Predictors of programme adherence and weight loss in women in an obesity programme using meal replacements

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Performance of weight loss programme with meal replacements

Abstract

Objective: To explore predictors of programme adherence and weight loss in patients participating in a weight management programme using meal replacements (MR).

Design: 150 healthy obese women, age 48.5(sd=8.3) years; weight, 97.6(13.4) kg; BMI 36.5(3.7), participated in a longitudinal study with a 16-week acute weight loss phase (Phase 1) followed by one year of a trial of weight loss maintenance (Phase 2). Energy intake during Phase 1 totaled 900 kcal (3.7MJ) a day from a diet including two meal replacements (MR). Energy intake during Phase 2 consisted of either MR or a low fat diet with a calculated energy deficit of 600 kcal/day (2.5MJ).

Methods: Weight, height and waist circumference were measured and body composition assessed by air plethysmography (Bodpod). Glucose and insulin were measured by standard immunoassays and insulin sensitivity assessed by Homeostatic Model Assessment (HOMA).

Results: At the end of 16 weeks, 114 subjects (76%) completed Phase 1 and achieved a mean weight loss of 8.95(3.38) kg. Adherence to Phase 1 was predicted by weight loss over the first two weeks ($p<0.001$). Weight loss during Phase 1 was predicted by initial weight and initial systolic blood pressure. Adherence to Phase 2 was not predicted by physiological measures. Weight loss maintenance in Phase 2 (not gaining more than 3% of the weight at start of phase 2) was predicted by cholesterol and triglyceride measured at the start of Phase 2 but otherwise was not predicted by the physiological measures. Initial insulin sensitivity did not predict weight loss in either phase.

Conclusion: Participants whose weight loss over the first two weeks falls in the bottom third may need additional intervention if they are to continue in this type of programme. A battery of physiological measures at entry to a MR weight loss and maintenance programme explains only a very small proportion of the variation in weight loss.

INTRODUCTION

There are two aspects that may be considered as relevant to the success of a weight reduction programme: continued adherence to the programme and the extent of weight loss among those who continue. However, there are few biological predictors known to predict these outcomes. Accurate or sensitive predictors would be useful in selecting an appropriate treatment regimen for individual obese patients. Earlier studies suggest that a positive family history [1], repeated weight loss in the past and extreme body dissatisfaction were important factors in predicting weight loss [2]. Higher pre-treatment body weight, [3] resting metabolic rate (RMR), fat cell hyperplasia and upper body fat distribution [4] were associated with greater weight losses. Recently a trial of diet and pharmacotherapy showed positive associations of weight loss at 6 months with pre-treatment body weight, height, fat-free mass, fat mass and resting metabolic rate [5]. Other factors implicated as predictors include a low ratio of fat to carbohydrate oxidation [6], high basal 24-hour energy expenditure, plasma noradrenaline and androgens [7].

Hyperinsulinemia, hypertension and insulin resistance are frequently observed in obesity. The relationship between hyperinsulinemia, insulin resistance and weight change is not straightforward. Previous studies have yielded conflicting results. While the CARDIA (Coronary Artery Risk Development in Young Adults) study showed a positive association between fasting insulin and weight gain, the ARIC (Atherosclerosis Risk in Communities) study showed a lower rate of weight gain with greater fasting hyperinsulinemia [3,8]. Odeleye et al found that greater insulin resistance predicts weight gain [9] whereas Swinburn et al found that the greater the insulin resistance, measured by glucose disposal rates, the lower the risk of weight gain in obese non-diabetic Pima Indians [10]. Conversely, Schwartz et al, found that relative hypoinsulinemia independently predicted weight gain [11]. Other studies have shown no correlation between fasting insulin and weight gain [12]. Most of these studies were observational retrospective analyses without any intervention. McLaughlin et al explored insulin sensitivity as a weight loss

predictor, by measuring insulin mediated glucose disposal using steady state plasma glucose in 20 obese female subjects on a hypocaloric diet. Insulin resistance did not predict weight loss in this setting [13].

