

# Compliance, clinical effects, and factors predicting weight reduction during a very low calorie diet regime

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*Objective* – To study compliance, clinical effects, and factors predicting weight reduction in obese patients treated with a very low calorie diet (VLCD) regime.

*Setting* – A general practice in Oslo, Norway.

*Subjects* – 253 obese volunteers, aged 15–72, with a mean body mass index (BMI) of 33.4 (25–51) kg/m<sup>2</sup>.

*Design* – Open, non-comparative trial. Patients used a VLCD for eight consecutive weeks to achieve weight loss. The following were recorded every second week: weight, blood pressure, anthropometric measurements, compliance, side-effects, and patient acceptability. Blood parameters were tested before and after the trial.

*Results* – VAS-measurements showed that patients found it easy to comply with treatment, and 87.0% completed the study. Mean weight loss was 13.2 (2–33) kg. Blood pressure, serum lipids, and anthropometric measurements were significantly reduced. Side-effects were few and occurred mainly during the first two weeks of the trial. Main factors predicting weight reduction were gender, initial weight, initial BMI, and age. There was no correlation between weight loss and duration of obesity or reported number of weight reduction attempts. By VAS-measurements good acceptability of satiety and taste was recorded, and patients reported improved physical fitness and better quality of life after weight reduction.

*Key words:* compliance, weight reduction, VLCD, BMI, LBM, obesity.

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Obesity is a considerable contributing factor to morbidity and mortality (1), and its prevalence in Western countries is increasing (2). Very low calorie diets (VLCD) are a compromise between therapeutic starvation, with its unwanted medical effects (3), and conventional low calorie diets, which, even when prescribed by health professionals, have a poor success rate (4,5). The first commercialized VLCD in the United States during the mid-1970s and onwards were nutritionally deficient and even led to deaths after prolonged

use (6). Because of dangers concerning these liquid protein diets, VLCD in general got a bad reputation, with health professionals and with the public, which led to a focus on safety by most of the research in the 1980s. Modern high quality VLCD are today regarded as safe (7). The VLCD used in the present study has been reported to give 75% fat loss and 25% reduction of lean body mass (LBM) (8), which is regarded as satisfactory.

What has been poorly documented is patient

acceptance of VLCD regimes. Drop-out rates of one third to one half are reported (9,10). The objective of the present study was to evaluate compliance and clinical effects, and to determine factors that might predict variation of weight loss during a VLCD treatment.

## Material and methods

Two hundred and fifty three patients were studied, 152 female and 101 male, aged 15–72 years (median 41.6). Their body weight ranged from 70–157 kg (median 99.7), and BMI from 25–51 kg/m<sup>2</sup> (median 33.2). All the patients were self selected after reading about a new VLCD in newspapers or weekly magazines. They used the regime for eight weeks, while continuing to work in their usual jobs. Patients were recommended to avoid alcohol during treatment. No subject's participation was rejected because of other concurrent diseases.

### Protocol

The study was performed as an open non-comparative trial. The VLCD (Nutrilett; Nycomed Pharma, Norway) was given 5 times a day, providing a total of 430 kcal (1800 kJ)/day, and containing 61.5 g high quality protein, 30.5 g carbohydrate, 6 g vegetable fat, and 17.5 g fibre. The subjects also received a daily fish oil capsule containing essential omega-3 fatty acids (EPA, DHA) (11), and a daily tablet containing Nordic Recommended Daily Allowances (RDA) (12) of the vitamins, minerals, and trace elements that did not occur sufficiently in the nutrition powder. In addition to the liquid diet, patients were told the importance of drinking at least 1–1.5 litres per day of low calorie liquids, and they were allowed to eat small amounts of vegetables.

### Ethics

The study was performed in accordance with the Helsinki II declaration, and informed written consent was obtained from all patients. The regional ethics committee had no objections to the trial.

### Measurements

Weight, blood pressure, and anthropometric measurements of waist, hip, thigh and upper arm

were recorded every second week. Based on results from the first half of the study, questionnaires were systematized for the second group of patients (n=140). Compliance and patient acceptability regarding satisfaction with weight reduction, feeling of hunger, and judgement of taste, were measured using a 10 cm visual analogue scale (VAS-scores). A score close to 0 or 10 would indicate a worse or better value, respectively. Concerning side-effects, patients were specifically asked about dryness of mouth, bad breath, breathing difficulty, fatigue and lethargy, abdominal pain, borborygmus, headache, and if they had other complaints. VAS-measurement for quality of life and physical fitness were recorded at the end of the study, as a comparison with pre-trial measurements.

