and cancer risks

Dr Jane Wilcock
 GP Silverdale Medical Practice, Salford CCG, co-year 3-4 Director and Tutor University of Liverpool School of Medicine

CASE STUDY

Barbara is a 20-year-old student and attends her GP with cystitis, for which she has tried some over-the-counter sachets, which haven't helped. She has a cheerful demeanour and the GP notices that she is obese and wonders whether to bring the topic up and offer health advice.

Epidemiology and diagnosis of obesity

Much of our time as GPs is spent advising patients to lose weight and exercise more. This is largely to prevent the increased obesity-related risks of cardiovascular disease (CVD) and Type 2 diabetes (T2DM), which are well recognised. For women there are also obesity-related risks of contraception, subfertility, pregnancy and cancers, which are less well known. Talking to our patients about these so they can enter pregnancy or post-menopausal life stages in the best possible health is a difficult area which this article seeks to discuss.

The UK has seen a marked increase in obesity rates over the years. In 1993 16% of women were obese; in 2011 this rose to 26%.¹ Conversely, the proportion of women with a healthy body mass index (BMI of 18.5-25) fell to 39% in 2011. The NHS five yearly check² for people aged 40-74 and related NICE guidance reflects the increasing risks of T2DM in ethnic groups and their increased risks of CVD; risks of illness start at a lower BMI of 27.5 or over for individuals from Indian, Pakistani, Bangladeshi, other Asian and Chinese ethnicity categories, and this is their threshold for obesity classification.

NICE do not recommend routinely measuring waist circumference, but it can be helpful in discerning visceral obesity (which is related to waist size) if the patient's BMI is below 35.³ Women with a waist measurement of 88cm (34ins) or more risk developing

the metabolic syndrome, but for those of S. Asian or Chinese ethnicity this is lower at 80cm (31.5ins).⁴

Obesity is related to lifestyle changes. Supermarkets arrived in the 1950s and convenience and takeaway foods are now cultural norms. In addition, more than 77% of households in the UK have a car and the combination of lack of activity and easily obtainable high calorie foods, resulting in reduced metabolism and over consumption, is the main driver for the obesity epidemic. In Victorian England, women required 3-3.5,000 Kcal/day⁶ as most jobs were long hours with heavy manual labour, often as domestic servants, and their diets contained less high calorie foods. The recommended intake for women nowadays is 2,000 Kcal/day.

In addition, after the menopause, calorie requirements reduce and visceral fat increases with age, although the mechanism for this is not clear.⁷ Social deprivation is also associated with obesity; 17% of women with a degree are obese whereas 33% of women with no qualifications are obese. There are complex interactions of calorie availability, including in alcohol, psychology and alternative lifestyles to consider in facilitating a patient's behavioural changes.

Science of obesity

The science of obesity is not completely understood and for women involves complex relationships between fat, gastrointestinal tract (GIT), ovaries and brain. Appetite is signalled by a number of peptides secreted from the GIT and fat cells (adipocytes). Appetite and satiety are triggered by a number of hypothalamic nuclei processing information related to reward, taste, smell, sight, circadian clock and input from the GIT.⁸

GIT factors

The vagus nerve is stimulated by stomach distension and signals to the hypothalamus to reduce appetite.

Ghrelin, a fast acting hormone secreted from an empty stomach, acts on the hypothalamus to increase hunger, gastric acid secretion and GIT motility, so stimulating appetite. Prader-Willi syndrome patients have both an insatiable appetite and obesity, and have been found to have translocation defects at chromosome 15, resulting in high ghrelin levels. It would be expected that obese patients would have low ghrelin levels as they do not require hunger but ghrelin levels are not usually reduced in obesity.⁹

Other appetite-related peptides produced from the GIT are glucagon-like peptide (GLP-1), which reduces

TABLE 1: CLASSIFICATION OF OBESITY IN ADULTS (WHO CRITERIA):⁵

BMI (kg/m ²)	classification
25-29.9	Overweight
30-34.9	Obesity 1
35-39.9	Obesity 2
40 and over	Obesity 3

appetite, YY peptide, insulin and cholecystokinin. In diabetic therapy GLP-1 agonists such as exenatide (incretin drugs that are injected to prevent GIT breakdown) increase insulin secretion, reduce glucagon secretion, reduce appetite and have a tendency to weight loss. They are not at present licensed for therapy of obesity in the UK.

Adipocyte factors

Adipocytes are endocrine organs and secrete adiponectin, leptin and oestrogen.

