Norges Teknisk-Naturvitenskapelige Universitet

# Impact of speed of weight loss on body composition, resting metabolic rate and exercise efficiency

Master thesis in Clinical Health Science – Obesity and Health

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Trondheim, May 2014

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# Acknowledgement

Throughout this past year I have learned several new things about myself, the use of equipment and about the research process. It has, at times, been very challenging, and I could not have done it without the exceptional help I received.

First of all I am very grateful to my supervisor, Catia Martins, for her indispensable guidance, dedication of time and valuable advice throughout the entire process. I am also very thankful to Silvia dos Santos Ribeiro F. Coutinho for practical help and good advice every day of the project. I am very grateful! I would also like to give a sincere thanks to Turid Follestad for taking the time to help me with the statistics.

Moreover, I would like to thank my coworkers at the lab: Jeanette Jørgensen, Linn Christin Torgersen, Hege Tevik Bjøru, Sissel Salater, Linn Bøhler og Marie Flataas. We have been a very good team, and I really appreciate all of you. Thanks to all the participants who showed great patience, and took the time to participate in the project. It would not have been possible to conduct this project without you!

Last, but not least, I want to thank my friend Emilie Aamodt for proofreading, and my boyfriend Fredrik Rålm, family and friends for all the support and encouraging words throughout this year. Thank you!

Trondheim, May 2014

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# Abbreviations

FFM: Fat free mass

FM: Fat mass

WL: Weight loss

BW: Body weight

RMR: Resting metabolic rate

RQ: Respiratory quotient

ExEff: Exercise efficiency

PA: Physical activity

VLCD: Very low calorie diet

LCD: Low calorie diet

NREE: Non resting energy expenditure

GME: Gross mechanical efficiency

RCT: Randomized clinical trial

# Abstract

**Background:** There is a common belief that losing weight fast leads to a greater loss of fat free mass (FFM) and larger reduction in resting metabolic rate (RMR) compared with more gradual weight reduction. Unfortunately, well-designed studies in this area are lacking.

**Purpose:** The primary aim of this study was to determine if a similar weight loss (WL) achieved fast versus gradually induces the same changes in body composition, more specifically regarding the loss of FFM. Secondary aims were to assess if speed of WL has an impact on RMR and exercise efficiency (ExEff).

**Material and method:** 35 sedentary, healthy obese (BMI ≥30kg/m$^2$) adults (18-55 year old) were randomized to lose 9-10 % of their baseline weight rapidly (very low-calorie diet (VLCD) for 4 weeks) or gradually (low-calorie diet (LCD) for 8 weeks). Body composition (fat mass (FM) and FFM), RMR, respiratory quotient (RQ) and ExEff (at 10, 25 and 50W) were measured before and after the intervention.

**Results:** A significant reduction in body weight (ca. -9%), FM (kg and %) FFM (kg) and RQ and an increase in FFM (%) were observed over time, with no significant differences between groups. A significant reduction in RMR was observed in the fast WL group (-129±118, $P<0.0001$, but not in the gradual WL group (-24±136, $P<0.05$), and difference between groups were significant ($P<0.05$), even after adjusting for loss of FFM and RMR at baseline ($P<0.01$). A larger increase in ExEff at 10 and 25 W was observed in the rapid compared with the gradual WL group ($P<0.01$), and the difference were still evident after adjusting for absolute WL and ExEff at baseline ($P<0.01$).

**Conclusion:** This study does not support the general belief that rapid WL leads to a larger loss of FFM, but rapid WL seems to lead to a larger reduction in RMR, as well as a greater increase in ExEff at low intensity levels and a greater decrease in RQ (increase in fat oxidation). However, further research is needed in this area.


# Relevance

Obesity is an increasing problem worldwide, and it is, therefore, necessary to identify appropriate treatments, which can induce the best results in terms of long-term WL maintenance. This study will provide evidence regarding the speed of WL associated with the most favorable modifications in body composition, skeletal muscle efficiency and RMR. Changes in these variables are most likely to modulate long-term maintenance of a reduced body weight (BW).

# Background

Obesity has become a global epidemic worldwide (1) and Norway is no exception (2). Obesity is defined as large amounts of excess body fat accumulated in the body to the extent that it might adversely affect health (1). According to the World Health organization (WHO), 24 % of the adult population is overweight and 11 % obese, and the worldwide prevalence has more than doubled since the 1980s (1). The public health consequences and associated socio-economic costs are immense (3). Obesity is a risk factor for many chronic diseases such as; hypertension, dyslipidaemia, sleep-apnea, cancer, cardiovascular disease, non-alcoholic fatty liver disease, and type 2 diabetes (4, 5). A large amount of excess fat accumulated around the organs is also positively correlated with the Metabolic Syndrome (6). The good news amidst this alarming picture is that a WL between 5-10% of initial weight, if sustained, can have large health benefits for the obese patient (7). Lifestyle interventions involving diet, exercise and behaviour therapy should be the first line option in obesity treatment. However, for the morbid obese patient, more drastic treatment options such as bariatric surgery can also be used as a help to lose weight (5). Despite variable outcomes, lifestyle treatment of obesity can result in clinically significant WL (8). However, a large review from 2000, found that only 15% of those who go through a WL program seem to be able to maintain all of the WL for at least three years (9), while the majority will experience significant weight regain (10, 11).

