

**Pre pregnancy weight loss in obese women requesting removal of their intra uterine
contraceptive device in order to conceive: a pilot study of full meal replacement.**

Lisa Brackenridge¹, Nick Finer², Rachel L Batterham³, Kosar Pedram¹, Tao Ding⁴, Judith
Stephenson¹, John Barry¹, Paul Hardiman¹

¹Institute for Women's Health, University College London, ²Institute of Cardiovascular Science,
University College London, ³Centre for Obesity Research, University College London, ⁴Department
of Statistical Science,.

Corresponding author.

Paul Hardiman, Senior Lecturer, Institute for Women's Health, University College London, Rowland
Hill Street, London NW3 2PF. Tel: +44 (0)20 7830 2563. Email: p.hardiman@ucl.ac.uk

Keywords: Obesity, Preconception care, Low calorie diet, Body weight change.

Running title: Pre pregnancy weight loss in obese women

What is already known.

1. Obesity during pregnancy is associated with increased morbidity for mother and baby
2. Current practice aiming to limit gestational weight gain is not effective
3. Normalising (or reducing) body weight before conception is clinically worthwhile and cost effective (NICE)

What this study adds.

1. Two thirds of women requesting removal of their intrauterine contraceptive device because they were planning a pregnancy, agreed to engage in a weight management programme that included eight weeks full meal replacement.
2. Omitting one subject who dropped out for reasons unrelated to the intervention, 46.2 % of women who started the programme completed it.
3. Including drop outs, the mean BMI decreased by 6.6%.

Summary

Obesity during pregnancy is associated with an increased risk of severe morbidity including thromboembolism, gestational diabetes, pre-eclampsia, miscarriage, congenital anomaly, macrosomia and stillbirth. Current practice is directed at reducing gestational weight gain although the available evidence suggests this is ineffective. The present study was designed to assess the acceptability of an intensive weight management programme, IWMP (8 weeks each of full meal replacement followed by partial meal replacement and then weight stabilisation: with behaviour modification throughout) to achieve sufficient weight loss that could reduce the risks for obese women requesting removal of their intrauterine contraceptive device (IUCD) in order to conceive. 65% of the 26 eligible consented to participate in the IWMP; three received as routine NHS care in the University College Hospital clinic and 14 agreed to participate in this study. The commonest reasons given for not participating were dislike of milk, anxiety and lack of support from family and friends. Omitting one woman who dropped out because of problems unrelated to the intervention, the completion rate was 46.2%. Including all women who started the programme, mean BMI decreased significantly ($p=0.005$) from 37.8 to 35.3 kg/m². The median percentage decrease was significantly ($p=0.007$) greater for women who completed the study (14.2) compared to those who dropped out (1.2). These results suggest an impressive level of weight loss in about a third of all women offered the IWMP who had to defer what they were seeking (pregnancy) while following a challenging programme that they were not seeking. However, studies of other interventions such as partial meal replacement in women are still required.

Introduction

Maternal obesity is one of the most commonly occurring risk factors in obstetric practice (1). The prevalence has increased, from 9–10% in the early 1990s to 20% in 2015 (2) so that it is now one of the biggest risks to pregnancy (Chief Medical Officer for England 2015) with increased maternal rates of thromboembolism, gestational diabetes, pre-eclampsia, dysfunctional labour, caesarean section, postpartum haemorrhage, wound infection and fetal/ neonatal risks of miscarriage, congenital anomaly, macrosomia, prematurity, stillbirth and neonatal death compared to women with a normal BMI (3). The Confidential Enquiry into Maternal and Child Health's report on maternal deaths in the 2003–2005 triennium (1) showed that 28% of mothers who died were obese, whereas the prevalence of obesity in the general maternity population within the same time period was 16-19%. Children born to obese mothers are less likely to be breast fed and have a lifelong increased risk of being themselves obese.

