THE FORMULA FOR EFFECTIVE WEIGHT LOSS

Safe, effective weight loss and maintenance with sustained health benefits using formula low-calorie and very low-calorie diets. A digest of recent research using Cambridge Weight Plan.

By Anthony R. Leeds

Cambridge Weight Plan®

Real people, real support, real results.

WHAT IS CAMBRIDGE WEIGHT PLAN?

Cambridge Weight Plan is a dietary weight loss and maintenance programme that is based on nutritionally balanced formula foods delivered by Cambridge Consultants in a community setting who provide regular support and guidance on lifestyle and physical activity. Amounts and rates of weight loss are generally higher than with conventional food restricted diets.

Cambridge Weight Plan is a flexible series of dietary energy intake levels (1500, 1200, 1000, 800, 600kcal/d), allowing titration of energy intake against the client or patient's response.

This is interesting historically because in the late 19th century a step-wise titration upwards of dietary energy was offered to people with diabetes, following a fast to clear the urine of reducing sugars. Now this remarkably precise titration process (precise because it includes formula food products rather than non-formula foods alone) can be applied with a step-wise reduction or increase of energy intake according to need.

Very low-calorie diets (VLCDs 800kcal/d or less) give the most effective weight losses, but sometimes a part-formula and part-food diet can achieve remarkable weight loss. Dietary adherence tends to be poorer at the higher energy intake levels and patients tend to be hungrier, but nevertheless energy intake levels above 800kcal/d can give good results.

Formula diet programmes, whether VLCD or low calorie diets (LCD >800kcal/d), as total diet replacement, or as part conventional food, part formula-food diets at 800kcal/d and above, are now used more widely because the level of evidence for their use to achieve weight loss, weight maintenance and health benefit has risen rapidly over the last few years.

> "Weight loss with formula diet programmes... has been proven to deliver a package of health benefits rather than simply weight loss and weight maintenance."
>
> (see page 4)

CONTENTS

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INTRODUCTION: THE FORMULA FOR EFFECTIVE WEIGHT-LOSS

The requirements for weight loss and maintenance need to be defined in terms of degree of obesity, both in terms of whole body fat and local fat in target organs, age, demographic and health characteristics of the subject group, proven amount of change needed for given health or cosmetic benefit, type and setting of the intervention and an analysis of the costs and benefits.

Formula diet programmes have been under-investigated, underused and undervalued since they were dismissed on flimsy grounds and without adequate evidence by some scientists, especially in the United Kingdom in the 1980s. Elsewhere, especially in Scandinavia, formula diets have been used in practice to a greater degree.

The rising prevalence of obesity and obesity-related diseases, and a recognition that morbid (BMI >40) and super obese (BMI >50) patients are increasing in numbers and need more than conventional dietary and lifestyle advice to correct their problems, has prompted innovative surgery and renewed investigations of potential use for formula diets in this group too.

As manufacturers of one of the world's most successful formula food brands, Cambridge Weight Plan has embarked on a significant medical research programme.

THE CAMBRIDGE WEIGHT PLAN MEDICAL RESEARCH PROGRAMME IS BASED ON CLEARLY DEFINED NEEDS AND OBJECTIVES AND HAS BEEN CONSTRUCTED TO PROVIDE EVIDENCE FOR:

- Effective weight reduction in specific groups (defined by disease state, gender and age) and in specific settings (secondary care research clinic, primary care, community programme, etc).
- Effective weight maintenance in specific groups and settings.
- Health benefit by measurement of accepted disease endpoints by accepted methods.
- Sustained health benefit with weight maintenance.
- Nutritional status changes with evidence of maintenance of changes with weight maintenance.
- Change of cardiovascular risk factors with weight loss and maintenance.
- Body composition changes with weight loss and maintenance, especially lean mass loss.
- Retention rates (or drop-out rates).
- Cost of interventions in defined settings.

The research work described here has not been 'commissioned' as such, but has taken place following negotiation and facilitation, and has been undertaken with an absolute understanding that data ownership remains with research teams. There must be full transparency with all evidence (all adverse events published) and funding (all interests declared), and results must be published promptly to fully inform the next round of research work.

WHAT IS THE DISTINCTIVE MECHANISM OF ACTION OF FORMULA DIET PROGRAMMES?

- Formula diet programmes can provide a range of energy intakes from just over 400kcal/d to 1500kcal/d.
- Use of formula products at the lower end of the energy intake scale is the only way to ensure adequacy of intake of micronutrients on a daily basis.
- Lower energy intakes result in a greater deficit between energy requirement and dietary energy intake resulting in greater rates of weight loss.
- Rates of weight loss greater than a half to one kilogramme per week result in rapid improvement in symptoms, such as reduction of pain, decreased shortage of breath, improved mobility and often reduction of medication use, than after conventional diet programmes.
- Rapid weight loss and symptom improvement is highly motivating and this is likely to improve compliance.
- The physiological ketosis developed at lower energy intake levels may facilitate compliance through suppression of appetite.

SUMMARY OF EFFECTS

- Weight loss rates of 1 to 2kg per week can be achieved. This can give a 15kg weight loss, which is associated with a symptomatic response in osteoarthritis, sleep apnoea, psoriasis and diabetes, in eight to 12 weeks.
- Weight loss can be maintained in compliant individuals, and maintenance of more than 10kg or more than 10% of initial body weight is possible, following a VLCD or low-calorie liquid diet, by using partial replacement of conventional food with formula food, by following a high protein diet or by the use of drug therapies.
- Health benefits following weight loss in osteoarthritis, sleep apnoea and psoriasis have been demonstrated and maintenance of these benefits has been demonstrated in some cases.
- Cardiovascular risk factor profiles are improved and some aspects of these can be maintained with weight maintenance.
- Secondary prevention of coronary heart disease can be facilitated with a 10% weight loss followed by weight maintenance.
- Lean mass loss associated with weight loss has been shown to be lower than expected in obese people with osteoarthritis.
- There is some evidence for improved vitamin D status and bone health in the elderly obese with osteoarthritis.
- Drop out rates in clinical trials have been shown to be lower than expected.

OSTEOARTHRITIS IN OBESE PEOPLE

Obesity and osteoarthritis both reduce mobility. Obesity is a risk factor for osteoarthritis. Osteoarthritis causes people who are overweight and obese to exercise less and possibly eat more than is appropriate for their low activity levels.