The aim of this study was to explore predictors (in particular initial insulin resistance) of programme adherence and weight loss and weight loss maintenance in patients participating in a weight management programme using meal replacements.

METHODS

Phase 1-Weight Loss Phase

During this phase, subjects were provided free a 900-calorie/ day diet consisting of 2 SlimFast Meal Replacements ™ (SFMR) each providing 200 calories, and one low fat meal of 300 calories; in addition patients were allowed 3 items of fruit and 2 servings of vegetables. Subjects attended biweekly for a one-hour dietetic and cognitive behavioural therapy (CBT) session delivered by a dietician with special skills in CBT. Monthly medical checks were carried out. Initially only subjects who achieved ≥10% weight loss after 16 weeks entered Phase 2. This was based on a 75% compliance with a theoretical calculation of weight loss based on the expected caloric deficit. However, on compassionate grounds a protocol amendment was made to allow a further 13 women who achieved at least 9% but less than 10% weight loss to be admitted to Phase 2.

Phase 2 - Weight Loss Maintenance

During this phase, subjects were given a weight maintenance regimen including group dietetic and lifestyle therapy, behavioural modification and advice on increased physical activity based on the CHANGE programme [14]. Dietary advice was modified to allow the use of at least

10 SlimFast ready-made liquid or powder meal replacements each week. The limited use of two meal replacements per day was permitted in patients tackling temporary relapse (no more than two weeks in any eight week period). Patients were asked to return used Slim-Fast tin lids, which were recorded to assess compliance. New tins were dispensed according to participants' usage of the diet supplement and the numbers of lids returned.

Subjects continued to attend the Research Centre for weighing monthly, and for group therapy sessions monthly, for the first six months, bi-monthly, for the next six months, and were planned to attend quarterly for the second year.

These data relate to the 16 weeks of Phase 1 and the first year of the weight loss management (WLM) phase. The study was terminated after the first year of the WLM phase because of the high attrition rate.

Subjects and Methods

188 healthy, obese women aged between 35 and 65 with a BMI range of 30 to 45 were screened through advertisements in local news media. Subjects were excluded if they were dieting, had a secondary cause of obesity, were on drugs known to affect energy balance, had a history of eating disorder, had lactose intolerance or if they had significant co-morbidity (uncontrolled hypertension, recent myocardial infarction, recent CABG, diabetes requiring insulin, gallstones, chronic illness or malignancy). This left 150 subjects who took part in the trial. The local Research Ethics Committee approved the study and all subjects gave informed written consent prior to participation.

Weight: was taken with the patient in light clothing and bare feet on Tanita (310) body composition analyser, calibrated to the nearest 0.1 kg.

Height: was taken by standing the subject against a wall-mounted stadiometer and to the nearest 0.5 cm

Body Mass Index (BMI): was calculated as weight in kg divided by the square of the height in metres.

Waist Circumference (WC): was measured according to the WHO criteria. It was taken at the midpoint between the lowest point of the costal margin and the highest point of the anterior superior iliac spine.

Hip circumference (HC): was taken at the level of the greater trochanters bilaterally with the tape measure passing round the widest part of the buttock and the symphysis pubis.

Body Composition: was measured using air plethysmography on the principle of air displacement [15]. Whole body density is measured and from this the relative proportion of fat and lean body mass is calculated using standard equations. The procedure has been shown to be safe, quick, non-invasive, accurate and reproducible [16].

Laboratory Measurements

All samples were taken after a 10-hour overnight fast. **Glucose:** was measured by the glucose oxidase method. **Insulin** was estimated using Microparticle Enzyme Immunoassay. The cross reactivity with proinsulin is negligible (<0.005). The sensitivity is 0.03 μIU/ml. The co-efficient of variation (CV) for intra-assay, inter-assay and total precision is 3.1%, 3.8% and 5% respectively. **Insulin sensitivity** was assessed using the mathematical model devised by Matthews et al. with the formula: insulin resistance = (fasting insulin x fasting glucose) ÷ 22.5 [17]. Patients were further classified according to whether or not they met the ATPIII criteria for metabolic syndrome [18].