Normalising (or reducing) the BMI before conception is likely to be clinically more effective than restricting weight gain during pregnancy (4) and therefore more cost effective. This strategy was advocated by NICE, "Health professionals should use any opportunity, as appropriate, to provide women with a BMI of 30 kg/m² or more with information about the health benefits of losing weight before becoming pregnant (for themselves and the baby they may conceive). This should include information on the increased health risks their weight poses to themselves and would pose to their unborn child".

Current efforts to reduce this excess morbidity are generally directed towards limiting weight gain in women after conception but do not attempt to induce weight loss because of the risk of restricting fetal growth (5). However this practice has little to no impact (4) suggesting that it would be more effective to intervene before women become pregnant. There is therefore an urgent need to increase public awareness of the additional risks posed by obesity to mothers and their babies, establish from interventional trial evidence that pre-conception weight loss in women with obesity is beneficial, and to provide interventions to promote weight loss which induce clinically relevant weight loss over a time period for which women are prepared to defer their desire to conceive.

The present study was designed to assess the willingness of women with obesity to delay removal of their IUCD in order to reduce their weight prior to conceiving to potentially improve their health and the outcomes of a future pregnancy. Women with obesity were asked to participate in an intensive weight management programme (IWMP) comprised of an initial 8-week total diet replacement low energy diet in order to reduce weight by 10% or greater (6). Total diet/meal replacement programmes, followed by gradual reintroduction of food have been extensively developed through continuous improvement methodology and offered within UK National Health Service Tier 3 (specialist) obesity clinics and shown to induce weight loss in excess of 10% in a mixed population of patients and is used in NHS clinics. In this pilot study, the aims were to assess women's willingness to postpone pregnancy when subjects were made aware of the risks of obesity to themselves and their babies and to obtain some preliminary data on the effectiveness of this intervention in this patient group.

Materials and Methods

Recruitment

Eligible patients recruited from one of four Margaret Pyke Sexual Health Clinics in North London or Gynaecology clinics at the Royal Free, University College and Whittington Hospitals between August 2014 and July 2015. The doctor or nurse explained the risks to their baby and themselves resulting from their obesity and that a clinical trial was underway to assess the acceptability to women of an intervention designed to promote weight loss, which could reduce these risks. Women who expressed an interest in participating in the trial, gave their contact details (with verbal consent) to the research nurse who subsequently called the woman to give a brief description of the trial and offered to send a copy of the Patient Information Leaflet. Those who called back to say they wished to take part were given an appointment to see a doctor who took a history and general physical examination to ensure there were no contra indications to the IWMP. The research nurse then obtained written consent and had the first consultation to explain the details of the intervention and trial design.

Inclusion Criteria.: Women with obesity (BMI>30 kg/m²) aged 18 - 40 years who told the clinic doctor or nurse that they wished to discontinue their contraception in order to become pregnant.

Exclusion criteria: Women using hormonal contraception, those with severe psychiatric disorders and those already participating in a study that may have conflicted with this protocol.

The Intensive Weight Management Programme

This intervention which combines a low energy liquid diet and behaviour modification providing 966 - 1220 kcals/day and 82-103g protein daily, is divided into three 8 week phases (Fig 1):

Subjects were also instructed to progressively increase daily exercise (walking) from five minutes to one hour per day over the 24 weeks of the programme. The IWMP was delivered by a research nurse, who had been trained to deliver the IWMP and motivational support in a Tier 3 adult obesity clinic (UCLH). Participants were given 15-minute individual appointments in the Community Gynaecology clinic at the Royal Free Hospital to see the research nurse every two weeks throughout the 24 weeks of the intervention. If the participant could not attend the hospital because of family/ work commitments a telephone consultation was used.

Statistical Analysis

The two sample paired t-test was used compare the mean BMI and weight before and after the programme. However, when the data were not normally distributed, the Wilcoxon rank-sum test was used to compare the median of the outcome of interest. Subgroup analysis was used to examine the change in BMI and weight for those who completed the programme and those who dropped out of the programme.