Women with osteoarthritis have slightly reduced lean mass relative to their body weight. Thus, losing and maintaining weight is difficult for people with osteoarthritis. Many individuals may have complicating factors such as cardiovascular disease, which means that bariatric surgery may not be an option, even if they are otherwise eligible. Thus a new solution for weight issues in osteoarthritis is needed.

WEIGHT LOSS WITH FORMULA DIET VLCD AND LCD IN OLDER OBESE PEOPLE WITH KNEE OSTEOARTHRITIS

192 patients were treated with a VLCD (415 to 540kcal/d) or LCD (810kcal/d) liquid diet for eight weeks, then a 1200kcal/d diet (which included two formula diet portions) for eight weeks, combined with education given weekly to groups of eight subjects delivering a total of 17 sessions.

More than 12% of initial body weight was lost in both groups, with 60% in both groups having a good symptom response.

Eight out of 96 dropped out of the VLCD group, six out of 96 dropped out of the LCD group.

Thus for this group of individuals there appeared to be no advantage in terms of weight loss to using a VLCD over an LCD.

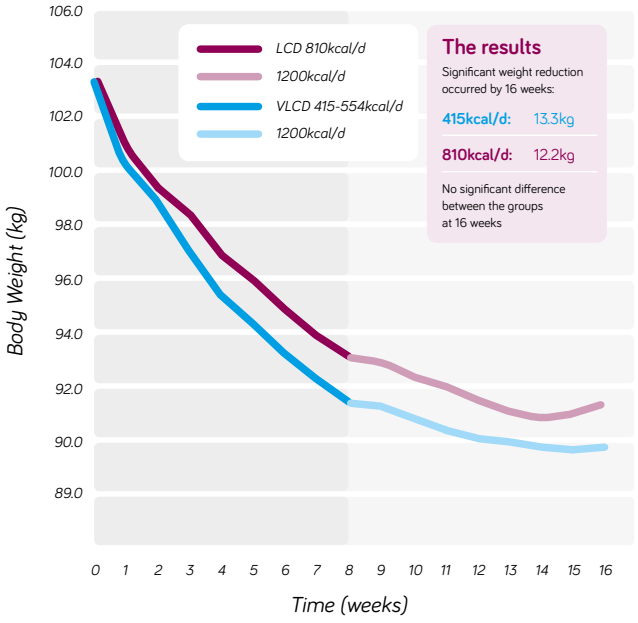

Figure 1. Mean drop in body weight from baseline. Blue/pale blue lines: very low-energy diet for eight weeks followed by eight weeks 1200kcal/d diet. Dark red/ pale red lines: low-calorie diet for eight weeks followed by eight weeks 1200kcal/d diet.

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Figure 1: Redrawn from: Christensen P, Bliddal H, Riecke B F, Leeds A R, Astrup A, Christensen R. Comparison of a low-energy diet and a very low-energy diet in sedentary obese individuals: a pragmatic randomised control CD trial. Clinical Obesity Article first published online: 21st March 2011 | DOI: 10.1111/j.1758-8111.2011.00006.x.

WEIGHT MAINTENANCE WITH FORMULA DIET IN OLDER OBESE PEOPLE WITH KNEE OSTEOARTHRITIS

This paper reports the 'secondary' end-points of the one-year maintenance phase of the Copenhagen trial of weight loss in older obese people with knee osteoarthritis. Patients were re-randomised into one of three groups for a maintenance phase of 52 weeks. The three groups were:

- Diet maintenance (in which one formula product was used in place of one conventional meal each day, and dietary messages were reinforced at a monthly meeting with a dietitian).
- Knee exercises (in which patients were trained to do knee exercises by a physiotherapist under direct supervision in hospital and also at home).
- A control group (in which subjects received no further contact, advice or intervention until recalled at 68 weeks).

In both the preparation (weight loss) phase and during maintenance, the primary end-points were symptoms and body weight. Variables relating to body composition (fat mass and lean body mass), cardiovascular risk (blood pressure, blood lipids, and blood glucose) and nutritional status (vitamin D, bone density, bone mineral, vitamin B12 and blood ferritin) were classified as secondary variables.

The primary overall purpose of the whole trial was to determine whether or not diet maintenance was superior to a knee exercise intervention in maintaining a symptom benefit after weight loss.

The paper published in 'Obesity' shows that there were some very statistically significant differences which demonstrated the advantages of following the dietary maintenance programme.

DIETARY MAINTENANCE LED TO GREATER CHANGES THAN THE KNEE EXERCISES PROGRAMME, IN THE FOLLOWING VARIABLES (AT 68 WEEKS, THAT IS AFTER ONE YEAR OF MAINTENANCE):

- Body weight (11kg weight loss after diet, 6.3kg weight loss after knee exercises). Significant p=0.0023.
- Waist circumference (down 8.4cm after diet, down 4.6cm after knee exercises). Significant p=0.0073.
- Fat mass (down 5.1kg after diet, down 2.4kg after knee exercises). Significant p=0.001.
- Vitamin D3 (up 28.5nmol/L after diet, up 18.7nmol/L after knee exercises) Significant p=0.035.
- Proportion of participants who were vitamin D3 deficient (down to 8% after diet, down to 24% after knee exercises). Significant p=0.054.
- Parathyroid hormone PTH (down 1.02pmol/L after diet, down 0.03pmol/L after knee exercises). Significant p=0.0006.
- Proportion of participants with high PTH (down to 12.5% after diet, down to 28% after knee exercises). Trend but not significant p=0.09 (thus there was a trend towards dietary maintenance reducing the secondary hyperparathyroidism more than knee exercises).

THE EFFECT OF WEIGHT LOSS FOLLOWED BY WEIGHT MAINTENANCE IN ALL GROUPS WAS ASSOCIATED WITH:

- A reduction and maintenance of lowered systolic and diastolic blood pressure, reduction to a degree that would appreciably reduce cardiovascular risk.
- An improvement in vitamin B12 blood levels (trend towards greater rise in the diet treated group).
- A reduction of bone mineral loss to levels much less than expected according to body weight (and relative to fat mass loss).
- Low lean mass losses of between 9% to 13% of body weight lost (no significant difference between groups).