Statistical Analyses

Data were analysed using SPSS version 11. Logs to the base 'e' were taken of the HOMA-IR and HOMA-IS measures before statistical analysis to correct for the skewed distributions of the

raw values. Summary statistics are expressed as means (sd), Pearson correlations, percentages or odds ratios. Confidence intervals are 95% and are shown as (*lower limit* to *upper limit*). T-tests and Mann-Whitney non-parametric tests were used to test differences between groups. Multi-level models were used to estimate mean rates of weight loss. Ordinal logistic regression and Cox Survival Analysis were used to explain continued adherence and weight loss in terms of various measures. p-values refer to two-sided tests.

RESULTS

Descriptive Statistics

The physical and demographic characteristics of the 150 subjects on entering Phase 1 are shown in Table 1, and a CONSORT description of the progress of subjects through the study is in Figure 1.

114 subjects (76%) completed Phase 1 and achieved a mean weight loss of 8.9(3.4) kg (9.1% of initial weight). Out of these 114 Phase 1 completers, 70 (61%) achieved the target weight loss of ≥9%. Of the 57 failing to achieve the required 9%, 27 lost between 5% and 9% and 17 less than 5% (Figure 1). There were no baseline differences in any individual measures between completers and non-completers of Phase 1 or between successes and failures in achieving 9% weight loss. The mean rate of weight reduction over Phase 1 was 0.45 kg per week (0.41 to 0.50) for the 68 patients who completed Phase 1 only and 0.64 kg per week (0.60 to 0.69) for the 46 who completed Phase 1 and Phase 2. See Figure 3.

Of the 114 who completed Phase 1, not all had complete Phase 1 physiological measurements. Since patients did not always know prior to attendance that they might have achieved the target loss to proceed to Phase 2, it was sometimes necessary for them to return fasting within 1-2 days for blood samples or body composition. The numbers of subjects for each measure, and the

changes, are shown in Table 2. The baseline values for the women with incomplete data did not differ from those of the women with complete data.

Forty-six (66%) of the 70 participants who entered the weight loss maintenance phase, Phase 2, completed the phase to its end at 12 months. They experienced an overall regain of total body weight, BMI, absolute fat mass, waist circumference, cholesterol and HDL-C. Although reaching statistical significance, these increases over Phase 2 were small compared to the decreases achieved over Phase 1. The overall levels observed at the end of Phase 2 continued to be lower than at baseline. During Phase 2 HOMA-IR decreased and HOMA-IS increased although both were 50% below baseline levels at the end of Phase 2. There were no statistically significant changes in lean body mass, plasma glucose, LDL-C and fasting triglyceride during Phase 2.

The dropout rates were 24% and 34% over Phase 1 and Phase 2 respectively. The main reasons given were work and family commitments. Five subjects had to be withdrawn at the end of Phase 1 for medical reasons.

What Predicts Continued Participation ?

There was a pattern of trend to earlier drop-out with younger age and higher values for HOMA, WHR, waist circumference and bodpod fat although when considered one at a time none of these measures reached statistical significance. However, a linear logistic ordinal regression showed that, in combination, older age, smaller waist and higher BMI at baseline predicted probability of continuation beyond 10 weeks or beyond 16 weeks ($p=0.022$). (See Table 3).

Cox survival analysis found that, in Phase 1, continuation in the study was in part predictable from weight loss over the first two weeks. Greater weight loss measured at week two related to longer

continuation in the trial. ($p<0.001$). See Fig 2 where weight loss after two weeks is categorised into tertiles.

What Predicts Weight Loss ?