Results

34 women (16 from Margaret Pyke clinics, 17 from Consultant Gynaecology clinics at the Royal Free, University College and Whittington Hospitals, one from her GP) contacted the research nurse to express an interest in the study. Eight were not eligible, five because their BMI was less than 30 kg/m², two were using hormonal contraception and the other because her IUCD had already been removed. Nine of the eligible subjects declined; one said the study would be too difficult, one could not understand the study, one did not like milk and six did not give a reason. In total therefore, 17 (65.4%) of the 26 eligible women started IWMP, 14 by agreeing to participate in this study and 3 outside the study.

The mean ages of the subjects who completed or dropped out of the program, were not significantly different (32 and 35 years, respectively). Six (42.9%) subjects completed the 24-week programme. Three did not miss any scheduled appointments (for two subjects all appointments were face to face and the other 11 face to face and one telephone appointment). The remaining three subjects each missed one appointment. Eight (57.3%) of the 14 who started the programme within the study discontinued programme after a mean of 5.3 (2-16) weeks. The reasons for discontinuing the study are shown in Table 1. Omitting the subject who dropped out because of problems with IUCD (unrelated to the IWMP), the completion rate was 46.2%.

Including all women who started the IWMP, including those who dropped out, the mean BMI decreased by 6.6%. Considering the mean of the individual changes in the BMI and weight, the IWMP induced a significant decrease. The effect was significantly ($p=0.002$) greater for women who completed the IWMP (-14.2%) compared to those who dropped out (-1.2%).

Discussion

As far as we are aware, this is the first time an intensive intervention, using meal-replacements combined with behavioural modification has been assessed in a group of women with obesity who had decided to discontinue contraception because they wished to conceive. This pilot study attempted to

find out how many women would be prepared to delay their plans to become pregnant when they were made aware of the additional risks to themselves and their babies posed by their obesity. The results of this study also give an indication of the proportion of women who are able to adhere to a 24-week weight management programme and the percentage weight loss achieved. Equally important we now have preliminary data to understand why women who start the weight loss programme, are unable to complete it.

The answer to the first question, 'are women motivated to enter a weight loss programme even when this requires her to postpone conception for six months', was encouraging with 65% of the eligible subjects enrolling in the IWMP. This rate of uptake is very similar to that reported for this intervention in a general population (male and female). It is disappointing that two thirds of the women who were eligible to take part, but declined, did not give any reason for their decision. For those that gave a reason, the major dissuading factors include dislike of milk, anxiety and lack of support from family and friends.

This programme was effective for those women who were able to adhere to it, with a median BMI decrease of 14.2%; five of the six women losing more than 9%. The degree of weight loss in this population of women who were planning a pregnancy was even higher than that found in the DiRECT study (7) of (male and female) patients with type 2 diabetes randomised to an intervention based on total diet replacement. This degree of weight loss before conception is likely to be clinically beneficial; rates of gestational diabetes, being 42% lower in women with a BMI in early pregnancy similar to that in our subjects before the IWMP compared to that after the intervention (4.4 and 7.6% respectively).

The answer to the second question, 'are women able to adhere to the weight loss programme' was that 43% completed the full weeks. This dropout rate was higher than that found in a randomised study (8) comparing a low carbohydrate, high protein diet with a commercially available very low-calorie diet but the attrition rates in the two groups were not significantly different. However, one of the early subjects who dropped out, had an eating disorder and this is known to be associated with a lower success

rate in weight loss programmes. As reported previously with this intervention, unacceptable hunger was an uncommon reason, despite the fact that the intervention provides about 100g of carbohydrate daily and is therefore not ketogenic (9). The commonest reasons were dislike of milk, nausea/ diarrhoea and anxiety. Gastrointestinal symptoms were alleviated in 3/14 subjects who completed the programme by switching to lactose free milk. Anxiety can be alleviated with support from the nurse or dietician. Training of the clinicians delivering the intervention has been shown to improve their effectiveness.