An energy deficient of 500-1000 Kcal/day, giving a WL between 0.5-1 kg/week, is usually recommended as the best speed of WL for obese individuals undergoing conservative treatment (12-15). There is a common belief that losing weight rapidly leads to a greater loss of FFM (16) and a greater reduction of RMR (17). However, the reasons behind such believes are likely to be based on poor evidence (16, 18). A large review that has tried to identify the proportion of weight lost as FFM by various WL interventions, found that significantly more studies using VLCD reported loss of FFM above what they estimated to be the mean loss of FFM (27 % men, 20% woman), compared with studies using LCD (16). Sénéchal and colleges (2012) placed post-menopausal women through a WL intervention aiming at a weight reduction of at least 5 % of initial BW. They found that those who had a rapid WL (-5 % in 5 weeks) lost significantly more FFM and less FM, compared with those who had a slow WL (-5 % in 15 weeks) (18). However, the very small sample size is a major limitation of that study. So, despite the generalised assumption that rapid WL leads to increased loss of FFM and consequently a disproportional reduction in RMR, the evidence is inconclusive (15, 17,

19, 20) and limited by the fact that WL is not matched, meaning that a higher rate/speed of WL is usually also associated with a larger overall weight reduction.

Another reason a slow rate of WL is recommended relates to WL maintenance. Studies claim that losing weight fast is detrimental because most the weight is regained afterwards (21). However, more recent studies have shown that losing weight fast, namely with VLCD, is associated with better WL maintenance in the long term, compared with losing weight gradually (22-27). Studies have also found that even though RMR decreases significantly with energy restriction, it does not predispose to weight regain if energy balance is restored after the WL intervention (28, 29), or if the decrease in RMR is compensated by elevated levels of daily physical activity (PA) (29). One study even found that a greater initial WL might provide a better WL maintenance, despite the reduction in FFM and RMR (23).

FFM contains highly metabolic active tissue, such as muscle and organs, and low metabolic bone and connective tissue (30), and is the most important determinant of RMR (31-33). RMR is defined as the rate of energy expenditure measured at rest, after an overnight fast (34), and is for most people, the largest determinant of total energy expenditure. However, other factors such as age (35, 36), sex (37) and genetic factors (36) have also been shown to have an impact on RMR. Given that FFM is the most important determinant of RMR, loss of FFM may aggravate the reduction in RMR observed with WL (4, 38), which could potentially slow the rate of WL and predispose to weight regain (4). Due to this potential reduction in RMR, it is very important to preserve as much FFM as possible under a WL program. Unfortunately, in most cases, there will also be some loss of FFM. The expected loss of FFM after a diet-induced WL is of approximately 25% (15, 39, 40). However, a high protein diet seems to help to preserve FFM when compared with a high carbohydrate diet (41). Moreover, studies report that diet restriction combined with intensive training programs is helpful in preserving FFM (38, 42). If speed of WL can modulate the loss of FFM and reduction in RMR observed with weight reduction remains a matter of debate.

As mentioned previously, changes in FFM have been found to have a significant effect on RMR, but also on non-resting energy expenditure ((NREE (non-exercise activity thermogenesis (NEAT) and activity-related energy expenditure) (43). Leibel and colleges (1995) found that, even after adjusting for FFM, NREE decreased by 15 % after a 10% WL (43). Studies have also found NREE to be the component of total energy expenditure most affected by weight change (43, 44). Moreover, studies report that the energy expended in

particular at low intensity levels of PA is lower than what could be explained by changes in body weight and composition after WL (45, 46). If the changes in NREE are permanent or a temporary response of weight reduction, it would be of interest regarding weight maintenance. Unfortunately, the literature is inconclusive. Leibel et al. study (1995) and Rosenbaum et al. study (2008 and 2003) found the changes in NREE and RMR were still evident, even after a period of WL maintenance (43-45). In contrast, Camps and collaborators (2013) found NREE returned to baseline levels (before WL), after a period of WL maintenance (47). Since the decline in NREE observed with WL, cannot be entirely explained by changes in body weight and composition, one explanation may be changes in skeletal muscle efficiency after WL (43).

Diet-induced WL has been shown to lead to a significant increase in ExEff (meaning a decrease in the energy spent for a given PA (same duration and intensity)), particularly at low intensity levels (44). This is particularly relevant given that PA at low intensities (walking, recreational cycling) may be most representative of the PA patterns of sedentary obese adults. It has been suggested that the increase in skeletal muscle efficiency at low intensities of PA has an important role in mediating the reduction in exercise energy expenditure that occur with WL (44). This reduction in exercise-induced energy expenditure could increase the risk of weight regain, if not compensated by lowered energy intake or increased PA level. This may explain why exercise is a well-known success factor in the maintenance of a reduced body weight (43). Other compensatory mechanisms observed in the weight reduced state is an increased appetite (48, 49), and a reduction in fat oxidation (50).

The challenge of WL maintenance seems to be due to a combination of metabolic, behavioural, neuroendocrine and autonomic responses that oppose the maintenance of a reduced BW (51). Besides the behavioural and motivational factors, there are physiological mechanisms that try to restore energy balance and bring the BW back to its baseline. A combination of all these mechanisms is likely to explain why it is so difficult to maintain a reduced BW in the long term.

Given the lack of research on the impact of speed of WL on the mechanisms previously described, more studies in the area are needed. The knowledge generated would be of great value in designing WL interventions aiming at minimizing the loss of FFM, the reduction in RMR and the increase in exercise efficiency, for a more successful long-term WL management.

## Aims and hypothesis

The primary aim of this study was to determine if similar WL achieved fast versus gradually induces the same changes in body composition, more specifically regarding the loss of FFM. Secondary aims were to assess if rate of WL had an impact on RMR and ExEff.

The main hypothesis of this project was that a rapid WL leads to a similar loss of FFM, both in absolute (kg) and relative (%) terms, compared with gradual WL. It was also hypothesized that losing weight rapidly induces a similar reduction in RMR and ExEff as losing weight more gradually.