Adiponectin regulates fatty acid and glucose metabolism and increases insulin sensitivity. It can be thought of as an insulin enhancer.¹⁰ There are low levels of adiponectin in obesity, with associated dyslipidaemia, insulin resistance and atherosclerosis. Levels are also reduced in T2DM. Thiazolidines, also known as glitazones, of which pioglitazone is used in diabetic therapy in the UK, modulate the transcription of insulin-sensitive genes involved in the control of glucose and lipid metabolism in muscle, fat and liver. Pioglitazone increases adiponectin levels and so increases fatty acid metabolism, reduces liver glucose production and increases sensitivity to insulin. Metformin does not influence adiponectin levels.

Leptin is secreted by adipocytes when lipid levels are high and regulates fat stores. Leptin acts to reduce appetite by actions at the hypothalamus. Genetic lack of leptin is very rare and causes obesity.⁹ Surprisingly, there are increased leptin levels in obesity and it is postulated that chronic over-eating creates receptor resistance at the hypothalamus, so obese patients are leptin resistant.

Adipocytes also secrete oestrogen which becomes an important source of oestrogen in the postmenopausal woman and partly explains the increased oestrogen-related cancer risks in postmenopausal obese women.

Subcutaneous fat doesn't seem to increase health risks, but white fat around the abdomen proliferates, secretes inflammatory cytokines like interleukin-6 and tumour necrosis factor- α , causing cell death and disease; in that sense obesity can be viewed as a low grade inflammatory process. This may contribute to the increased risks of cancer.³

The science of obesity is not completely understood and for women involves complex relationships between fat, gastrointestinal tract (GIT), ovaries and brain

The mechanisms of obesity are not yet completely understood, but 135 genes have been identified as related to obesity. FTO gene defects at chromosome 16 are most commonly recognised, as changes to this genetic site are linked with increased appetite at the brain and adult obesity, but the full mechanism of action is not yet known. In addition, epigenetics (chemical markers attached to DNA but not part of the nucleotide pairs) is thought to be a potential mechanism for foetal programming and may explain why obese mothers are more likely to have obese children; that is obese mothers may create chemical changes outside of the gene pairing to DNA which is then inherited.

General disease risks associated with obesity

Patients with obesity are at risk of the metabolic syndrome. This is a condition of glucose disorder with two or more of: central obesity, hypertension, dyslipidaemia and microalbuminuria.¹¹ Metabolic syndrome confers a three-fold increased risk of CVD or stroke and a five-fold increased risk of T2DM. Excess body fat contributes to 58% of T2DM and 21% of CHD. The South Asian population has a six-fold increased prevalence of T2DM and their rates of CHD are 50% higher,⁴ which is why obesity is diagnosed at a lower BMI and waist circumference.

In the USA, 75% of hypertension diagnoses are estimated to be related to obesity. Blood pressure reduces by 1mmHg per 1kg weight loss with a 6mmHg reduction at 10kg weight loss.¹² There are also risks of gallstones, non-alcoholic fatty liver disease (NAFLD), steatohepatitis (NASH), liver cirrhosis and hepatocellular carcinoma.¹³ There is an increased risk of snoring/sleep apnoea and disruption of the gastro-oesophageal junction.¹⁴ Obese patients are more likely to have leg oedema, suffer a DVT and have osteoarthritis of their knees. Leg oedema in obese patients may be due to varicose veins, related to increased abdominal pressure, DVT and post-thrombotic syndrome, postural pooling from inactivity in the severely obese, congestive cardiac failure, and increased risks of cellulitis and lymphoedema. Importantly, obese women are more likely to lack confidence and have depression.

FAT CELLS ARE ENDOCRINE ORGANS

Secrete Adiponectin

which regulates fatty acid, glucose metabolism and increases insulin sensitivity. Low levels in obesity.

Secrete Oestrogen



Secrete Leptin
to cause satiety. But obesity has high leptin levels but leptin resistance.

Cancer risks associated with obesity

Although cancer can occur at any age, it is age related and is more prevalent in the older women. In 2010 there were estimated to be more than 10,000 excess deaths among women due to obesity, and these are mainly due to cancers of the oesophagus, gallbladder, pancreas, colorectal, post-menopausal breast cancer, endometrium and kidney.¹⁵ In 2015 Cancer Research UK stated that obesity causes a relative risk increase of postmenopausal breast cancer of 1.25, endometrial cancer 2.31 and adenocarcinoma of the oesophagus 2.4.¹⁶ Physical activity can reduce endometrial cancer risk by 20-30%, but 50% of obese people do not think that weight loss reduces their risk of cancer.