In summary, this pilot study of an intervention based on a LELD was acceptable to around two thirds of obese women who were planning a pregnancy. The degree of weight loss achieved by those who completed the programme is very likely to improve pregnancy outcomes for mother and baby. Further studies are required to identify interventions which are both acceptable and effective in this important patient group.

Conflicts of interest.

None declared.

Acknowledgements

PH principal investigator, study design, manuscript editing. JB, KP and TD, statistical analysis. LB subject recruitment and drafting the manuscript. RB, data interpretation and drafting the manuscript. NF study design, supervising physician and drafting the manuscript. JS, identifying recruiting centres and drafting the manuscript. The Royal Free Charity provided funding for the Research Nurse (LB).

Subject	Weeks completed	Reason for discontinuing programme
1	6	Irregular bleeding with IUCD (presumed unrelated to programme)
2	2	Disliked milk
3	2	Diarrhoea, 'fed up with milk'
5	8	Pressure from relatives to eat
6	4	Headaches, nausea and hunger
7	2	No reason given
8	2	No reason given
14	16	Pressure from relatives to eat, anxiety and diarrhoea

Table 1. Subjects who discontinued the intensive weight management programme.

	Weight (kg) before programme	Weight (kg) after completing/ dropping out from programme	BMI (kg/m ²) before starting	BMI (kg/m ²) at time of completing/ dropping out	Median of individual % BMI changes	P
All subjects starting n=14	108.6	91.5	37.8	35.3	-2.1	0.005
Subjects completing n=6	101.5	89.5	36.9	31.7	-14.2**	0.004
Subjects who dropped out n=6	111.6	109.1	38.5	38.0	-1.2**	0.006

**p = 0.007 for difference in % change (post v. pre WMP) between subjects who completed and dropped out of IWMP

Table 2. Mean weight and BMI before and after the intensive weight management programme.

Figure 1. Patient eligibility, enrolment and adherence to the intensive weight management programme