# Materials and methods

## Study design

Randomized clinical trial (RCT), in which participants were randomized to one of two intervention groups: (1) a rapid or (2) a gradual WL. Both interventions aimed at a WL of 9-10% of baseline weight. Groups were matched for age, gender ratio and BMI.

## Subjects

Obese healthy men and women, with a body-mass index (BMI) between 30 and 45kg/$m^2$ were recruited for this study through advertisement posted in the local newspaper and also on the Intranet at NTNU and St. Olavs Hospital. To participate, subjects had to be weight stable during the last three months (no more than ± 2kg), not currently dieting to lose weight and with an inactive lifestyle. Sedentary lifestyle was defined as not engaged in strenuous work or in regular brisk leisure time exercise more than once a week or in light exercise for more than 20 minutes/day in more than 3 times/week. Given that RMR has been shown to vary across the menstrual cycle in normally ovulating women (52), but not in those taking the contraceptive pill (53), only women taking hormonal contraceptives, with a regular menstrual cycle or post-menopausal were included in the study.

Subjects with history of endocrine/cardiovascular/pulmonary/kidney disease, lactose intolerance, anemia, gout and depression or other psychological disorders, eating disorders, drug or alcohol abuse within the last two years and current medication known to affect appetite or induce weight loss were excluded. Those with a planned surgery during the study period or participating in another research study were also not accepted to take part in this study.

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and was approved by the regional Ethics Committee (Midt Norge, Trondheim, Norway. REK nr. 2013/888). Written informed consent was obtained from all participants before enrolling in the study. The study was registered in clinicaltrial.gov under the number NCT01912742.

## Detailed protocol

The rapid WL group was asked to follow a VLCD for 4 weeks, while the gradual WL group was asked to follow a LCD for 8 weeks. All participants in both groups were asked not to change their PA levels.

The duration of the intervention, for both groups 1 and 2, was estimated using the Body Weight Simulator (54) aiming at a weight reduction of approximately 9-10% of baseline weight. As examples for this simulation, we used a 45-year old man, with a body weight of 100kg, a height of 175cm (32.7 $kg/m^2$) and a light physical activity level. Using a VLCD (660kcal/day) and a LCD (1500 kcal/day), 4 and 8 weeks of treatment would be needed in order to achieve a 9-10% loss of baseline weight, respectively. For a hypothetical woman, of similar age, weight, height and PA levels, using the gender-specific recommendation regarding VLCD (550kcal/day) and LCD (1200kcal/day), a similar duration would be needed in order to induce a 9-10% loss of baseline weight.

At the end of the WL phase all participants were given an individual consultation with a nutritionist who prescribed individualized diet plans aiming at weight stabilization.
Before and after the intervention, the following assessments were performed:

- Anthropometric measurements (weight and height) using standard procedures;
- Body composition using air displacement plethysmography (BodPod);
- RMR using indirect calorimetry;
- RQ using indirect calorimetry;
- ExEff in a graded ergometer cycle, using indirect calorimetry.

## Dietary intervention

The rapid WL group followed a commercial VLCD (Allevo, Cederroth, Sweeden) for 4 weeks (table 1). The participants randomized to this group followed a 550 Kcal/day (women) – 660 Kcal/day (men) diet. The VLCD products from Allevo provide 110kcal/pack and include a variety of shakes, smoothies and soups. In addition to VLCD products, the subjects were allowed to eat some low-starch vegetables (maximum 100 gram/day): cauliflower, broccoli, tomato, cucumber, cabbage, eggplant, peppers, lettuce, celery, spinach, radishes, mushrooms, leek, and squash.

Table 1: Dietary plan for the VLCD group.

| **Meal** | **Women** | **Men** |
|---|---|---|
| Breakfast | 1 Shake | 1 Shake |
| Lunch | 1 Soup<br>+<br>Max 50g of low-starch vegetables | 1 Soup<br>+<br>Max. 50g of low-starch vegetables |
| Snack | 1 Shake | 1 Shake |
| Diner | 1 Soup<br>+<br>Max 50g of low-starch vegetables | 1 Soup<br>+<br>1 Shake<br>+<br>Max 50g of low-starch vegetables |
| Snack | 1 Shake | 1 Shake |

The slow WL group followed a LCD for 8 weeks: women: 1200 kcal/day, men: 1500 kcal/day, using meal replacements (Allevo, Cederroth, Sweeden) (such as smoothies, milkshakes, soups and cereal bars) and conventional foods (table 2).

Table 2: Dietary plan for the LCD group.

| **Meal** | **Women** | **Men** |
|---|---|---|
| Breakfast | 1 Shake (Product) | 1 Shake (Product) |
| Lunch | 1 Soup (Product)<br>+<br>1 knekkebrød+<br><br>15g low fat cheese (9%) **or** 15g ham | 1 Soup (Product)<br>+<br>1 Cereal Bar (Product) |
| Snack | 1 Cereal Bar (Product) | 1 Cereal Bar (Product) |
| Diner | 200g of low fat fish **or** meat **or** 3 eggs<br>+<br>50g of cooked pasta/rice, **or** 80g of raw potatoes **or** 30g of bread<br>+<br>165g of low-starch vegetables (described above)<br>+<br>1 (medium size) fruit (pear, apple, orange, peach) | 250g of low fat fish **or** meat **or** 3 eggs<br>+<br>50g of cooked pasta/rice, **or** 80g of raw potatoes **or** 30g of bread<br>+<br>165g of low-starch vegetables (described above)<br>+<br>1 (medium size) fruit (pear, apple, orange, peach) |
| Snack | 200ml of low fat milk (0,1%) **or** 125g of law-fat yoghurt<br>+<br>1 knekkebrød<br>+<br>1 15g low fat cheese (9%) **or** 15g ham | 200ml of low fat milk (0,1%) **or** 125g of law-fat yoghurt<br>+<br>2 knekkebrød<br>+<br>1 45g low fat cheese (9%) **or** 45g ham |

In both groups, the participants were allowed to have calorie-free drinks (coffee, tea), some diet soda (maximum 0.5 L/day), and were advised to drink at least 2.5 liters of water. The LCD was designed to match the macronutrient composition of the VLCD: 38.9% of the energy from protein, 16.4% from fat, 40% from carbohydrates, 5.9% from fiber and 0% from alcohol.