FOUR YEAR (ONE PLUS THREE YEARS) WEIGHT MAINTENANCE

- 153 of 175 subjects who had completed the one year weight maintenance randomised controlled trial were then re-randomised either to a regular substitution of one formula product each day or to intermittent use of five weeks low energy liquid diet (LELD) (800kcal/d) three times each year for three years. The average weight loss (from the original baseline weight of 102.5kg) of those 153 subjects at the start of the three year weight maintenance phase was 11.3kg.
- 108 completed the three year maintenance study. Those who used one product per day regained 1.78kg (they had maintained 9.5kg weight loss, this being 68% of their original 14kg weight loss), those who used intermittent LELD regained 0.71 kg on average (they had maintained 10.6kg weight loss, this being 76% of their original 14kg weight loss). There was no statistically significant difference between the weight changes in the two groups.
- The initial start weight was 102.5kg, so the weight loss maintenance at four years was approximately 9-10% of the original weight (9.5/102.5 = 9.3%, and 10.6/102.5 = 10.3%).
- Of the weight lost initially (14kg) between 68% and 76% of that weight loss was maintained in those who completed the programme.

IMPLICATION OF THESE RESULTS

A good weight loss and maintenance method for obese people with osteoarthritis is one which gives sufficient weight loss to reduce symptoms, especially pain, and improve mobility, while maintaining or improving body composition (losing fat, retaining lean tissue), improving cardiovascular risk and improving or maintaining vitamin D status and bone health status (during and after weight loss bone-remodelling usually results in mineral loss).

Thus the approach to weight loss with formula diet programmes described in these papers has been proven to deliver a package of health benefits rather than simply weight loss and weight maintenance.

OBSTRUCTIVE SLEEP APNOEA IN OBESE PEOPLE

Obstructive sleep apnoea is said to be present when the airflow through the mouth and nose stops for more than 10 seconds at least 30 times during a seven-hour sleep. Some surveys suggest that one in four people with diabetes mellitus may have OSA and others that four out of five obese people with diabetes may be affected. There is uncertainty about the rate of OSA in the general population; perhaps one in 25 is affected, perhaps more.

Obstructive sleep apnoea can be a factor in causing raised blood pressure. Those who have suffered from but survived a stroke often give a history showing that they had sleep apnoea before they had their stroke. Sleep apnoea is thus a condition which is best avoided.

DOES SLEEP APNOEA MATTER?

OSA causes snoring interrupted by pauses in breathing, choking and gasping during sleep, restless sleep and excessive daytime sleepiness and perhaps falling asleep at work or while driving a motor vehicle. Quality of life may be seriously impaired by general fatigue, poor concentration, irritability, forgetfulness, morning headaches, depression and sexual dysfunction.

WHAT CAUSES SLEEP APNOEA?

Factors linked to OSA include variations in the shape and size of the upper airway, being overweight and obese, and having a family history of OSA. Scientific studies have shown that in OSA the airway is narrowed and that there is more fat next to the airway in those who are overweight and obese. The muscles supporting the airway may be less effective at holding the airway open, causing it to collapse and obstruct.

WEIGHT LOSS IN MILD OBSTRUCTIVE SLEEP APNOEA

A recently published study reports a randomised controlled trial undertaken in Finland by Tuomilehto et al (2009) of a very low-energy calorie diet with supervised lifestyle modification compared to routine counselling in 72 overweight patients with mild OSA.

At the end of one year, the group treated initially with VLCD (n=35) lost an average 10.7kg body weight, compared to a loss of 2.4kg in the routine counselling group (n=37). The number of apnoea-hypopnoea episodes was reduced significantly in the VLCD group by four, compared to a slight rise in the routine counselling group. Other measures of severity of sleep apnoea were also improved significantly in the VLCD group, compared to the routine counselling group.

A recently published study from the USA has shown that people with diabetes and sleep apnoea who lose more than 10kg with formula diet and who maintain that weight loss for one year, also maintain the improvement in sleep apnoea (Foster et al 2009). What was lacking until December 2009 was high quality research in the form of a randomised controlled trial of weight loss in people with moderate or severe sleep apnoea.

THE SWEDISH STUDY ON MODERATE AND SEVERE OBSTRUCTIVE SLEEP APNOEA

Johansson and colleagues at the Karolinska Institute in Stockholm reported that 63 obese men with moderate and severe OSA were allocated to one of two groups. Thirty men followed a seven-week Cambridge Weight Plan VLCD (554kcal/d), followed by two weeks of rising dietary energy intake, in preparation for a one-year maintenance programme, and 33 men (the control group) received no treatment and followed their usual diet.

IN THE CAMBRIDGE WEIGHT PLAN VLCD TREATED GROUP:

- Average weight loss was 18.7kg (average baseline weight was 113.4kg).
- There was a 3.8cm reduction in neck circumference (baseline was 45.1cm).
- A little over one quarter of body fat (30.1 percent at baseline) was lost by nine weeks.
- 22 out of 30 were not obese (BMI under 30) after nine weeks.
- Five improved sufficiently to be classed as 'cured' of their OSA.
- 26 out of 30 saw improvement in their OSA.
- No-one dropped out from the VLCD treated group (in contrast, two subjects out of 33 dropped out from the control group).

IN THE CONTROL GROUP:

- There was a small weight gain of 1.1kg (average) and very slight increases in neck circumference and body fat.
- Four subjects saw improvement in their OSA, five deteriorated and 24 out of 33 stayed unchanged.
- The differences between the VLCD group and the control group were highly significant.

THIS PAPER IS IMPORTANT BECAUSE:

- It is the first published randomised controlled trial of a VLCD in moderate and severe sleep apnoea.
- It provides high quality evidence that a relatively short period of a VLCD diet can result in effective weight loss and improve OSA in a majority of male patients.

LONGER TERM EFFECTS: ONE YEAR MAINTENANCE RESULTS

THE SWEDISH STUDY ON MODERATE AND SEVERE OBSTRUCTIVE SLEEP APNOEA: ONE YEAR RESULTS

After nine weeks those who had been in the control group then followed the nine-week diet programme. All subjects were then offered a maintenance programme with continued support from a dietitian and an option to use formula product to maintain weight for one year.

After one year the apnoea-hypopnea index had improved by 17 compared to baseline and body weight was 12kg less than at baseline. Thirty out of 63 no longer required CPAP and six out of 63 had total remission. Those who lost the most weight or had the most severe sleep apnoea at baseline benefited most.