Mean weight at various stages of the study is described by the line graphs in Figure 3. Since the intervention represents a fixed energy intake of 900 cals per day, it is to be expected that heavier subjects will experience a larger deficit and hence lose more weight. This was confirmed by correlation of weight at week 0 to weight loss at week 16 of 0.422 ($p<0.001$). Clearly initial weight predicts weight loss through Phase 1. As a consequence, any measure which is correlated with initial weight will also appear to predict weight loss. To examine the extent to which other measures predict weight loss independently of their association with initial weight it was therefore necessary to partial out initial weight from their correlations with weight loss. Table 4 shows the partial correlations of baseline levels of systolic and diastolic blood pressure, HOMA, glucose, insulin, cholesterol, hdl and triglyceride with weight loss at week 16 of Phase 1 and at 1 year at the end of Phase 2. Only systolic blood pressure had a relationship with weight loss at week 16. The relationship was positive, that is, higher values of blood pressure corresponded with greater weight loss. There were no differences, at any stage of the study, between the mean weight losses of women with and without metabolic syndrome. Higher cholesterol and lower HDL at baseline related to less weight loss at year 1. Weight loss maintenance in Phase 2 (not gaining more than 3% of the weight at start of phase 2) was predictable in a logistic regression analysis only by cholesterol and triglyceride measured at start of year 1 and otherwise was not predicted by the physiological measures. Higher cholesterol ($p=0.021$) and lower triglyceride ($p=0.044$) related to higher odds for not increasing weight by more than 3%.

DISCUSSION

This study set out to explore physiological predictors of continued study participation and weight loss in the study participants including the role of insulin sensitivity in prediciting weight loss. Since patients who demonstrated a greater weight loss after two weeks of participation in the trial were more likely to continue in the trial it may be assumed that those who did not continue to participate were not successful in losing weight. Hence continuation of participation is of prime importance and progress during the first two weeks should be given particular attention in future trial designs.

The contribution of body shape (smaller waist, higher BMI) and age (but not metabolic variables such as insulin resistance or secretion) to continued participation suggests a psychological dimension which should be the subject of further research.

The attrition rate in this study was higher than expected, and similar rates have been reported in previous studies with meal replacements. The reasons for this are not immediately obvious. The study was conducted on patients attending as out-patients within the setting of the UK National Health Service. Patients received no covert or overt incentives to remain on the programme other than the initial provision of the meal replacements. However drop-out rates in obesity trials are high. A trial using 16 weeks of VLCD followed by intermittent or on demand periods of VLCD showed only 35% of patients completed two years [19]. A randomised controlled trial of four commercial weight loss programmes in a community based sample of obese adults was conducted by the British Broadcasting Corporation under scientific supervision. It recruited 293 subjects (the largest such study in the UK) and reported a drop-out rate of 28% at six months [20] . A recent trial of dietary therapy in the US, also showed comparable drop-out rates after one year: 39 percent of participants on an Atkins-type diet dropped out compared with 43 percent of those on the conventional diet [21]. Even in drug trials where there is an apparent greater and more medicalised intervention, drop-out rates are high. For example in a one year trial of diet

with orlistat or placebo in the UK, the drop-out rate was 48% in the placebo group and 39% in the orlistat group [22]. The relatively small numbers completing Phase 2 represented a limitation to the power of this part of the analysis. In looking at weight loss to the end of Phase 2 a sample correlation had to be at least 0.29 to qualify for statistical significance.

In keeping with earlier studies, baseline weight predicted weight loss[5,23,24]. Other predictors include baseline BMI, age, sex and hormonal and metabolic variables like RMR, fat oxidation, plasma dihydrotestosterone and plasma noradrenaline[7]. Insulin sensitivity as assessed by the Homeostatic Model Assessment (HOMA) did not predict weight loss in an adult, obese healthy female Caucasian population. These findings are in accordance with those concluded by McLaughlin et al . However, they do not agree with earlier studies using hyperinsulinemia as a predictor of weight gain and vice versa. There are a few reasons for this discrepancy. Firstly, with the exception of McLaughlin et al who used a treatment intervention, all other studies only followed up patients without a therapeutic programme. Thus the effect of insulin on weight gain was explored extensively, unlike the present study which has looked at the effect of insulin and insulin resistance on weight loss. Secondly, the methods used for assessing insulin sensitivity were differrent in the various studies. Two of the studies employed the euglycemic hyperinsulinemic clamp techniques [10,25], one used the isotope dilution method for glucose disposal and the last used only the fasting insulin as a surrogate measure of insulin resistance [26]. In the study by Sigal et al, hyperinsulinemia estimated by the acute insulin response to intravenous glucose predicted weight gain while fasting insulin in the same study showed no correlation. Thirdly, the differences could be explained by the different ethnic population groups and sample sizes. These involved Pima Indians, Hispanic and non-Hispanic whites, Europeans and offspring of Type 2 diabetic parents, adults and children.