## Variables measured

### Anthropometric measurements

Height and body weight were measured with the Seca 217 altimeter (Hamburg, Germany) and Seca 877 scale (Hamburg, Germany) in the morning, after 10 hours of fasting.

### Body composition

Body composition was measured using air-displacement plethysmograph (Bod Pod, Life Measurement, Inc., Concord, CA, USA). The machine and weight scale were calibrated every morning. All subjects were tested in the morning, after 10 hours of fasting, only wearing underwear and a Lycra swim cap. They were also asked to take of all jewelry before the test.

### Resting metabolic rate and Respiratory Quotient

RMR was measured for at least 15 minutes by indirect calorimetry (Vmax Encore 29N, Care Fusion, Germany). All participants were measured in the morning, after a 10-hour overnight fast and in a supine position. During the 10-hour of fasting, the participants were asked not to smoke or drink anything except water (55). The participants were asked to sit on a chair/bench upon arrival for at least 10 minutes and after that they had to lie down on a bench. A canopy was then placed around the head and oxygen uptake ($VO_2$) and carbon dioxide ($VCO_2$) production measured continuously for at least 15 minutes, or as long as needed to obtain at least 5 minutes of stabile data. The first five minutes were always excluded from the calculations, and RMR (kcal/day) and RQ were derived by taking an average of at least 5 minutes of stabile data (55).

### Exercise efficiency

ExEff was measured in a graded cycle ergometer (Monark, Eromedic 839E, GIH, Sweeden). Approximately three hours before this test, participants were placed in a waiting room, served a standard breakfast (approximately 600kcal; macronutrient distribution: 48% carbohydrates, 17% protein, 35% fat), and asked not to drink anything besides water, not to smoke or to be active. The participants started the test with a period of light cycling to get used to the equipment. After a period of accommodation, the participants pedaled at 60 rpm against

graded resistance to generate 10, 25 and 50 Watt of power in sequential 4-min intervals. $VO_2$ consumption, $VCO_2$ production and RQ were measured continuously using a metabolic cart (Vmax Encore 29N, CareFusion, Germany). Exercise efficiency was expressed as gross mechanical efficiency (GME), which is defined as power output (PO)/PI ((kcal/min, 1W=0,01433kcal/min)/ (VO2-average VO2 during steady state period (lasts 2 minutes of each stage) times the oxygen equivalent)) (44).

## Measures of compliance

### Armbands

To check for compliance regarding maintenance of PA levels, participants were asked to use Sense Wear armbands (BodyMedia, Inc., Pittsburg. PA, USA) for one week, before the start of the study and again at week 4 (group 1) and 8 (group 2). The Sense Wear armband collects information through multiple sensors, including a two-axis accelerometer and sensors measuring heat flux, galvanic skin response, skin temperature and near body ambient temperature (56). The minimal criteria for data analysis were 4 days of complete data collection; 3 weekdays and 1 weekend day. The following variables were analyzed: time spent on sedentary, light, moderate, vigorous and very vigorous activities and steps/day. The following cut points for the different activity levels were used: Sedentary <2.0 MET, Light activity 2.0-3.0 MET, Moderate activity 3.0-6.0 MET and Vigorous to Very vigorous activity >6.0 MET (56, 57).

### Weekly follow ups

To facilitate compliance with the program, participants were asked to keep daily food records and were scheduled for weekly visits for weighing and diet follow up with the nutritionist. For the gradual WL group the food diaries for week 2, 6 and 8 were analyzed and for the fast WL group the food diaries from week 2 and 4 were analyzed. The program “Mat på data” version 5.1 (Mattilsynet og Helsedirektoratet, Norway), was used to analyse the food diaries.

In the fast WL group, the adherence to the diet was also evaluated each week through assessment of urine acetoacetic acid concentration (mmol/L) using Ketostix reagent strips (Bayer, Basel, Switzerland). Participants with urinary ketone concentrations ≤1.5 mmol/L, indicative of negative or trace values were educated as to the appropriate dietary protocol. If a participant had negative ketone concentrations more than once, he/she was excluded from the analysis.

## Power calculation

This study was part of a larger RCT aiming at assessing the impact of speed of WL on several compensatory mechanisms, both at the level of energy intake and energy expenditure, activated with weight reduction. A power calculation was performed based on expected differences in postprandial release of GLP-1 between groups. A sample size of 12 participants would be needed to detect a difference of 4pM x hour/L in the postprandial AUC (area under the curve) for GLP-1 between the two intervention groups, assuming a standard deviation for this variable of 2 pM x h, at a power of 80%, and a significance level of 5%. However, to allow for a predicted dropout rate of around 25% a sample size of 15 participants/group would be necessary.

Given that the main aim of this study was to assess the impact of speed of WL on body composition, another power calculation was performed *a posteriori* based on expected differences in the loss of FFM between groups (18). Since the study of Sénéchal (2012) was designed to induce a WL of 5 %, and not 9-10 % as in our study, we extrapolated the minimal detectable difference from 2.5 to 5kg. With a minimal detectable difference between groups of 5 ± 6.8 kg of FFM, a power of 0.8 and a significant level of 0.05, a total of 62 (31/group) participants would be needed.