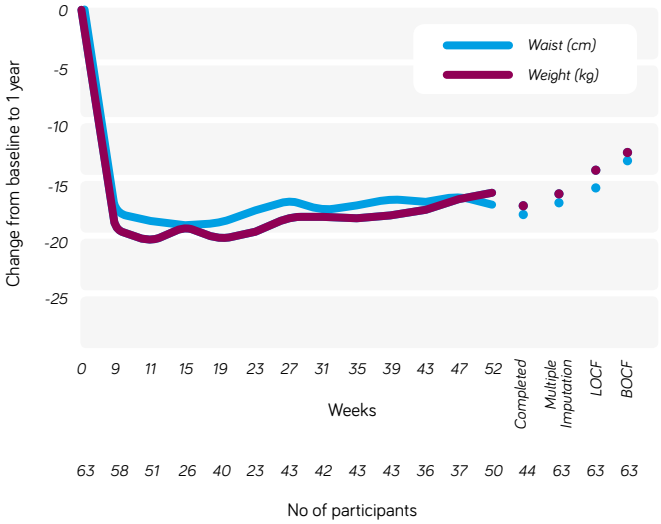

Figure 2. Mean change from baseline in weight, waist circumstances during and after treatment with very low energy diet for patients completing weight loss maintenance programme (n=44) and sensitivity analysis for missing data with multiple imputation (n=63), last observation carried forward (LOCF; n=63), or baseline observation carried forward (BOCF; n=63). Attendance was low at 15 and 23 weeks because of summer holidays.

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Figure 2: Redrawn from Johansson K, et al. BMJ 2009; 339: b4609 doi10.1136/bmj.b4609.

WEIGHT MAINTENANCE AFTER WEIGHT LOSS WITH VLCD OR FORMULA LCD

A popular belief has been that weight regain occurs rapidly after weight loss with VLCD or formula LCD, probably reflecting the failure of practitioners to put in place effective maintenance strategies. How best to maintain a lower dietary-energy intake (approximately 250kcal/d for every 10kg body weight lost) and a higher physical activity level have been the subject of ongoing investigations for many years.

This meta-analysis was designed to evaluate the effects of anti-obesity drugs (sibutramine and orlistat), diet or exercise on weight- loss maintenance after an initial very low-calorie diet (VLCD) or low-calorie diet (LCD) period (less then <1000 kcal/d). It consisted of a systematic review of English articles using MEDLINE, Cochrane Controlled Trial Register, EMBASE from 1981 to February 2013, and by contacting clinical experts, etc. Included studies were randomised controlled trials specifically evaluating weight loss maintenance strategies after an initial VLCD/LCD period.

Twenty studies with a total of 27 study arms and 3017 participants were included. These were studies on anti-obesity drugs (three arms, n=658), meal replacements (four arms, n=322), high protein diets (six arms, n=865), dietary supplements (six arms, n=261), other diets (three arms, n=564) and exercise (five arms, n=347).

During the VLCD/LCD period, the pooled mean weight loss was 12.3kg (median duration: eight weeks, range 3-16weeks).

Compared with placebo or control, the intervention changed weight-loss maintenance statistically significantly as follows:

- Anti-obesity drugs by -3.5kg (95%CI -5.5,-1.5: median duration 18 months, range 12-36 months).
- Meal replacements by -3.9kg (95%CI -5.0,-2.8: median duration 12 months, range 10-26 months).
- High protein diets by -1.5kg (95%CI -2.1,-0.8: median duration five months, range 3-12 months).

In contrast the differences in the following groups were not significant: exercise (0.8kg: 95%CI -2.8,1.2: median duration 10 months, range 6-12 months) and dietary supplements (0.0kg: 95%CI -1.4,1.4: median duration 3 months, range 3-14 months).

Thus anti-obesity drugs, meal replacements and high protein diets were associated with improved weight-loss maintenance after a VLCD/LCD period.

CONCLUSION

Since sibutramine has now been withdrawn from use in Europe, the only interventions currently proven to result in significantly better weight maintenance after weight loss with VLCD or LCD are orlistat, partial replacement of conventional food with formula meal replacement product and use of a high protein diet.

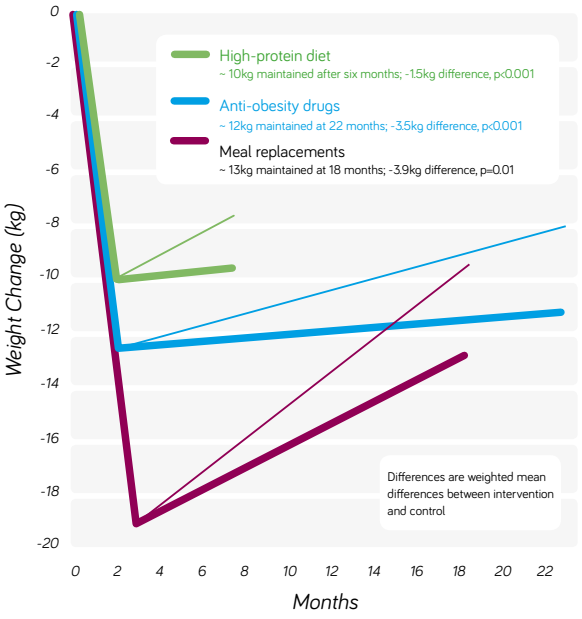

Figure 3. Body weight change during the VLCD or LCD period followed by the weight loss maintenance period. The thin lines represent the control subjects in each category, while the thick lines represent the active intervention.

TRANSLATION INTO PRIMARY CARE

A care package which included an initial weight loss with a Cambridge Weight Plan total diet replacement (TDR, 810-833kcal/d liquid diet comprised of soups and shakes) followed by food re-introduction and weight maintenance (the Counterweight programme), delivered more than a 15kg weight loss after one year in one third of participants in a primary care setting.

The study, reported in February 2013 in the British Journal of General Practice by Professor Mike Lean and colleagues from the University of Glasgow and the Counterweight programme team, described the results of the weight-loss intervention in 91 people with BMI >40 living in rural and small-town Scotland (Lean et al 2013). Severe obesity is increasing rapidly in Scotland: 6% of men and 11% of women have BMI over 35, and for those over 55 years 3% of men and 5% of women have BMI over 40. Potentially eligible for surgery, many of these people with BMI in excess of 40 are unlikely to get that treatment in today's circumstances, and yet the 15-20kg weight loss needed to correct the metabolic derangement in type 2 diabetes cannot be achieved by conventional dietary regimens. Formula diet programmes, providing a nutritionally replete diet, achieve a higher energy deficit than conventional reducing diets, resulting in 1-2kg weekly weight loss, in turn giving the weight losses needed. These higher rates of weight loss have been shown to be safe (adverse event profiles are fully published, Johansson et al 2011, see page 6) and lean mass losses were reported as remarkably low in older Danes with osteoarthritis (Christensen et al 2011, see page 4).