Contraception and obesity

The Faculty of Reproductive and Sexual Health Care (FRSH)¹⁷ suggest that the risks of DVT and hypertension should be considered in prescribing the combined hormonal contraceptive pill (CHC). Women with a BMI of 35 or more should not take the CHC as the risks of disease outweigh the benefits. Women with a BMI of 30-34.⁹ should have their risks carefully weighed, but using the CHC may be acceptable.

The use of the progesterone only pill (POP) is recommended and Nexplanon, the progesterone containing subcutaneous implant, can be used in obese women without restriction or reduction in efficacy. The progesterone IM injection, Depo-provera, is also recommended but may cause an increase in weight.

The progesterone containing intrauterine system (LNG-IUS) and the copper coil (IUCD) may be difficult to insert but are recommended.

All forms of emergency contraception are recommended in obese women if required.

Subfertility and obesity

NICE CG¹⁸ states that over 80% of normal couples having regular sex, in whom the woman is below 40 years old, conceive in 12 months rising to 90% of couples after 2 years. Unfortunately, obese women are more likely to be subfertile as they are more likely to have oligomenorrhoea, menstrual irregularity and anovulation. They may require early referral for infertility investigations but actually require help to normalise their weight before embarking on pregnancy if possible. Participation in a group programme of exercise and dietary change leads to more pregnancies than weight loss advice alone.¹⁸ Obese women are more reluctant to come for help with subfertility and if the woman has a BMI > 40 she is unlikely to be accepted for fertility treatment due to health risks, and the rates of IVF success are lower in obesity. Even in ovulatory obese women there is an increased rate of subfertility.¹⁹ After they have conceived, obese women have an increased miscarriage rate.

GPs should also enquire about the male partner as the obese man is more likely to have low testosterone,

In the USA, 75% of hypertension diagnoses are estimated to be related to obesity

Low LH and FSH, reduced spermatogenesis, erectile dysfunction and reduced libido.²⁰

Pregnancy related risks and obesity

The obese woman is at increased risk of DVT, T2DM, gestational diabetes, pre-eclampsia (PET), severe haemorrhage and increased rates of maternal death.²¹ The obese woman is more likely to have labour induction, shoulder dystocia, delivery by caesarean section, general anaesthesia and anaesthetic complications and poor wound healing as obese tissue is relatively avascular and so hypoxic. There are also poorer perinatal outcomes of macrosomia, stillbirth and neonatal death.

In ante-natal care it is recommended that all women have their BMI and waist measured at booking. Obese women should be referred for dietary and exercise programmes, but are not advised to lose a lot of weight in pregnancy – the emphasis is on not gaining a lot of weight. Obese women are known to be nutritionally deficient; they have lower folic acid levels than

CONCEPTION AND PREGNANCY

Early onset obesity is related to oligomenorrhoea, menstrual irregularity, anovulation and subfertility. Increased rate of miscarriage. Reduced IVF if BMI > 30 women are less likely to come for help with fertility and if BMI > 40 less likely to be accepted for treatment. Ovulatory obese women have an increased rate of subfertility but may have less sex.



Maternal death
DVT
DM
PET
Severe haemorrhage
Labour induction
Shoulder dystocia
Delivery by caesarean section
General anaesthesia and anaesthesia complications.

Male obesity

Associated with low testosterone.
Low LH and FSH.
Reduced spermatogenesis.
Increased ED
Reduced libido

counterparts with a normal BMI and an increased rate of babies born with neural tube defects. Therefore, they should be offered folic acid 5mg a day pre-conceptually to week 12²¹ and 10mcgs vitamin D supplementation daily during pregnancy and while breastfeeding. This vitamin D recommendation is the same for all pregnant women but obese women are more at risk of vitamin D deficiency, and cord blood on delivery has shown lower vitamin D levels in babies of obese mothers compared to those of a normal BMI.²¹

GPs, midwives and obstetricians should consider risks of T2DM and hypertension through the pregnancy and often patients are given heparin (DVT prophylaxis) and aspirin (if one other risk factor for pre-eclampsia and also obese). A glucose tolerance test (GTT) is arranged routinely by the obstetrician at 24-28 weeks gestation for obese pregnant women. Detecting and controlling a woman's gestational diabetes (GDM) through dietary advice, blood glucose monitoring and therapy significantly reduces the risk of perinatal death, shoulder dystocia, bone fracture, and nerve palsy compared to routine care when GDM had not been diagnosed.²¹ Glycosuria at routine ante-natal testing in a well woman should prompt a GTT for GDM. The levels of glucose for diagnosis of GDM in pregnancy are not the same as those used in the normal non-pregnant population. In addition, the use of HbA1c is not reliable in pregnancy. Lastly, a number of pregnant women will be known to have diabetes and NICE has specific guidance for this group.²²

In severely obese women multidisciplinary teams are required to consider equipment, handling, IV access, labour and operative risks.