## Statistical analysis

Data was analysed using SPSS version 21 (SPSS Inc., Chicago, IL). To check for normality, the Kolmogorov-Smirnov test was used, together with visual inspection of normal Q/Q plots and Box Plot. Results are expressed as mean ±S.D and significance level was set at $P<0.05$, unless otherwise stated.

Differences between groups at baseline were assessed using independent sample T-test (for normally distributed variables) and Mann-Whitney U test (for not normally distributed variables). To check for changes over time, within each group, paired-sample T-tests and Wilcoxon matched-pair signed-rank test were used, as appropriate. To look at changes overtime (from baseline to end) between groups, independent sample T-test or Mann-Whitney U-test, have been used. ANCOVA test was used to look at differences in RMR and ExEff between groups at the end, using baseline data (RMR and ExEff, respectively) and changes in FFM and body weight, respectively, as covariates.

# Results

## Study participants

Thirty-five subjects entered this study; eighteen were randomized to the fast WL group and seventeen to the gradual WL group. One participant had to withdraw because of illness and one because of personal reasons (see flowchart in attachment 4). This happened one week after baseline testing. The remaining 33 participants completed the study (17 in the fast WL group, 16 in the gradual WL group). The baseline characteristics of all participants who completed the intervention can be seen in table 3.

Table 3: Baseline characteristics of the participants

| | All | Fast | Gradual | P value |
|---|---|---|---|---|
| **Age (years)** | 39.3 ± 9.7 | 42.2 ± 10.0 | 36.2 ± 8.7 | NS |
| **Gender ratio (women:men)** | 24:9 | 14:3 | 10:6 | NS |
| **Body weight (kg)** | 97.9 ± 12.0 | 96.6 ± 12.2 | 99.4 ± 12.1 | NS |
| **BMI (kg/m$^2$)** | 33.5 ± 2.8 | 33.4 ± 3.0 | 33.5 ± 2.6 | NS |

Values are presented as mean +/-SD.
P value for the comparison between intervention groups.

At baseline, there were no significant differences in age, gender ratio, body weight or BMI between the fast and gradual WL group.

## Compliance with the intervention

### Ketone bodies

Throughout the 4-week intervention period for the fast WL group, there were two different participants who had negative ketone bodies in the urine at one time point.

### Macronutrient composition of the diet

The macronutrient composition of the VLCD and LCD can be seen on table 4.

Table 4: Macronutrient composition of the diets in the fast and gradual WL groups

| | Fast, VLCD | | | Gradual, LCD | | | P value* | P value** | P value*** |
|---|---|---|---|---|---|---|---|---|---|
| | All | Women (n=14) | Men (n=3) | All | Women (n=10) | Men (n=6) | | | |
| **Energy (kcal/day)** | 593.1 ± 45.1 | 573.4 ± 10.8 | 685.1 ± 11.2 | 1325.6 ± 124.1 | 1234.8 ± 27.5 | 1477 ± 29.2 | <0.001 | <0.001 | <0.05 |
| **Protein %** | 38.5 ± 0.4 | 38.6 ± 0.3 | 38.4 ± 0.6 | 36.9 ± 1.5 | 36.2 ± 1.0 | 38.0 ± 1.6 | <0.001 | <0.001 | NS |
| **Fat %** | 15.1 ± 0.9 | 14.9 ± 0.6 | 15.9 ± 1.8 | 17.9 ± 1.4 | 17.9 ± 1.3 | 17.9 ± 1.7 | <0.001 | <0.001 | NS |
| **CHO %** | 39.0 ± 0.5 | 39.1 ± 0.4 | 38.8 ± 0.9 | 41.3 ± 1.5 | 42.1 ± 0.9 | 39.9 ± 1.2 | <0.001 | <0.001 | NS |
| **Fiber %** | 6.0 ± 0.2 | 6.1 ± 0.2 | 6.0 ± 0.4 | 3.5 ± 0.2 | 3.4 ± 0.1 | 3.7 ± 0.1 | <0.001 | <0.001 | <0.05 |
| **Alcohol %** | 0 | 0 | 0 | 0.1 ± 0.3 | 0.1 ± 0.3 | 0.1 ± 0.4 | NS | NS | NS |

Values are presented as mean +/-SD
*P value for comparison between groups, with all participants included (men and women)
** P value for comparison between groups in women only
*** P value for comparison between groups in men only

There was a statistical significant difference in total energy intake and the macronutrient composition of the diet between groups, with the exception of alcohol. The intake of protein and fiber was significantly higher, and the intake of fat and CHO was significantly lower in the fast compared with the gradual WL group, both for all participants and women. Between men in the two groups, there were only significant differences in total energy intake and fiber.

### Physical activity level

Changes in physical activity levels overtime in the two groups can be seen in table 5.

Table 5: Physical activity levels overtime in the two intervention groups

| | VLCD (n=11) | | | LCD (n=14) | | | P value** |
|---|---|---|---|---|---|---|---|
| | **Baseline** | **End** | **P value*** | **Baseline** | **End** | **P value*** | |
| **Steps/day** | 6288 ± 2031 | 5996 ± 2492 | NS | 6425 ± 2640 | 5816 ± 2391 | NS | NS |
| **Sedentary (min)** | 1220 ± 128 | 1244 ± 95 | NS | 1230 ± 91 | 1208 ± 112 | NS | NS |
| **Light (min)** | 119 ± 62 | 132 ± 67 | NS | 116 ± 53 | 115 ± 66 | NS | NS |
| **Moderate (min)** | 55 ± 22 | 50 ± 26 | NS | 54 ± 22 | 45 ± 20 | NS | NS |
| **Vigorous- Very vigorous (min)** | 0.6 ± 1.8 | 0.2 ± 0.6 | NS | 0.4 ± 0.9 | 1.1 ± 1.7 | NS | NS |

Values are presented as mean +/-SD
*Change from baseline to end, within group
**Changes from baseline to end, between groups

No significant differences in activity levels (steps/day, time spent on sedentary/light/moderate/vigorous-very vigorous activities) were observed between the fast and gradual WL groups at baseline or end. Moreover, changes in PA levels overtime were not significantly different between groups.