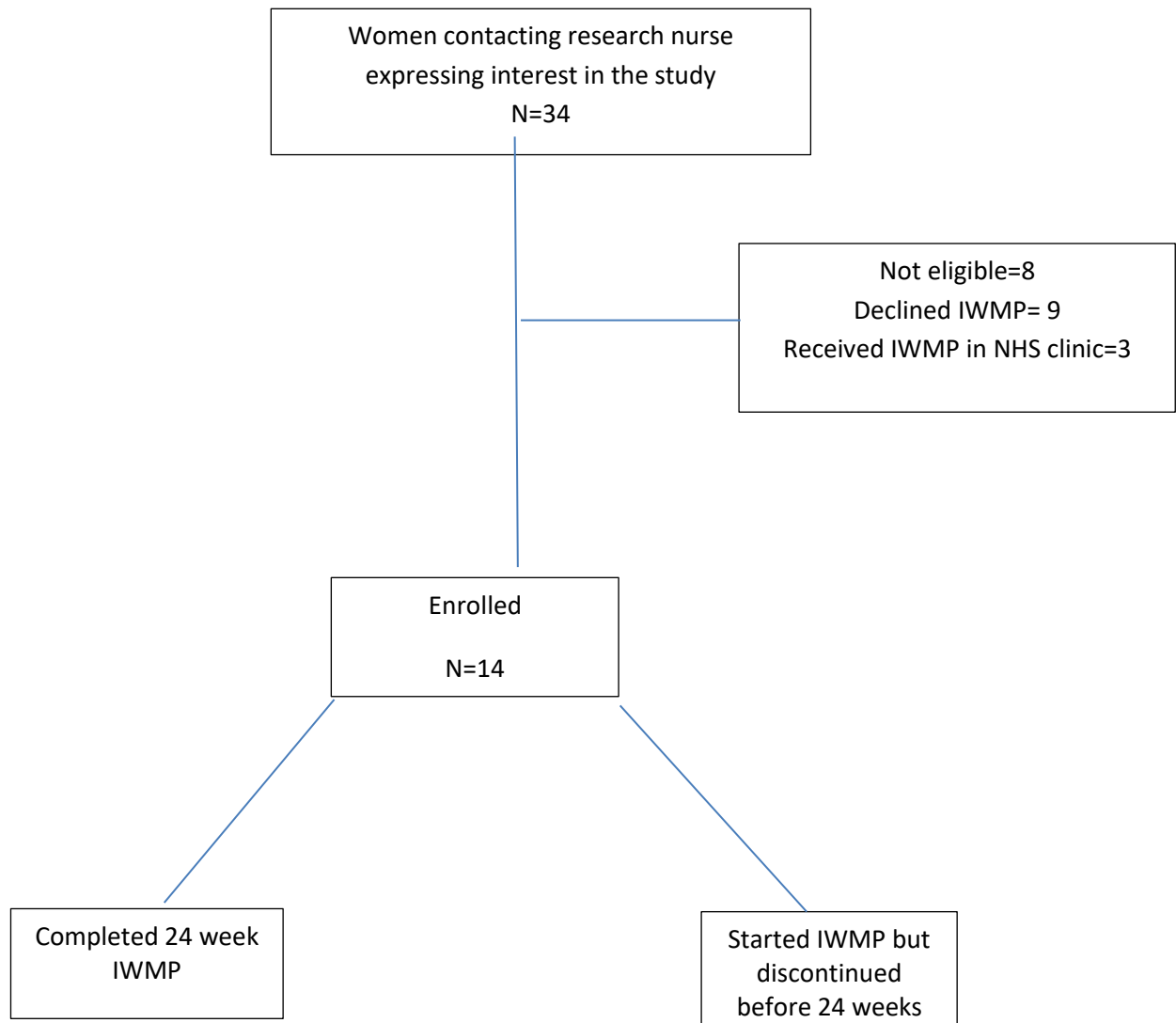
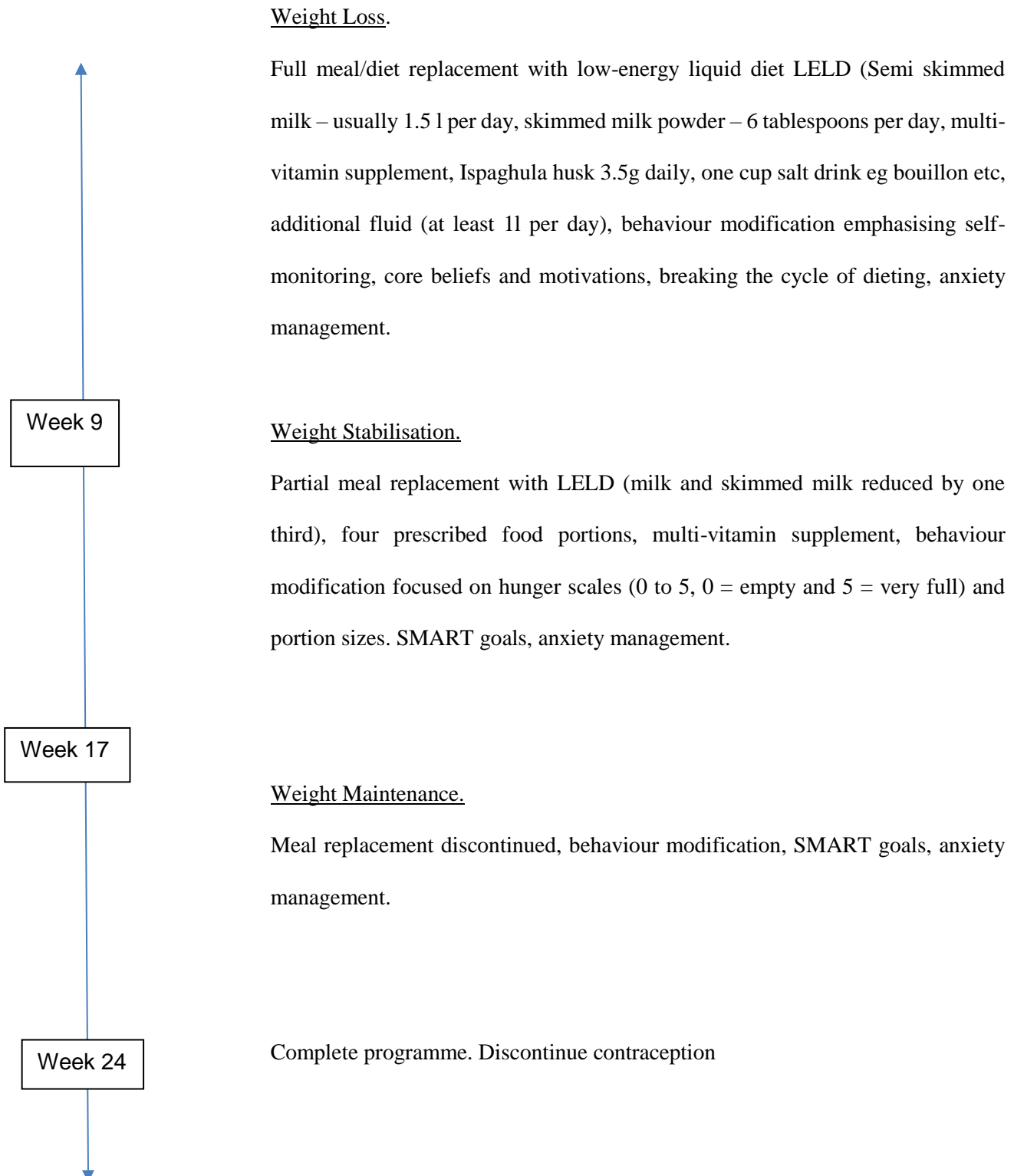