In the Counterweight total diet replacement weight loss and maintenance programme, 91 patients (mean BMI48) entered the programme and 58 completed the liquid diet phase (82 initially chose the commercial programme over the 'home-made' version). The mean weight loss during the liquid diet was 16.9kg, and during food re-introduction was 2.1kg.

Fifty-two patients commenced the maintenance phase, 27 achieving a loss of more than 15kg at one year. 44 had accepted use of orlistat to facilitate maintenance at some point during the year and those taking orlistat showed a weight-loss of 20.1kg at one year, while those not taking it showed an average loss of 14.1kg at one year.

The cost, carefully calculated to include all components, including practice nurse time and cost of product and telephone calls, was estimated at £861 per participant or, since three participated in order for one to lose 15kg, the cost (given in the paper) was £2611 per patient with a documented 15kg weight loss at one year.

A qualitative analysis showed that participants were 'very satisfied' with the rate and degree of weight loss with the formula diet. Transient constipation and dizziness occurred in some people but there was more concern over social and occupational consequences such as difficulties at family meal times.

The participants in this feasibility trial were largely non-diabetic patients, so there is now a need to undertake a similar study in those with type 2 diabetes. Strategies for reducing drop-out need to be devised and methods to enhance weight maintenance beyond one year need to be tested. In the weight loss trial in elderly Danes with osteoarthritis (Christensen et al 2011, see page 4), at the end of the first year of maintenance patients were re-randomised to one of two active intervention programmes. The first allowed the daily use of one formula product to substitute for one meal to help achieve the daily reduction of dietary energy intake of about 400kcal/d needed after a 15kg weight loss, with tight monitoring of weight and a short-term use of an 800kcal/d liquid diet if weight rose by 2kg. The second provided an opportunity for a five week 800kcal/d liquid diet every four months. This three-year randomised controlled trial will determine whether or not weight maintenance is possible and which of these two interventions gives the best outcome. Publication of these results is expected in early 2017.

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Lean M, Brosnahan N, McLoone P, McCombie L, Bell-Higgs A, Ross H, Mackenzie M, Grieve E, Finer N, Reckless J, Haslam D, Sloan B, Morrison D, Feasibility and indicative results from a 12-month low-energy liquid diet treatment and maintenance programme for severe obesity. Br J Gen Pract 2013; DOI: 10.3399/bjgp13X663073.

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PSORIASIS

Psoriasis is a chronic recurring inflammatory skin condition characterised by patchy red, thick and scaly skin, which varies in severity from time to time. Environmental and genetic factors play a part in the causation of psoriasis. It is associated with obesity, it is not seen in very slim individuals, may become more severe with increasing body weight and in some people seems to respond to weight reduction. Until the publication of the work described below, there was no good clinical trial evidence that weight loss could be helpful.

Sixty obese patients with psoriasis randomised to either usual management (control) or an 800-1000kcal/d Cambridge Weight Plan diet programme for eight weeks followed by a 1200kcal/d diet for eight weeks in preparation for a maintenance programme. The diet-treated group lost 15.4kg more than the control group at 16 weeks. The dermatology life quality index (DLQI) improved significantly after the formula diet compared to control and the Psoriasis Area and Severity Index (PASI) showed a trend towards improvement.

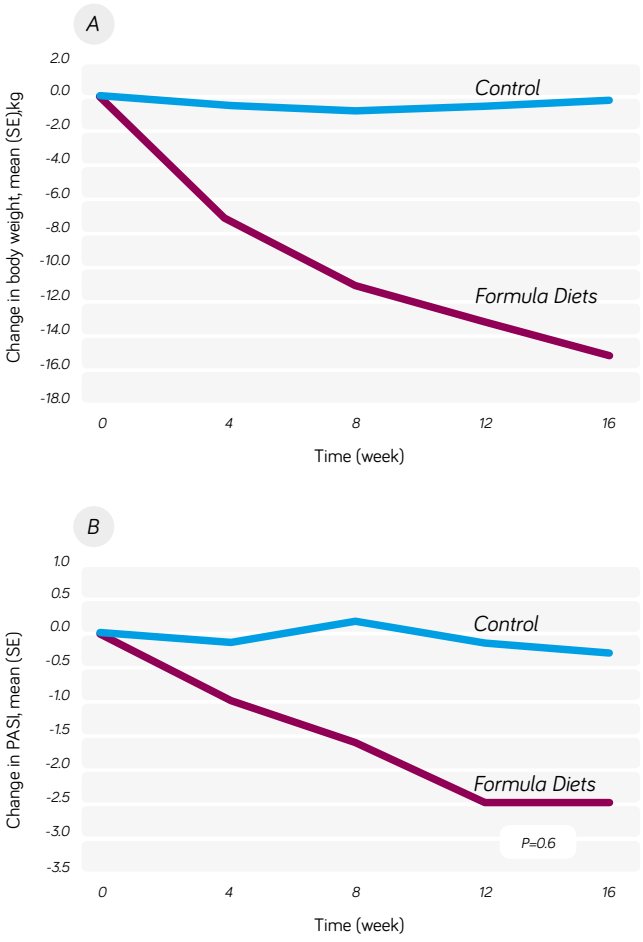

Figure 4. Mean changes over time from baseline body weight (A) and Psoriasis Area and Severity Index (PASI) (B). The dark red line represents low-calorie diet group; blue line represents the control group.

ONE YEAR FOLLOW-UP:
EFFECT OF WEIGHT LOSS ON SEVERITY OF PSORIASIS

Following completion of the randomised controlled trial described above, subjects in the control group were offered weight loss with formula diet over 16 weeks. After weight loss, subjects from both groups were offered weight maintenance with replacement of two meals daily with formula diet products and support from a dietitian at eight weekly intervals. Body weight, Psoriasis Area and Severity Index (PASI) and Dermatology Life Quality Index (DLQI) were measured.

Thirty-two subjects completed the one-year follow-up programme. During their initial 16-week weight loss programme, they lost on average 15kg. After one year they had maintained about 66% of that initial loss – approximately 10kg (a significant change from baseline $p<0.001$). The improvement in PASI seen at 16 weeks was maintained at one-year follow-up (a significantly lower score compared to baseline, $p<0.001$). The significantly improved DLQI seen at 16 weeks was maintained at one year.