## Body measurements

### Body composition

Changes in body weight and composition overtime in both groups can be seen in table 6.

Table 6: Changes in body composition overtime in the two intervention groups

| | Fast | | | | Gradual | | | | P value** |
|---|---|---|---|---|---|---|---|---|---|
| | **Baseline** | **End** | **Change** | **P value*** | **Baseline** | **End** | **Change** | **P value*** | |
| **Weight (kg)** | 96.6 ± 12.2 | 87.7 ± 11.5 | -8.9 ± 1.3 | <0.001 | 99.4 ± 12.1 | 90.1 ± 10.8 | -9.3 ± 2.1 | <0.001 | NS |
| **FM (kg)** | 42.8 ± 8.1 | 36.2 ± 8.4 | -6.6 ± 1.2 | <0.001 | 43.1 ± 6.2 | 35.6 ± 6.3 | -7.6 ± 1.7 | <0.001 | 0.07 |
| **FFM (kg)** | 53.7 ± 7.1 | 51.5 ± 6.5 | -2.2 ± 1.4 | <0.001 | 56.3 ± 9.0 | 54.5 ± 8.4 | -1.7 ± 1.1 | <0.001 | NS |
| **FM (%)** | 44.2 ± 4.7 | 40.9 ± 5.8 | -3.2 ± 1.6 | <0.001 | 43.6 ± 4.7 | 39.5 ± 5.4 | -4.0 ± 1.4 | <0.001 | NS |
| **FFM (%)** | 55.8 ± 4.7 | 59.1 ± 5.8 | 3.2 ± 1.6 | <0.001 | 56.5 ± 4.7 | 60.5 ± 5.4 | 4.0 ± 1.5 | <0.001 | NS |

Values are presented as mean +/-SD
*Change from baseline to end within group
**Changes from baseline to end between groups

Both the fast and the gradual WL group lost a significant amount of weight (-9%), FM (in kg and %) and FFM (kg), and increased their percentage of FFM (P<0.001). No significant differences were found between groups regarding the change in body weight, BMI, FM or FFM, but there was a tendency for the gradual WL group to lose more FM (in kg) than the fast WL group (P=0.07).

### RMR and RQ

Changes in RMR and RQ overtime in both groups can be seen in table 7.

Table 7: Resting metabolic rate and Respiratory Quotient overtime in the two intervention groups

| | Fast | | | | Gradual | | | | P value** |
|---|---|---|---|---|---|---|---|---|---|
| | Baseline | End | Change | P value* | Baseline | End | Change | P value* | |
| **RMR** (Kcal/day) | 1319± 179 | 1190± 131 | -129 ± 118 | <0.001 | 1359 ± 201 | 1335± 168 | -24 ± 136 | NS | <0.05 [A] |
| **RQ** | 0.85 ± 0.05 | 0.75± 0.03 | -0.1 ± 0.06 | <0.001 | 0.86 ± 0.05 | 0.81± 0.05 | -0.05 ± 0.08 | 0.01 | NS |

Values are presented as mean +/- SD
*Change from baseline to end within group
**Changes from baseline to end between groups.
[A] After adjusting for baseline RMR and changes in FFM, there continued to be a significant difference in RMR at the end between groups (p<0.01)

At baseline there were no significant differences between the two groups regarding RQ and RMR. Change over time, in RMR, between groups differed significantly (P<0.05). While RMR in the fast WL group decreased significantly over time (P <0.001), RMR of the subjects in the gradual WL group showed no significant change. Differences at the end between groups were still significant after adjusting for baseline RMR and loss of FFM (P <0.01). Both groups experienced a significant decrease in RQ (P <0.001 fast, P <0.01 gradual), but differences between groups were not significant.

### Exercise efficiency

Average GME at 10, 25 and 50 Watt at baseline and end in both intervention groups, and changes over time are presented in table 8.

Table 8: Exercise efficiency overtime in the two groups

| | Fast | | | | Gradual | | | | P value** |
|---|---|---|---|---|---|---|---|---|---|
| | Baseline | End | Change | P value* | Baseline | End | Change | P value* | |
| **GME at 10W** | 0.059 ± 0.01 | 0.068 ± 0.02 | 0.01 ± 0.01 | <0.001 | 0.058 ± 0.01 | 0.057 ± 0.01 | -0.00 ± 0.01 | NS | <0.01 [A] |
| **GME at 25W** | 0.115 ± 0.02 | 0.123 ± 0.02 | 0.01 ± 0.01 | <0.01 | 0.120 ± 0.01 | 0.112 ± 0.02 | -0.01 ± 0.02 | NS | <0.01 [A] |
| **GME at 50W** | 0.161 ± 0.02 | 0.163 ± 0.02 | 0.00 ± 0.01 | NS | 0.165 ± 0.02 | 0.160 ± 0.02 | -0.00 ± 0.02 | NS | NS [B] |

Values are presented as mean +/- SD
*Change from baseline to end within group
**Changes from baseline to end between groups
[A] After adjusting for ExEff at baseline and absolute loss of BW, there continued to be a significant difference in ExEff at 10 and 25W at the end between groups (P 0.01)
[B] After adjusting for ExEff at baseline and absolute loss of BW, there continued to be no significant difference in ExEff at 50W at the end between groups.