Figure 2. The intensive weight management programme.



References

1. Centre for Maternal and Child Enquiries. "Saving Mothers' Lives: Reviewing maternal deaths to make motherhood safer: 2006–2008." *BJOG: An International Journal of Obstetrics & Gynaecology*.2013; **118**: 1-203.
2. NHS Digital. <https://digital.nhs.uk/catalogue/PUB19869>
3. Opray N, Grivell RM, Deussen AR et al. "Directed preconception health programs and interventions for improving pregnancy outcomes for women who are overweight or obese." *Cochrane Database Syst Rev* 2015; **7**: Cd010932.
4. Rogozinska E, Marlin N, DODDS JP et al. Effect of diet and physical activity-based interventions in pregnancy on gestational weight gain and pregnancy outcomes: Individual participant data (IPD) meta-analysis of randomised trials. *British Medical Journal* 2017.
5. American College of Obstetricians and Gynecologists. ACOG Committee opinion no. 548: weight gain during pregnancy. *Obstetrics and gynecology* 2013; **121**: 210.
6. Barrett P, Finer N, Fisher C et al. Evaluation of a multimodality treatment programme for weight management at the Luton and Dunstable Hospital NHS Trust. *Journal of Human Nutrition and Dietetics* 1999; **12**: 43-52.
7. Lean ME, Leslie WS, Barnes AC et al. Primary care-led weight management for remission of type 2 diabetes (DiRECT): an open-label, cluster-randomised trial. *The Lancet* 2017.
8. Rolland C, Hession M, Murray S et al. Randomized clinical trial of standard dietary treatment versus a low-carbohydrate/high-protein diet or the LighterLife Programme in the management of obesity. *Journal of diabetes* 2009; **1**: 207-217.
9. Gibson AA, Seimon RV, Lee CM et al. Do ketogenic diets really suppress appetite? A systematic review and meta-analysis. *Obesity reviews* 2015; **16**: 64-76.

<https://fetalmedicine.org/research/assess/gdm> (cannot find where this is cited, please check!)