A new finding in this study is that systolic blood pressure and cholesterol were predictors of initial weight loss and weight loss maintenance at 1 year, respectively. The relationship between

these baseline characteristics and weight loss were significant even after adjusting for baseline weight suggesting an independent mechanism. It is recognized that blood pressure is related to weight gain, glucose intolerance and insulin resistance [27]. Many studies have suggested that insulin resistance is the metabolic link between obesity and hypertension [28]. In this study, while blood pressure predicted weight loss, insulin resistance did not predict weight loss. Patients were unaware of their biochemistry results, so it does not seem likely that knowledge of blood pressure or cholesterol would have lead to improved dietary compliance.

In conclusion, this study showed that 76% of patients achieved a mean weight loss of 9% within 16 weeks using of a meal replacement diet programme. A minority of patients continued on a weight maintenance diet and behaviour programme for one year, but those that continued in therapy maintained much of their loss. It remains the challenge for obesity treatment to find ways of improving the retention of patients in treatment, and that this is perhaps a more important target than increased weight loss itself.

Figure 1. Flow of participants through weight loss programme

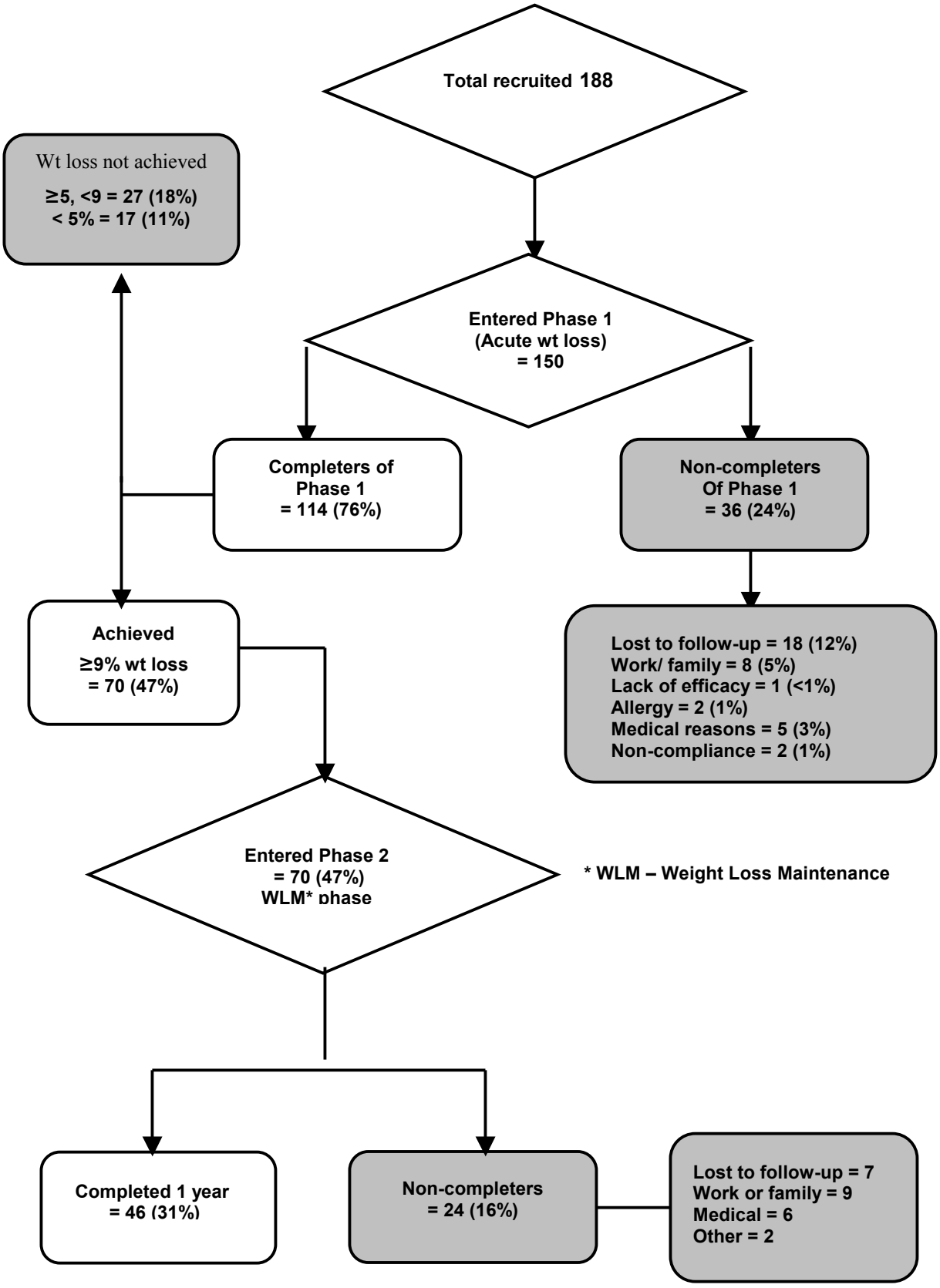

Figure 2:
Continured participation in Phase 1 by tertile of weight loss in first two weeks