The following laboratory tests were carried out at the beginning and end of the study: urine testing for blood, glucose, and protein; and blood analyses, which comprised: total-cholesterol, HDL-cholesterol, triglycerides, glucose, creatine, uric acid, ALAT, ASAT, gamma-GT, alkaline phosphatase, potassium, manganese, sodium, chloride, total protein, albumin, haemoglobin, haematocrit, red blood cells, white blood cells, thrombocytes, SR, MCV, MCH, MCHC. Blood tests were all taken non-fasting.

### Drop-outs

Thirty three patients (13.0%), 18 female and 15 male, did not complete the treatment. Ten patients dropped out because of travelling, four due to treatment for other diseases, four because of other personal reasons, and 15 persons failed to attend the consultation without giving any cause. Females in the drop-out group had a mean weight reduction of 6.6 kg, and males 8.8 kg, equivalent to 83.5% and 75.2% of the weight loss after 4 weeks of the rest of the group, respectively; the drop-out was therefore not caused by lack of efficacy of the VLCD. Drop-out populations of females and males did not differ significantly from the populations that concluded the study, with respect to body composition or blood analyses.

### Statistical analyses

A two-tailed Wilcoxon signed-rank test was applied for mean changes from before to after treat-

ment. Correlations were calculated using Pearson's correlation coefficient. A multiple regression analysis was used to determine the effects of factors predicting variation in weight reduction. A 5% significance level was used for each significance testing. VAS measurements are given with one standard error of the mean (S.E.M.)

## Results

Patients reported ease of complying with the VLCD treatment (VAS mean score  $7.2 \pm 0.23$ ), and 87.0% of patients completed the eight-week course. Table I shows reductions in weight, BMI, blood pressure, and anthropometric measurements during VLCD treatment. Mean weight loss was 13.2 kg; females losing 11.1 kg, and males 16.6 kg. Mean BMI was reduced by  $4.4 \text{ kg/m}^2$ . Weight loss during the first two weeks of the study was larger than during the following weeks (Figure 1), and the difference between sexes was significant ( $p < 0.001$ ). The distribution of weight loss varied considerably, partly caused by intake of other foods by some patients (Figure 2).

Reductions in systolic and diastolic blood pressures were significant ( $p < 0.001$ ) and occurred during the first two weeks of the study. Anthropo-

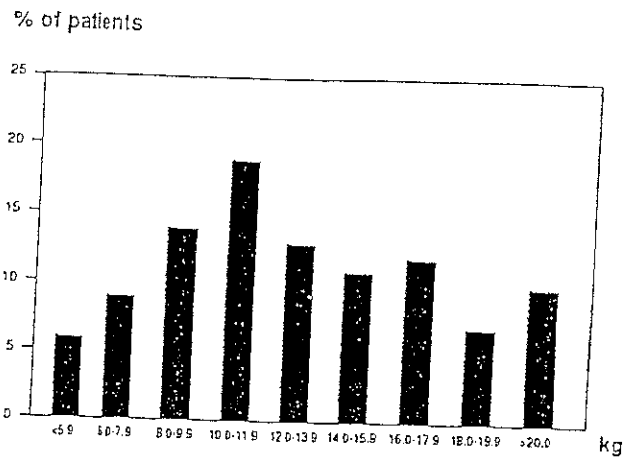


Figure 2. Distribution of weight reduction (n=220).

metric measurements were significantly reduced. Waist circumference was the only measurement that was reduced significantly more in males ( $p = 0.003$ ).

Blood lipids were all reduced significantly (Table II). Blood glucose level was lowered, one of the liver function tests, Gamma-GT, was reduced by nearly one third, and there was a slight rise in uric acid. The mean values of all the other blood tests were within normal limits, both before and after the study; in particular, there were no major changes in protein or electrolyte tests, including serum potassium. Analyses taken during the second half of the study showed that there were fewer patients with blood, glucose, and protein in the urine after weight reduction (Table II).

Side-effects were mainly mild, reported to be worst during the first two weeks of the trial. Fatigue and lethargy were reported by 16.4% of the patients before the study started, increasing to 25.5% in week two, and decreasing to 2.2% after eight weeks of treatment. Mouth dryness and bad breath also diminished after the two first weeks of the trial (Figure 39). Several symptoms were reduced during the VLCD regime (Table III). Surprisingly, and contrary to what was expected on the very restricted energy and food intake,