These results suggest strongly that effective weight loss with an 800 to 1000kcal/d formula diet programme can improve the severity of the skin lesions in psoriasis and that this can be maintained by partial use of formula diet in a weight maintenance programme. A full-scale multi-centre randomised

CARDIOVASCULAR RISK FACTORS IN PSORIASIS

A recently published meta-analysis of 75 relevant articles (Miller at al 2013) showed that psoriasis is associated with heart disease, diabetes, hypertension, dyslipidaemia, obesity and the metabolic syndrome, but not cardiovascular mortality. In the study reported by Jensen and colleagues described on page 10, cardiovascular risk factors were measured as well as markers of endothelial function.

Some traditional cardiovascular risk factors (see table right) showed significantly greater reduction following weight loss with formula diet (800-1000kcal/d Cambridge Weight Plan) followed by eight weeks of 1200kcal/d diet than after 16 weeks of 'usual care' control treatment.

Endothelial function had been assessed by measurement of soluble markers: intercellular adhesion molecule (ICAM)-1, vascular adhesion molecule (VCAM)-1 and tissue plasminogen activator inhibitor (tPAI)-1. Tissue plasminogen activator inhibitor showed a large fall following weight loss from 5.21 to 2.14ng/ml after weight loss with formula diet and a slight rise after the control treatment (4.53 to 4.94ng/ml), the difference between the groups being significant (p = 0.001), but (ICAM)-1 and (VCAM)-1 showed no significant change. Microvascular endothelial function was assessed using peripheral arterial tonometry but there was no significant change in the calculated reactive hyperaemia index.

Thus, some components of the cardiovascular risk profile were improved by weight reduction with a formula diet Cambridge Weight Plan programme.

Changes in variables from baseline to 16 weeks:

	Formula diet	Control	Difference	P value
Systolic blood pressure mmHg	-7	-2	-5	0.1
Diastolic blood pressure mmHg	-5	1	-6	0.002
Total cholesterol mmol/l	-0.4	0.04	-0.5	0.008
LDL-cholesterol mmol/l	-0.2	0.04	-0.1	0.06
Triglyceride mmol/l	-0.58	-0.24	-0.32	0.01
Plasma glucose mmol/l	-0.6	-0.1	-0.5	0.007
Glycated haemoglobin %	-0.7	-0.4	-0.3	0.007

controlled trial, with weight loss followed by at least a two-year weight maintenance programme, should now be undertaken to provide the evidence required for weight loss and maintenance guidance to be incorporated into psoriasis management guidelines. In the meantime clinicians may feel inclined to see whether or not obese individuals with psoriasis benefit from weight loss using formula diet weight reduction and maintenance programmes.

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Figure 4: Redrawn from: Jensen, P., et al Effect of Weight Loss on the severity of Psoriasis JAMA Dermatol doi: 10.1001/jamadermatol.2013.722 (published on line 29th May 2013).

SLIM FOR SURGERY: IS WEIGHT LOSS BEFORE BARIATRIC SURGERY NECESSARY?

There is clear evidence from the Scandinavian obesity registry, describing over 22,000 bariatric surgical cases observed from 2008-12, that the standard two to three week pre-op regimen of a very low-calorie diet (VLCD) resulted in variable weight losses (0.5% to 9% of initial weight in the 25th and 75th percentiles) and variable complication rates. Anastomotic leakage, deep infection or abscess, and minor wound complications were 24%, 37% and 54% lower in the group that achieved 9% weight loss compared to that with a 0.5% loss. The effects were most pronounced in patients with BMIs >46 compared to <40 (Anderin C et al. 2014). Another analysis of the same registry showed that those who achieved greater pre-op weight loss (75th percentile, ~9% of initial body weight, ~10kg from a baseline of 120kg) compared to those who lost least (25th percentile, ~zero) lost significantly more weight in the first year after surgery (38kg compared to 34kg). The difference persisted at two years after surgery (Gerber P et al. 2015A) and the effect was greatest in heavier patients (BMI >46). A review of 23 publications by Gerber et al (2015B) noted that 'high quality evidence is lacking' but added 'for post-operative complications robust studies are emerging suggesting that a pre-operative regimen should be approved'.

Bariatric surgeons in Denmark require that their patients lose 8% of their initial body weight before surgery. This is achieved either through use of formula diet programmes or conventional food restriction. As part of a study on the effects of Roux-en-Y gastric bypass surgery on energy expenditure, appetite and glycaemic control undertaken in Copenhagen, 30 subjects (average baseline weight 143kg, BMI46) scheduled for surgery were offered a liquid formula diet (800kcal/d) plus some non-starchy vegetables and yoghurt (200kcal/d) for 11 weeks (Schmidt et al 2016). Half received their RYGB after seven weeks and half after 11 weeks. The data on the first seven weeks show that on average they lost 12.7kg (9.7% of initial body weight), while the 15 subjects who followed the diet for 11 weeks before surgery lost an average further 4.9kg (total 17.6kg). On average the 8% weight loss target had been achieved by five-and-a-half weeks and 77% of subjects had reached it by seven weeks. In parallel with the weight-loss the metabolic profile improved and blood pressure was lowered (Nielsen LV etal 2016). These two papers show quite clearly that a Cambridge Weight Plan low-energy liquid diet combined with the local preference for a small conventional meal can deliver in seven weeks, a weight-loss close to the 10% target suggested by Anderin (2015).

To examine diet duration needed to reduce liver volume and fat, Bottin et al. (2014) in London compared two and six-week pre-op regimens of a low-energy liquid Cambridge Weight Plan diet with a conventional food-based 1000kcal/d diet in patients (BMI ~46) before Roux-en-Y surgery. Preliminary results showed that effective reduction of liver volume and fat (measured by MRI scanning and NMR spectroscopy respectively) was achieved in two weeks with formula diet compared to conventional diet, while greater visceral fat loss and neck circumference reduction was achieved in six weeks of formula diet.

Ability to mobilise in the post-operative period is important and some obese patients struggle to move as well as less heavy patients. In a randomised controlled trial of Cambridge Weight Plan 800kcal/d formula diet, in southern Denmark in patients awaiting total knee replacement in whom the treated group lost about 10kg (10%) of initial body weight in eight weeks, mobilisation on the first post-operative day was significantly improved in the weight-loss group (Liljensøe et al., 2014).

The evidence supports the use of 1000kcal/d liquid formula diet for two weeks for 'liver shrinkage' and for seven to eleven weeks to achieve the 10% body weight loss suggested by Anderin. Evidence suggests that heavier patients (BMI >46) may benefit most from pre-op diets given for extended periods, for whom the likely standard 'unit of care' will be 12 weeks of 1000kcal/d liquid formula diet.