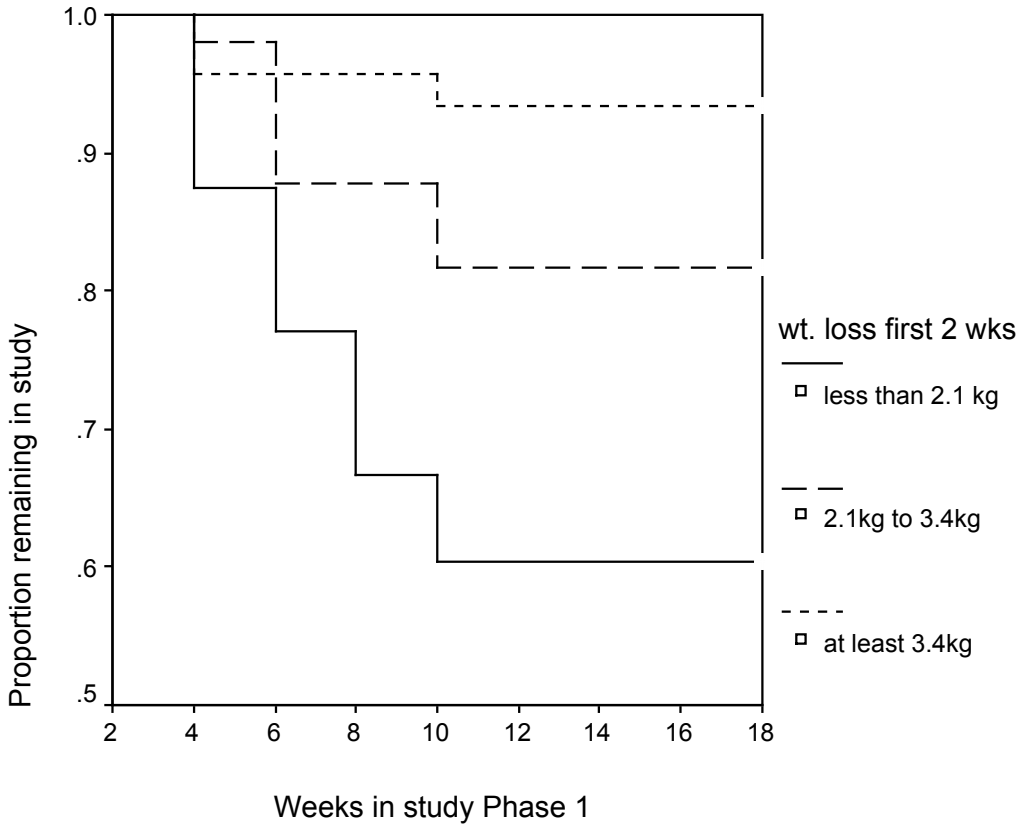

Figure 3: Means of weights of participants by phase completed

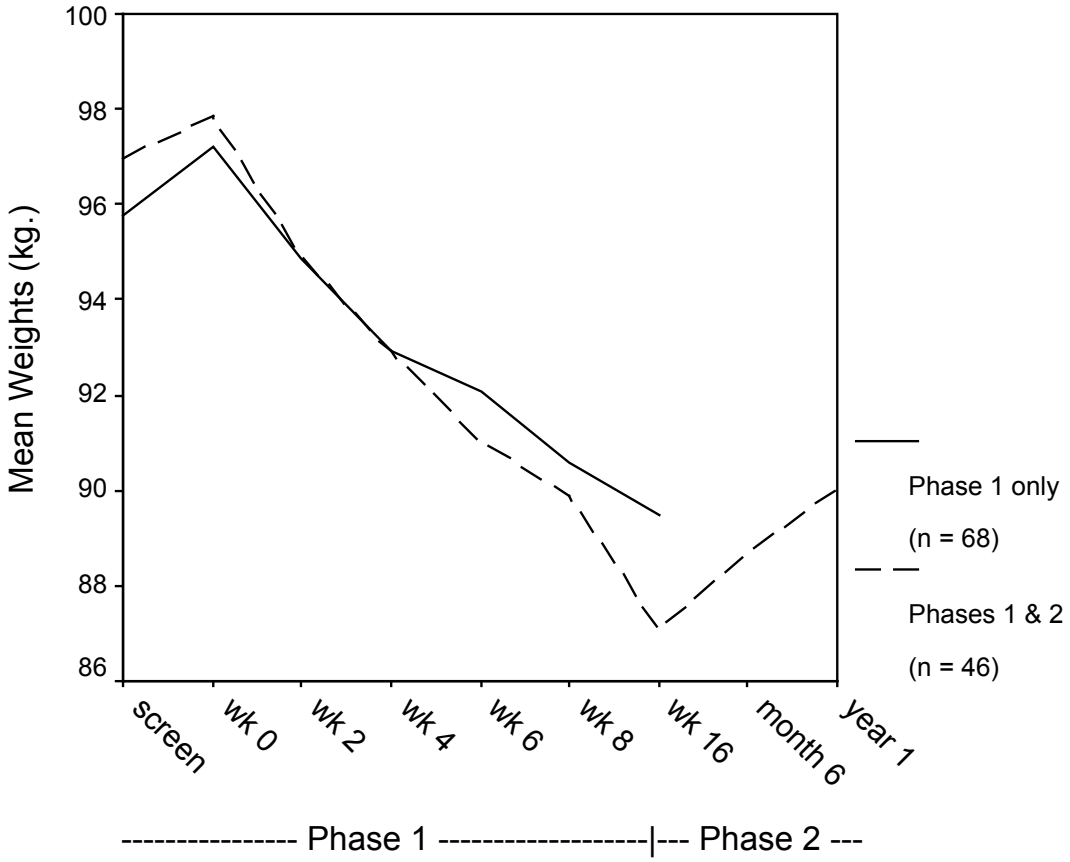

Table 1 Demographic profile of study subjects at baseline

N=150

	Mean (SD)
Clinical	
Age (yr)	48.5 (8.25)
BMI	36.1 (5.62)
Body Weight (kg)	95.1 (13.22)
Anthropometric	
Waist Circumference (cm)	105.0 (9.42)
Bodpod Fat Mass (kg)	46.81 (9.48)
Bodpod Lean Body Mass (kg)	49.07 (5.95)
Metabolic	
Resting Metabolic Rate [RMR] [kcal/24hrs]	1588 (139.9)
Total Energy Expenditure [TEE] [kcal/24hrs]	2384 (237.7)
Laboratory	
Fasting glucose (mmol/l)	4.9 (0.64)
Fasting insulin (Mu/l)	12.4 (5.67)
HOMA index	2.79 (1.18)
Fasting Cholesterol (mmol/l)	5.58 (1.06)
Fasting Triglycerides (mmol/l)	1.54 (0.88)
Fasting HDL (mmol/l)	1.43 (0.32)