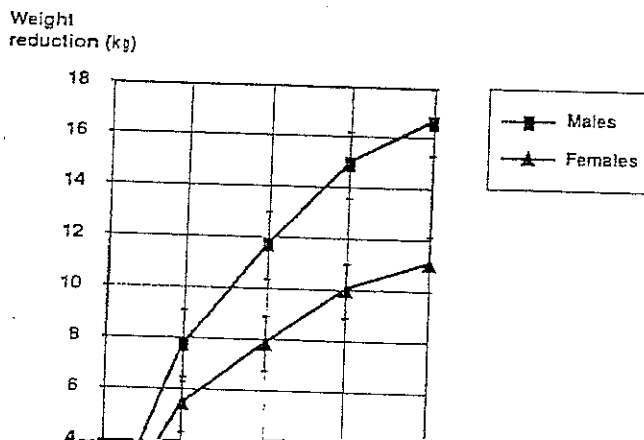


Table 1. Body weight, body mass index, blood pressure, and anthropometric measurements during the VLCD programme.

	Week		Reduction	
	0	8	0-8	%
<b>Body Weight (kg)</b>				
Total (n = 220)	99.7 ± 1.1 (70 - 157)	86.5 ± 0.9 (61 - 150)	13.2 ± 0.3* (2 - 33)	13.2
Females (n = 134)	92.8 ± 1.2 (70 - 157)	81.7 ± 1.1 (61 - 150)	11.1 ± 0.3* (2 - 20)	12.0
Males (n = 86)	110.5 ± 1.4 (84 - 150)	93.9 ± 1.3 (73 - 133)	16.6 ± 0.5* (5 - 33)	15.0
<b>Body Mass Index (BMI) (kg/m<sup>2</sup>)</b>				
Total (n = 218)	33.4 ± 0.3 (25 - 51)	29.0 ± 0.3 (21 - 49)	4.4 ± 0.1* (1 - 11)	13.2
Females (n = 134)	33.2 ± 0.4 (25 - 51)	29.3 ± 0.4 (21 - 49)	3.9 ± 0.1* (1 - 7)	11.8
Males (n = 84)	33.7 ± 0.4 (27 - 43)	28.6 ± 0.4 (22 - 38)	5.1 ± 0.1* (2 - 11)	15.1
<b>Systolic Blood Pressure (mmHg)</b>				
Total (n = 191)	141.1 ± 1.2 (100 - 186)	130.2 ± 1.0 (98 - 177)	10.9 ± 1.1* (-30 - 50)	7.7
Females (n = 113)	138.0 ± 1.5 (100 - 186)	129.0 ± 1.1 (98 - 155)	9.0 ± 1.4* (-30 - 40)	6.5
Males (n = 78)	145.7 ± 1.8 (111 - 186)	132.0 ± 1.7 (100 - 177)	13.7 ± 1.7* (-24 - 50)	9.4
<b>Diastolic Blood Pressure (mmHg)</b>				
Total (n = 191)	87.5 ± 0.7 (65 - 114)	80.6 ± 0.6 (60 - 106)	6.9 ± 0.6* (-16 - 25)	7.9
Females (n = 113)	85.3 ± 0.7 (68 - 106)	79.9 ± 0.7 (61 - 100)	5.4 ± 0.7* (-16 - 21)	6.3
Males (n = 78)	90.7 ± 1.1 (65 - 114)	81.6 ± 1.0 (60 - 106)	9.1 ± 1.0* (-15 - 25)	10.0
<b>Anthropometric Circumferences (cm)</b>				
Waist (n = 129)	109.0 ± 1.0 (80 - 140)	96.6 ± 0.9 (72 - 129)	12.4 ± 0.5* (1 - 43)	11.4
Hip (n = 128)	115.6 ± 0.9 (94 - 160)	106.1 ± 0.9 (87 - 155)	9.5 ± 0.4* (0 - 32)	8.2
Thigh (n = 127)	67.7 ± 0.6 (54 - 89)	61.3 ± 0.5 (49 - 74)	6.1 ± 0.3* (0 - 25)	9.0
Upper Arm (n = 128)	35.9 ± 0.3 (28 - 46)	32.8 ± 0.3 (27 - 44)	3.1 ± 0.1* (0 - 9)	8.6

Results are mean ± s.e.m. The range of values obtained is given in parentheses

\*P<0.001

(mean score  $8.2 \pm 0.18$ ) and improved physical fitness (mean score  $7.8 \pm 0.17$ ), than before the study.

Multiple regression analysis indicated that factors contributing significantly to weight reduction were gender (males more than females;  $r=-0.23$ ,  $p<0.001$ ), initial weight ( $r=0.47$ ,  $p<0.001$ ), initial BMI ( $r=0.23$ ,  $p=0.007$ ), and age ( $r=-0.21$ ,

$p<0.001$ ). These factors accounted for 37.0% of the variation in weight reduction.