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WEIGHT-LOSS AND SECONDARY PREVENTION OF CORONARY HEART DISEASE

In eight centres across Europe that contributed data to the European Action on Secondary Prevention through Intervention to Reduce cardiac Events survey (EUROASPIRE III), the prevalence of obesity rose from 25 to 38% in the ten years prior to 2007. In addition, data from 22 countries across Europe was used to assess the overweight and obesity among patients participating in secondary prevention of heart disease programmes. Only 18% of patients were found to achieve a reduction of body weight to below a BMI of 25 kg/m^2. Survey results suggested that a proportion of patients were largely unaware that they had a weight problem, and only half of those with BMI over 30 reported actively trying to lose weight in the month preceding questioning. The survey also showed a more frequent use of lipid-lowering and anti-hypertensive drugs in overweight and obese patients. The authors concluded that 'management of body weight should be given the highest priority in patients with coronary artery disease'.

To investigate the potential benefit of weight loss with a formula diet programme, 70 non-diabetic people with coronary artery disease aged 45 to 75 years and with BMI >28 kg/m^2, were randomised to aerobic interval training (AIT) at 90% peak heart rate three times weekly or a low-energy liquid diet (LED) Cambridge Weight Plan 800–1000kcal/d for eight to 10 weeks, followed by two to four weeks' weight maintenance diet with conventional food reintroduction (Pedersen et al 2013; Pedersen et al 2015A). Insulin sensitivity and glucose metabolism were assessed by 3h glucose tolerance tests with calculation of insulin sensitivity (Pedersen et al 2015B). Coronary microvascular function was measured before and after the intervention by measurement of coronary flow reserve (CFR) (Olsen et al 2015).

Three out of four successfully completed the AIT (n=26) and four out of five (n=29) successfully completed the LED. The LED group lost 10.6% of their initial body weight and 26.6% of their fat mass, whereas in the AIT group weight loss was 1.6% and fat mass loss was 5.5% (p<0.001 between groups for both variables). Systolic blood pressure was reduced significantly after AIT but not after LED and diastolic blood pressure did not change significantly. VO2 peak total (mL/min) increased significantly after AIT by 212 from 1999, but not after LED, there being a significant difference between the groups (Pedersen et al 2015A).

Fasting plasma glucose and fasting plasma insulin were significantly reduced after LED but not after AIT. Whole body and hepatic insulin sensitivity increased significantly after the LED but not after AIT, as did the beta-cell response (Pedersen 2015B). A significant reduction of small dense low density (LDL) lipoprotein occurred after LED only, indicating decreased lipoprotein atherogenicity (Pedersen et al 2016).

Baseline CFRs indicated poor coronary microvascular function, which increased significantly after both interventions by 0.26 from 2.27 after AIT and by 0.39 from 2.29 after LED, but there was no significant difference between the groups (Olsen et al 2015).

Following the initial 10 to 14 weeks' intervention, both groups continued supervised AIT twice weekly for 40 weeks and the LED group also continued a dietitian-supervised weight maintenance programme. The AIT followed by twice weekly AIT group maintained 1.6kg weight loss at one year, while the LED followed by weight maintenance plus twice weekly AIT group maintained 7.2kg weight loss of which 0.5kg was determined as lean mass loss. VO2 peak BW ML/min/kg was significantly improved at one year after LED followed by twice weekly AIT (23.7 compared to 20.5 at baseline) whereas after AIT VO2 peak BW was improved but not significantly (22.5 compared to 21.0 at baseline) (Jurs et al 2015). Publication of the one year CFR results is awaited.

These findings suggest that achieving an initial body weight loss of 10% followed by a weight maintenance programme with aerobic interval training is associated with increased insulin sensitivity, a less atherogenic blood lipid profile, a relatively small loss of lean mass, and improved cardiovascular fitness, and thus may contribute effectively to secondary prevention of coronary heart disease.

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DIABETES PREVENTION, TYPE 2 DIABETES REVERSAL AND IMPROVEMENT OF DIABETES CONTROL IN INSULIN-TREATED TYPE 2 DIABETES.

The International Diabetes Federation (IDF 2015) estimates that the global population of people known to have type 2 diabetes will rise from about 415 million in 2015 to 642 million in 2040.

Risk factors are known (a family history of diabetes; being overweight; physically inactive; and older than 45 years and, in women, having a history of diabetes in pregnancy) and diabetes prevention programmes are in place in a number of countries. The emphasis is on losing weight, being physically active and eating 'healthily'. Greater weight loss and maintenance leads to a greater proportion of people being diabetes free for longer. This was demonstrated clearly in the US Diabetes Prevention Program (US DPP) which, in a group treated by change in diet and lifestyle, diabetes-risk decreased by 10% for each percentage point of weight loss at six months (Maruther et al. 2013). Similarly Iwahashi et al (2015) showed that older Japanese men who lost and maintained >4.3% of their body weight developed no diabetes within three years, whereas over the same period, 30% of those who lost between 1.2 and 2.5% of their body weight developed diabetes. Thus diabetes programmes need to aim for large enough initial weight losses followed by sufficiently effective maintenance programmes to achieve, ideally, maintenance of 10% body weight loss for as long as possible. Achievement of normalisation of blood glucose by six months was found to be an independent indicator of risk of diabetes development. This shows that reversal of risk is probably also dependent on a large enough whole body weight and fat mass loss to achieve a depletion of the small amounts of excess fat in the liver and possibly the pancreas, thereby improving insulin sensitivity and facilitating beta cell recovery.

PREVENTION OF DIABETES THROUGH LIFESTYLE INTERVENTION AND POPULATION STUDIES IN EUROPE AND AROUND THE WORLD – PREVIEW TRIAL (FUNDED WITH AN EU PROGRAMME GRANT).

Over 16,000 people in eight countries† were pre-screened, nearly 6,000 were screened and over 2,300 entered a weight loss programme commencing with an eight-week 800kcal/d liquid formula diet programme (Cambridge Weight Plan) prior to randomisation into higher and lower exercise groups and randomisation into either higher protein, lower glycaemic index (GI) diet or a lower protein, higher GI diet for two years (Fogelholm M, et al 2015A). Based on the six-month results from the DIOGENES trial (Larsen et al 2013) the critical six-month weight reduction is expected to be best in the higher exercise, higher protein, lower GI group.

The average weight loss during the Cambridge Weight Plan 800kcal/d diet was 10.8% of starting weight (10.7kg) from an initial average weight of 99kg (Fogelholm M, et al 2015B). If maintained this weight loss would be expected to be associated with a reduction of 90% in diabetes risk over three years.