Table 2: Body composition and metabolic parameters before and after weight loss

	Baseline max n=114	Week 16 (end Phase 1) max n=114			Baseline Max n=46	Week 52 (end Phase 2) max n=46		
	Mean (SD)	Mean (SD)	n	p	Mean (SD)	Mean (SD)	n	p
Weight (kg)	97.47 (13.44)	88.52(12.40)	114	***	97.85 (13.70)	90.04 (14.02)	46	***
BMI	36.63 (3.79)	33.71 (3.62)	114	***	36.66 (3.82)	33.95 (4.07)	46	***
Systolic BP	140.41(17.77)	120.0 (12.96)	114	***	141.60 (21.12)	124.53 (13.81)	46	***
Diastolic BP	89.26 (9.19)	77.90 (8.99)	114	***	89.51 (9.57)	80.33 (9.18)	46	***
Fat Mass	46.43 (9.70)	39.76 (9.08)	85	***	47.34 (10.13)	42.01 (10.90)	46	***
LBM (kg)	49.16 (5.44)	47.26 (5.06)	85	***	49.70 (4.95)	48.03 (4.86)	46	***
RMR(kcal/24h)	1546 (244)	1510 (160)	80	0.094	1583 (155)	1536 (65)	46	***
Waist (cm)	104.9 (8.3)	98.69 (7.87)	80	***	104.2 (8.8)	99.7 (9.5)	46	***
Glucose(mmol/l)	4.96 (0.74)	5.13 (0.99)	85	0.011	4.93 (0.65)	5.08 (0.61)	45	0.086
Insulin (mu/l)	12.02 (5.75)	9.07 (4.18)	82	***	11.33 (6.32)	6.47 (3.67)	42	***
Ln(HOMA-IR)	0.922(0.419)	0.617(0.525)	82	***	0.868 (0.428)	0.213 (0.616)	42	***
Ln(HOMA-IS)	5.13 (0.62)	4.71 (0.56)	82	***	5.06 (0.59)	4.31 (0.66)	42	***
Chol (mmol/l)	5.59 (1.05)	4.95 (0.98)	85	***	5.42 (0.98)	5.35 (1.08)	45	0.513
HDL(mmol/l)	1.47 (0.32)	1.34 (0.24)	70	***	1.38 (0.30)	1.49 (0.39)	38	0.029
LDL(mmol/l)	3.59 (0.89)	3.21 (0.76)	70	***	3.55 (0.75)	3.51 (0.80)	38	0.673
TG(mmol/l)	1.50 (0.78)	1.21 (0.76)	85	***	1.40 (0.66)	1.13 (0.47)	45	**

Total number of patients at baseline=150; week 16=114; 1 year =46. Exact numbers available for analysis varies according to data availability. *** $p < 0.001$; ** $p < 0.01$

Table 3:
Ordinal regression to predict probability of continuation beyond 10 or 16 weeks (n=150).

measure	Regression coefficient	P value
Age (years)	0.0402	0.037
Waist (cm)	-0.0673	0.009
BMI	0.1203	0.052

Table 4: Correlations of baseline measures with subsequent weight loss after partialling out initial weight*

	weight loss week 16	weight loss year 1
SYSBP	-.223 (n=114) P= .018	-.195 (n= 46) P= .199
DIASBP	-.129 (n=114) P= .172	-.225 (n= 46) P= .138
Ln(HOMA)	.030 (n=114) P= .754	.065 (n= 46) P= .637
GLUC†	.067 (n=114) P= .476	.001 (n= 46) P= .995
INSUL	-.036 (n=114) P= .707	.159 (n= 46) P= .269
CHOL†	.099 (n=114) P= .293	-.367 (n= 46) P= .012
HDL	-.033 (n=104) P= .742	-.310 (n= 40) P= .054
TG	.093 (n=114) P= .328	-.249 (n= 46) P= .099

* mean of screening and week 0 weights used for this

† Glucose and Cholesterol did not correlate with initial weight hence their correlations were not adjusted for this.

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