Relative body weight reduction was significantly lower in females (12.0%) than in males (15.0%) ( $p<0.001$ ). No correlation was found between weight loss and duration of obesity ( $r=-0.21$ ,  $p=0.53$ ), or between weight loss and number of weight reduction attempts ( $r=-0.16$ ,  $p=0.08$ ).

Table II. Significant changes of laboratory tests during the VLCD programme

	Week		Difference	
	0	8	0-8	%
<b>Blood analysis</b>				
Total Cholesterol (mmol/l) (n = 220)	6.0 ± 0.09 (3.1 - 11.7)	4.8 ± 0.08 (2.2 - 9.3)	1.2 ± 0.08* (-2.2 - 6.0)	-20.0
HDL Cholesterol (mmol/l) (n = 198)	1.4 ± 0.03 (0.6 - 2.7)	1.2 ± 0.02 (0.5 - 2.4)	0.2 ± 0.02* (-0.6 - 0.9)	-14.3
Triglycerides (mmol/l) (n = 195)	3.1 ± 0.69 (0.6 - 13.6)	1.2 ± 0.04 (0.5 - 5.1)	1.9 ± 0.11* (-2.7 - 7.4)	-61.3
Glucose (mmol/l) (n = 219)	5.2 ± 0.10 (3.2 - 17.6)	4.9 ± 0.05 (3.3 - 7.7)	0.3 ± 0.11* (-22 - 13.4)	-5.8
Gamma - GT (U/l) (n = 220)	35.7 ± 1.76 (6.0 - 185.0)	25.4 ± 1.32 (6.0 - 165.0)	10.4 ± 1.38* (-68.0 - 98.0)	-28.9
Uric Acid (umol/l) (n = 219)	308.4 ± 6.75 (111.0 - 624.0)	330.1 ± 8.19 (95.0 - 1025.0)	-21.7 ± 7.63† (-530.0 - 284.0)	+ 6.7
<b>Urinary analysis</b> (Number of patients with positive findings)				
Glucose (n = 137)	4	2	2*	-50.0
Blood (n = 137)	12	9	3*	-25.0
Protein (n = 137)	4	3	1*	-25.0

Results are mean ± s.e.m. The range of values obtained is given in parentheses  
\*P<0.01 †P<0.05

Correlations between blood pressure reduction and weight loss showed that only the reduction in diastolic blood pressure and weight reduction was significant ( $r=0.27$ ,  $p=0.002$ ).

Mean duration of overweight was 39 months at the beginning of the study, and patients had tried on average three serious attempts to reduce their weight before the trial. Among other results, one woman diagnosed as infertile became pregnant after a 10 kg weight loss, three patients on antihyperglycaemic agents for diabetes II stopped medication, while one patient on insulin halved his dosage.

All patients continued their usual work while being on the diet.

## DISCUSSION

Few studies of VLCD have focused on compliance and drop-outs. Wadden et al. and Friedman reported drop-out rates varying from 33 to 50% (9,10). We have found only one study that discusses drop-out of patients using VLCD in general practice, which reported 51% drop-out in 443 patients using a VLCD for 4 weeks (13). In our study ease of compliance, few side-effects, and good acceptability resulted in fewer patients dropping out of the trial. Our positive results could partly be explained by high motivation of the patients, and partly by improved acceptability of the VLCD. A relatively high protein content of