Bariatric surgery follow up

NICE CG³ indications for considering bariatric surgery are BMI >40 or patients with a BMI of 35-40 and a significant disease aggravated by weight and failed non-surgical measures. The patient must be fit for a general anaesthetic and surgery, and agree to long-term follow up.

The British Obesity and Metabolic Surgery Society (BOMSS) has published excellent guidance for specialists and GPs²³ on follow up of patients after bariatric surgery and other weight loss procedures, as there is a requirement for long-term micronutrient supplementation. Follow up of patients is through secondary care outpatient clinics in the first 2 years then annual nutritional status and appropriate supplementation as a shared care protocol with GP practices; tables for blood tests and micronutrient prescribing for each weight loss procedure is available²³.

Patients are advised to avoid conception for 12-18 months post bariatric surgery, though there is limited evidence for this recommendation at present. While trying to conceive, and in early conception, women post bariatric surgery should take folic acid 400mcg daily, but as they should already be on long-term

multivitamin and mineral supplements (Forceval vitamin daily), they are already ingesting this dose of folic acid. If they have T2DM and/or obesity this dose should increase to folic acid 5mg daily to 12 weeks gestation – as in the advice above for pregnancy – related risks. There is a recommendation for blood tests for vitamin levels in every trimester of pregnancy for women after bariatric surgery; they should have bloods for ferritin, folate, vitamin B12, calcium and fat soluble vitamins (A,D, E and K).²³ Pregnant women are referred to a multidisciplinary team which includes a bariatric specialist dietician.

Conclusion

Treatment of obesity revolves around lifestyle weight management programmes, preferably in groups. Patients can self-refer or referrals can be through health and social care practitioners and care is integrated by local authorities, local providers and CCGs.²⁴ The aims are to lose weight or to prevent further weight gain through dietary and exercise change. There is no particular diet that is superior to others. NICE emphasises consultation skills which are non-judgmental and short GP interventions about diet and exercise have been associated with increased patient actions to lose weight.²⁵

Patients should undertake moderate exercise for 30 minutes five days a week. To prevent obesity 45-60 minutes of moderate intensity exercise is recommended a day but if a patient has lost weight, having been

There is evidence for health benefits if patients lose 5% of their body weight for life

obese, they may need 60-90 minutes of exercise to keep weight off³. This is a big commitment. National sources to recommend to patients are available online at Change 4Life²⁶ and NHS Choices.²⁷ Weight management programmes benefit patients with a BMI >30, or lower if from black and ethnic minority groups, or if there are other risk factors like T2DM. If there is capacity, programmes can be accessed at BMI 25-30; long-term dietary and exercise plans are provided and encouraged. There is evidence for health benefits if patients lose 5% of their body weight for life; the average weight loss is 3% but it is variable and long-term support is important. Services have outcomes measures of percentage of patients losing 5% of body weight, percentage of patients losing 3% of initial body weight, percentage of patients adhering to the programme, and weight at 12 months after the programme finished.

GPs may want to prescribe orlistat if the patient has a BMI >28 plus other risk factors, or a BMI >30 alone. If the patient does not lose 5% of their body weight at three months on orlistat they should have the medication discontinued. Orlistat interferes with fat absorption and so may affect fat soluble vitamins, A, D, E, K and use over 12 months needs discussion of benefits and harms.

The obese woman attending the GP or practice nurse should be thought of holistically, not just as a hypertensive or CVD risk. Risks regarding conception, pregnancy outcomes and cancer are not widely known and discussed and there is poor written patient literature at present. Timing the advice and not upsetting the doctor-patient relationship over a deeply personal issue requires a skill set that is inherent to general practice and continuity of care. There are some concerns in the elderly overweight and obese groups that dieting can cause loss of muscle (sarcopenia) and so weakness. There are a confusing number of stepped weight loss services and patients can self-refer to some of them. Services explore diet, cookery classes and gym membership so that exercise programmes are linked to long-term dietary plans and supportive behavioural change.

Clearly it is difficult to lose weight, and maintaining weight loss requires a lot of commitment but in achieving success the burden of illness among individuals and the benefits to society and NHS costs are highly significant. Governments have belatedly started to address the issues of a car-centric, high calorie convenience food society but there is a long way to go in obesity prevention.