At baseline there were no statistical significant differences between the groups in ExEff at 10, 25 or 50 Watts of power. Over time, participants in the gradual WL group did not change their ExEff at either of the resistance levels, while subjects in the fast WL group significantly increased their ExEff at 10 and 25 W (P<0.01), but not at 50W. Changes over time, were significant different between groups at 10 and 25W of power (P<0.01), and groups were still different at the end, at 10 and 25 W, after adjusting for ExEff at baseline and absolute loss of BW (P=0.01).

# Discussion

The present study aimed to assess the impact of speed of WL on body composition, RMR and ExEff. The main hypothesis of this project was that a rapid WL leads to a similar loss of FFM, both in absolute (kg) and relative (%) terms, compared with gradual WL. Moreover, it was also hypothesized, that losing weight fast would induce a similar reduction in RMR and increase in ExEff as losing weight gradually.

This study indicates that a similar WL (9% of baseline weight) achieved either fast (over 4 weeks) or gradually (over 8 weeks) induced similar changes in body composition (significant reduction in FM (in kg and %) and FFM (in kg), and increase in FFM (%)). However, fast WL was associated with a significant reduction in RMR, while gradual WL was associated with maintenance of RMR. Both groups decreased their RQ, but the fast WL group experienced a greater reduction. After adjusting for the amount of weight lost as FFM, which is known to be the main determinant of the RMR (31, 32, 34, 58), the difference in RMR at the end between the groups was still evident. Moreover, subjects within the gradual WL group did not change their ExEff at any resistant levels, while subjects in the fast WL group experienced a significant increase in ExEff at 10 and 25 W and differences between groups were significant, even after adjusting for the magnitude of WL.

The similar loss of FFM with both rapid and gradual WL observed in the present study is in contrast with the literature. A review from Chaston et al. (2000) aiming at identifying the proportion of weight lost as FFM by various WL interventions, which included studies from 1966-2006, concluded that there was clear evidence that the degree of caloric restriction and speed of WL impact on the amount of weight lost as FFM, and that a WL achieved with a VLCD induces a larger loss of FFM than a WL achieved with a LCD (16). However, the studies included in this review were not matched regarding WL (10-21kg), duration (6-52 weeks), diets or study design; they assumed that loss of FFM is equal at each week and compared the studies based on loss of FFM in percentage. However, and as that review points out, the lack of RCT`s prevents any firm conclusions to be taken. The present study is the first RCT, to my knowledge, aiming at assessing the impact of speed of WL on body composition changes.

Three original studies were specifically designed to look at speed of WL and loss of FFM (15, 18, 19), but none was an RCT. Sénéchal et al (2012) investigated the impact of speed of WL on body composition, in a pilot study in 10 post-menopausal women, and found that a rapid

WL induced a greater loss of FFM (18). However, besides a very small sample size (5 in each group), the participants were divided into slow/rapid group *after* the WL based on the rate at which they lost the weight. The two groups lost 5% of their baseline weight over a time period of 5 vs.15 weeks, which is very different from the present study with a WL of 9-10% over 4 vs. 8 weeks. While their slow and rapid WL groups lost on average 0.42kg/week and 1.2kg/week, respectively, our gradual WL group lost in average 1.2kg/week and the fast WL group on average 2.2kg/week. Due to these differences, our findings may not be comparable with the study of Sénéchal and colleagues (18). The second study, Arguin et al (2008), investigated the association between the rate of WL and changes in body composition in postmenopausal obese women (51-74 year), with a diet designed to give a WL of 1%/week over a 5 week period. They found the rapid rate of WL (-0.74 to – 1.38 kg/week) to induce greater reduction in FFM, compared with a low rate of WL (-0.44 to -0.72 kg/week), and conclude that a higher rate of WL is correlated with greater loss of FFM (15). A major limitation in the study of Arguin and colleagues (2008) is both WL groups reporting same energy intake. The very different rate of WL, and their study population being older than participants of our study, makes their study not comparable with our. The third study, Coxon et al (1989), was designed to achieve a WL of 1.1 kg/week vs. 1.9 kg/week, more similar to the rate of WL in our study, but over an 8-week time period for both groups (19). As expected, the rapid WL group lost a greater amount of weight and had, therefore, also a larger reduction in FFM. But, after adjusting for absolute WL, the differences in loss of FFM disappeared. They found a average loss of 0.42 (fast WL group) and 0.44 (slow WL group) kg FFM/ kg weight lost, that is greater than our findings: 0.24 kg FFM/kg weight lost (fast group) and -0.18 kg FFM/ kg weight lost (gradual). They conclude that their study does not support the concern that more rapid rate of WL is associated with disproportionate loss of lean tissue.

Regarding the impact of speed of WL on RMR, there is very little research done. The only study that has investigated this is the study of Coxon and colleagues (1989) (19). They found a significant reduction in RMR both after rapid and gradual WL and concluded that a drop in RMR of 20kcal/kg of body weight lost is expected regardless of the speed of WL. In contrast to our findings, they did not find a difference between groups in changes in RMR after adjusting for loss of FFM. However, both groups in our study are within the expected drop in RMR (Fast: -14.5Kcal/kg WL, Gradual: -2.5 Kcal/kg WL) proposed by Coxon and colleagues. Our rapid WL group being on diet for 4 weeks, opposed to subject of this studies

rapid group being on diet for 8 weeks, might explain why our results regarding RMR differ from Coxon and collaborators.

Given that FFM is the main determinant of RMR (31, 32, 34, 58), and that the present study did not find any difference in FFM loss between groups; the differences in RMR between groups were unexpected. The differences in RMR may be due to an improvement in the energy efficiency of metabolically active tissue (17), independently of the amount of FFM.