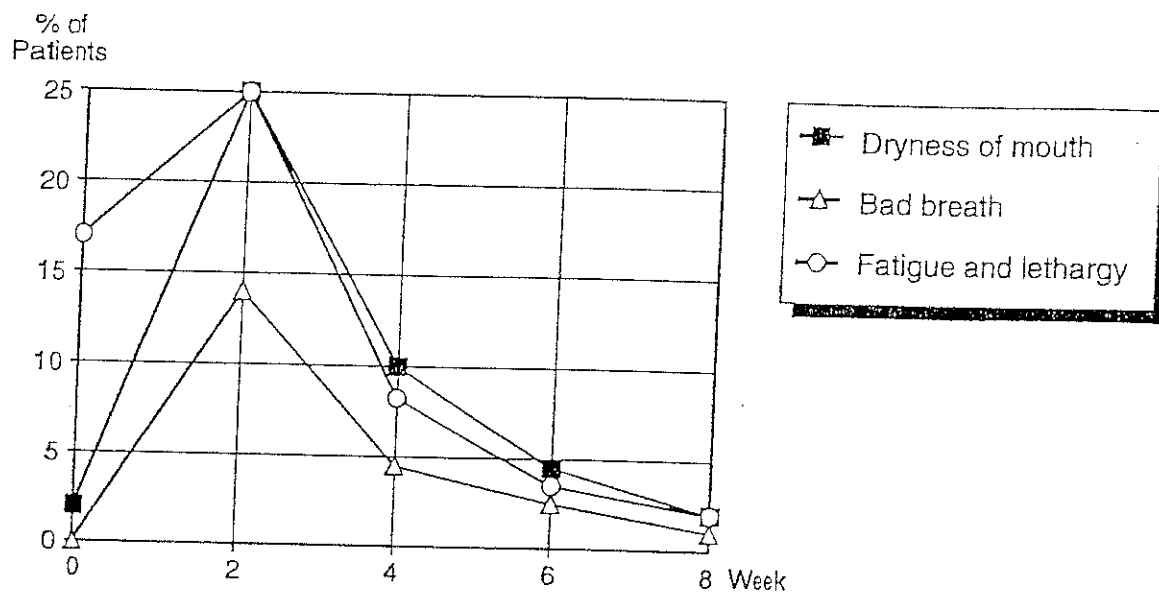


Figure 3. Reporting of side-effects during VLCD treatment (n=140).

the VLCD is necessary to preserve lean body mass (LBM) (14) and to diminish a feeling of hunger (15). A relatively low carbohydrate content diminishes intensity of ketosis and sodium loss (16). Satiety is achieved by frequent meals and fibre, apart from relatively high protein and low carbohydrate content. To compensate for the diet-induced thermogenesis, which diminishes when food intake is reduced (15), meals are taken approximately every three hours. Dietary fibre added to VLCD normalizes hunger and alleviates constipation (17). Fibre contained in the VLCD used in our study is derived mainly from soya

Table III. Reporting of symptoms during weight reduction (n=140).

	Number of patients with symptoms	
	Week 0	Week 8
Headache	31	3
Borborygmi	38	1
Myalgia and Muscular cramps	13	1
Abdominal pain	12	0
Constipation	6	0
Diarrhoea	3	0
Disturbed sleeping patterns	6	1
Lack of well-being	9	1

bean, which exerts a hypocholesterolaemic effect (18).

Weight reduction in our trial was similar to that found in other studies using VLCD (9). Initial rapid weight loss is partly caused by increased diuresis (16). Anthropometric measurements were reduced by nearly the same percentage, suggesting that weight loss is evenly distributed. The somewhat greater reduction of waist circumference than other anthropometric parameters may be caused by a lowering of the volume of the intestinal contents by the VLCD.

Medical benefits of VLCD, lowering blood pressure (19), reducing blood lipids (20) and blood glucose (21), are well documented in the literature. Because glucose is lowered substantially during the first week of treatment in diabetic patients (9,21), these patients were recommended to control their glucose level regularly. Uric acid increased only moderately in our study, as expected (4). Mean reduction of Gamma-GT by nearly one third may be explained by knowing that liver pathology, mainly steatosis, is common in the obese (22), and that patients were told to avoid alcohol during the weight reduction programme. The pregnancy of the "infertile" women after a 10kg weight loss may be coincidental, but it is known that obesity is associated with decreased fertility (23).

Obesity is related to higher resting metabolic

rate (RMR), caused by more lean body mass (LBM) (4,8). Gender prediction of the amount of weight reduction probably reflects females' lower initial weight and LBM than males. Our finding that relative body weight reduction was significantly lower in females than in males has been contradicted in other studies showing women reducing their initial weight by the same percentage as men (24).

Between the ages of 20 and 50, fat content increases by approximately 50% in females and 100% in males (2). This is accounted for by a reduction of LBM, and by an increase in body weight, which however only rises by 10 to 15 per cent (2). Since LBM is a more metabolically active tissue (15), the metabolic rate will diminish with age, which may explain our finding of decreasing weight reduction with increasing age. Other researchers have not found this coherence (13). Higher initial weight, or BMI, which corresponds to more LBM, has been found to increase weight loss (9), which we also found.

In our study there was a considerable variation among patients regarding duration of being overweight, and of the number of weight reduction attempts prior to the trial. These factors has however no effect on the amount of weight loss. Cycles of weight loss and regain that did not reduce RMR or increase body fat have also been documented in other trials (25, 26). There is a need to carry out follow-up studies to determine the long-term outcome of weight reduction by the VLCD regime used in our trial.

We observed excellent compliance, and reduction of risk factors and associated ailments of obesity during VLCD treatment. Our findings suggest that treatment of obese patients with VLCD may well be performed in general practice outside specialist clinics, which is of importance considering how widespread obesity is. We suggest that general practitioners should devote more time to treating this major health problem, with the aim of avoiding the development of other concurrent diseases.

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