References

- <http://www.nhs.uk/news/2013/02February/Pages/Latest-obesity-stats-for-England-are-alarming-reading.aspx> (accessed June 2015)
- NHS Health Check Best practice guidance February 2015 Public Health England http://www.healthcheck.nhs.uk/commissioners_and_healthcare_professionals/national_guidance/ (accessed June 2015)
- Obesity: identification, assessment and management of overweight and obesity in children, young people and adults NICE cg 189 Nov 2014 <https://www.nice.org.uk/guidance/cg189> (accessed June 2015)
- Assessing body mass index and waist circumference thresholds for intervening to prevent ill health and premature death among adults from black, Asian and other minority ethnic groups in the UK. NICE guidelines PH46 July 2013 <https://www.nice.org.uk/guidance/ph46> (accessed June 2015)
- Measurement of Obesity Public Health England. http://www.noo.org.uk/NOO_about_obesity/measurement (accessed June 2015)
- Clayton P, Rowbotham J. *International Journal of Environmental Research and Public Health*. 2009; 6(3): p. 1235-1253. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2672390/> (accessed June 2015)
- Estimated Calorie Needs per Day by Age, Gender, and Physical Activity Level. Dietary Reference Values for Energy 2011 Scientific Advisory Committee on Nutrition (SACN) https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/339317/SACN_Dietary_Reference_Values_for_Energy.pdf (accessed June 2015)
- Trivedi B. P. *Nature* April 2014; 508: p. 64–65
- Klok M.D., Jakobsdottir S., Drent M.L. *Obes Rev.* Jan 2007; 8 (1): p. 21-34
- Lihn A.S., Pedersen S.B., Richelsen B. *Obes Rev.* Feb 2005; 6: (1): p.13-21.
- The International Diabetes Federation consensus worldwide definition of the metabolic syndrome <http://www.idf.org/metabolic-syndrome> (accessed June 2015)
- Landsberg L., Aronne L.J., Beilin L.J. *et al. The Journal of Clinical Hypertension* Jan 2013; 15 (1): p. 14-28
- Muthuveloe T. and Wilcock J. *Guidelines in Practice* Jan 2008 at http://www.guidelinesinpractice.co.uk/jan_08_muthuveloe_nafld_jan08 (accessed June 2015)
- Lee, Y.Y., McColl K.E.L. *Diseases of the Esophagus* 2015; 28: p. 318–325
- Parkin D.M., Boyd I. *British Journal of Cancer* 2011; 105: p. 34 – 37
- <http://www.cancerresearchuk.org/about-us/cancer-news/press-release/2015-03-17-obese-women-40-per-cent-more-likely-to-get-cancer> (accessed June 2015)
- www.fsrh.org/pdfs/CEUGuidanceCombinedHormonalContraception.pdf (accessed June 2015)
- Fertility: assessment and treatment for people with fertility problems NICE cg 156 Feb 2013 <https://www.nice.org.uk/guidance/cg156> (accessed June 2015)
- van der Steeg J.W., Steures P., Eijkemans M. J.C. *et al Human Reproduction* 2008; 23(2) p. 324–328
- Paquali R., Patton L., Gaminer A. *Curr Opin Endocrinol Diabetes Obes* Dec 2007; 14(6): p. 482-7 www.ncbi.nlm.nih.gov/pubmed (accessed June 2015)
- CMACE/RCOG Joint Guideline Management of Women with Obesity in Pregnancy March 2010 <https://www.rcog.org.uk/globalassets/documents/guidelines/cmacercojointguidelinemanagementwomenobesitypregnancya.pdf> (accessed June 2015)
- Diabetes in pregnancy: management of diabetes and its complications from preconception to the postnatal period NICE guidelines [NG3] February 2015 <http://www.nice.org.uk/guidance/ng3/> (accessed June 2015)
- BOMSS Guidelines on perioperative and postoperative biochemical monitoring and micronutrient replacement for patients undergoing bariatric surgery Sept 2014 <http://www.bomss.org.uk/wp-content/uploads/2014/09/BOMSS-guidelines-Final-version1Oct14.pdf> (accessed June 2015)
- Managing overweight and obesity in adults – lifestyle weight management services NICE public health guidance PH53 May 2014. <http://www.nice.org.uk/guidance/PH53>
- Brief interventions for weight management April 2011 National Obesity Observatory <http://www.hse.ie/eng/health/child/healthyeating/weightmanagement.pdf>
- <http://www.nhs.uk/conditions/obesity/pages/introduction.aspx> eating/healthy-lifestyle/change-for-life.htm (accessed June 2015)
- <http://www.weightlossresources.co.uk/healthy> (accessed June 2015)