Full metabolic changes following the initial weight loss may be published in 2017 and two year outcomes in 2018/2019.

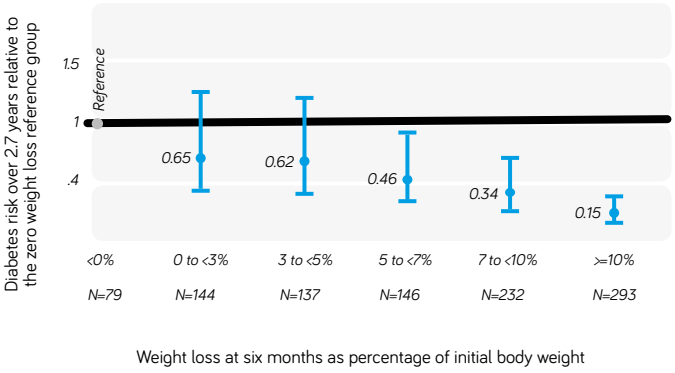

Figure 5. Greater weight loss gives greater reduction of diabetes development up to 2.7 years. Redrawn from 'Maruther NM et al 2013 Early response to prevention strategies in the Diabetes Prevention Program. J Gen Int Med 28 (12): 1629-1636.

†PREVIEW countries: Finland; Denmark; the Netherlands; the United Kingdom; Spain; Bulgaria; Australia; and New Zealand.

	Low-energy liquid diet	Best practice clinical care	Significance
Weight loss kg	9.8 + 4.0	2.2 + 2.2	p<0.001
Insulin reduction %	76	46	p<0.0001
Receiving insulin treatment at 12 weeks No	6/10	10/10	

Weight loss and insulin reduction in long standing type 2 diabetes. Data from Brown et al 2016

DIABETES REMISSION CLINICAL TRIAL - DIRECT

Reversal of early diabetes has been demonstrated by Lim et al (2011) using a very low-calorie diet, and has been shown by the same group to be sustainable for six months in 40% of subjects who achieved a fasting blood glucose of <7mmol/l at the end of the initial weight loss (Steven et al, 2016). Professor Roy Taylor, principal investigator in these studies, believes that type 2 diabetes mellitus is potentially reversible, in some people.

Based on this work and a translation into primary care pilot study reported by Lean et al (2013) (see page 9), a study on diabetes remission by weight loss and maintenance in a primary care setting is now underway (Leslie et al 2016).

280 participants (aged 20 to 65 years, BMI >27 and <45, time since diagnosis up to six years) were randomised to either usual care or a 12 to 20 week low-energy liquid diet (825-853kcal/d total diet replacement by Cambridge Weight Plan) followed by structured food re-introduction delivered within the Counterweight Plus programme. Practices in Scotland and North East England participated. The protocol includes a relapse management option to address weight regain or diabetes recurrence with options to use partial or total diet replacement with liquid formula for short periods, followed by food re-introduction. Participants will be followed for two years – the primary endpoints are body weight and reversal of diabetes (targets >15kg, HbA1c < 48 mmol/l). Results are expected by 2018.

WEIGHT LOSS WITH CAMBRIDGE WEIGHT PLAN IN INSULIN TREATED TYPE 2 DIABETES

To investigate the role of weight loss using formula diet in long-standing type 2 diabetes treated with insulin, 20 obese patients (average age 56 years, weight 100kg, time since diagnosis 13.6 years, duration of insulin treatment 4.7 years, insulin dose 64 units) were given either a Cambridge Weight Plan low-energy formula liquid diet (810-840kcal/d) or best practice clinical care (a 600kcal/d deficit diet) for 12 weeks. All received advice on physical activity and behaviour change.

Preliminary results on 20 participants were presented at the Diabetes UK 2015 conference and suggested that 'low energy liquid diet is a promising intervention in this patient group in whom weight reduction is difficult to achieve' (Brown et al, 2015).

Participants then followed a gradual and carefully managed food re-introduction programme over three months, followed by conventional food for six months. Full measurements were made at 12 months and results are anticipated by early 2018.

Weight loss with formula diet programmes, such as Cambridge Weight Plan's 800kcal/d total diet replacement, can deliver rates of weight loss of 1-1.5kg per week and 10 to 12kg in 8 weeks (15 to 20kg takes a little longer). These amounts of weight loss are critical to achieving sufficient change (depletion of fat) in target organs, including the liver and pancreas, thereby preventing type 2 diabetes, reversing early diabetes and improving the health and metabolic control of those who are insulin-treated.

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RESEARCH IN PROGRESS

COMPREHENSIVE TREATMENT OF ANGINA PECTORIS IN WOMEN WITH MICROVASCULAR DYSFUNCTION

To be undertaken by the team at Bispebjerg Hospital, Copenhagen, who reported the results described on page 13. The new study extends the application of weight loss with Cambridge Weight Plan in people with coronary microvascular disease, and subsequent aerobic interval training, to acquire further evidence for the benefit of weight loss using formula total diet replacement.

DIABETES INTERVENTIONAL ASSESSMENT OF SLIMMING OR TRAINING TO LESSEN INCONSPICUOUS CARDIAC FUNCTION: THE DIASTOLIC STUDY

Currently underway at Leicester Diabetes Centre, Leicester General Hospital, this study will determine whether there is a place for weight loss with Cambridge Weight Plan in reversing diastolic dysfunction in those with type 2 diabetes.

MALE INFERTILITY

A pilot study at Imperial College, The Hammersmith Hospital, is currently under way to investigate whether weight-loss with Cambridge Weight Plan can improve measures of infertility in obese men.

DOCTOR REFERRAL OF OVERWEIGHT PEOPLE TO LOW-ENERGY TREATMENT - THE DROPLET TRIAL

In this study, now under way at the Nuffield Department of Primary Care Health Sciences, University of Oxford, GPs located in practices throughout Oxfordshire offer clinically obese patients an opportunity to enter a trial of weight loss via a standard care pathway or by referral out to Cambridge Weight Plan Consultants working in the community. In this randomised controlled trial on 270 subjects, the participants will be observed for one year after weight loss. First results are expected in late 2017/early 2018.

> "We demonstrated that weight loss was superior to aerobic interval training in improving whole-body and hepatic insulin sensitivity which is associated with prognosis in coronary artery disease.
>
> Our results could have an impact on secondary prevention strategies for overweight, prediabetic people with coronary artery disease."
>
> (Pedersen et al 2015, see page 13)

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