Despite the general belief that diet induced WL leads to an increased RQ and decreased fat oxidation, potentially increasing the risk of weight gain (43, 59), our findings suggest the opposite. A study very similar to the present one, where a 10 % WL was induced by caloric restriction also found a decrease in RQ, meaning an increased whole body fat oxidation immediately after WL (60). Another study reported no change in RQ after 4 months on a 1200Kcal/day low fat or CHO dietary intervention, where the subject lost 9.8 kg (low CHO) and 6.1 kg (low fat) (61). Studies reporting increased RQ/ decreased fat oxidation with diet-induced WL seem to have in common that RQ was measured after some time of weight maintenance (in energy balance) (50, 62). A study that measured RQ both immediately after weight loss (10 %) and after a period of weight maintenance reported significantly higher RQ at weight maintenance than immediately after the WL intervention (43). This indicates that our findings may be an immediate response to negative energy balance and utilization of FFA, rather than the reduced weight, and that this may change after a period of weight maintenance.

A significant increase in ExEff at 10 and 25W was found in the fast, but not gradual WL group in the present study. Similar results have been reported by Rosenbaum et al (2003) (44), with a significant increase in muscle work efficiency at 10 and 25 W, but not at 50 W of power after a 10% WL. In that study, all the subjects were provided with a liquid formula diet consisting of 800 kcal/day, and were on the diet until they lost 10% of initial BW (~10.2 kg in 4-10 weeks). There are different factors making it difficult to compare the results of their and our study. Vague information about at what speed of WL participants lost their weight, the fact that Rosenbaum and colleagues looked at both overweight (BMI >28 kg/m$^2$) and normal- to overweight (BMI <28 kg/m$^2$), had their participants engaged in supervised exercise (bicycling or treadmill, at 80% of anaerobic threshold, 20-30 min, 3 times/week), tested the participants 14 days *after* intervention (weight stabile state) and used another weight loss method. All this aspects need to be taken in consideration when comparing the

results. Increased ExEff could mean that even though subjects maintain their PA-level, they will use less Kcal. In practise this could cause people to gain weight, if not the decreased energy-cost in low activity intensities is compensated by more PA or lower energy intake. Because we post-tested subjects immediately after WL intervention, we cannot be certain if our results are an acute response, or if it is a permanent change that could implicate WL maintenance.

## Strength and limitations

The present study has both strengths and limitations. The main strength of this study is the study design, Randomized clinical trial, which is considered the "gold standard" of experimental designs due to its ability to minimize the influence of different bias. Second, compliance with the intervention was thoroughly monitored over time in both groups (armbands monitoring PA levels, measurements of ketone bodies, food diaries and weekly follow ups) and was excellent. PA levels did not change over time and there were no differences between groups, ketones were positive in the fast WL group (except in two participants who had negative values only once) and participants ate what was prescribed. Third, with an intervention period of either 4 or 8 weeks, all the female participants were tested (pre and post-intervention) in the same phase of the menstruation cycle, preventing a potential impact of phase of menstrual cycle on RMR. Fourth, golden standard validated methods were used to measure RMR, RQ, ExEff and body composition. Last, both groups lost a similar amount of weight, meaning that differences between groups were due to speed of WL only.

This study also has some limitations. First of all, our study may be unpowered, due to a small sample size. Second, both groups were losing weight relatively fast (2.2 kg/week versus 1.2 kg/week), meaning that we cannot know if there exists differences between losing weight slowly at the present recommended levels (<1kg/week) and fast. Third, measurements were taken immediately after the end of the intervention, preventing to isolate the effect of WL from the effect of negative energy balance. Fourth, and last, significant differences were found in the macronutrient composition of the two diets. However, the differences were very small (average difference of 2.3%) and unlikely to have an important role on our outcome variables. We believe that this difference is due to the very small SD of the means (0.2 - 1.5), particularly in the VLCD group. When comparing the macronutrient composition of the two diets in this study with other studies, both diets fall under the same category: low fat - high

protein diet (63-65). Based on this, it is unlikely that the differences in macronutrient composition of the diets have confounded the results.

## Further studies

To be able to conclude whether a rapid rate of WL leads to a greater loss of FFM and a higher activation of compensatory mechanisms or not, more RCT's and studies with larger sample size are needed. Studies with more men included would also be of interest, to see if there exists a gender difference. Studies with measurements taken after a period of weight stabilization are needed to be able to separate the independent effects of negative energy balance from WL. As mentioned, both the fast and gradual WL group of this study lost weight rather fast. It would be interesting to compare VLCD with LCD (gradual) and LCD (slow/recommended 0.5 - 1kg WL/week), to see if there is a difference between losing weight at the recommended speed and more rapid. Studies of longer duration, to see how subjects manage to maintain their weight over time, after either a rapid or gradual WL, would also be of great importance in determining which rate of WL should be recommended.

## Conclusion

This study does not support the general belief that rapid WL leads to a larger loss of FFM. However, rapid WL was associated with a larger reduction in RMR and a greater increase in ExEff at low intensity levels of PA compared with more gradual WL. Further research is necessary to be able to draw firm conclusion about the impact of speed of weight loss on body composition and compensatory mechanisms activated with WL.

## Conflict of interest

The dietary products were provided by Allevo (Cederroth Norge A/S).

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## Appendix 1: Consent firm

# Forespørsel om deltakelse i forskningsprosjekt

*Hastighet av vekttap og kompensatoriske mekanismer som aktiveres under vekttap*

### Bakgrunn og hensikt

Vi vet i dag at når man slanker seg iverksetter kroppen en rekke mottiltak (såkalte kompensatoriske mekanismer) for å opprettholde sin opprinnelige vekt. Dette dreier seg om ulike appetitthormoner, samt justeringer i forbrenning, som trolig har stor betydning for risiko for tilbakefall/vektøkning.

Hensikten med denne studien er å sammenligne effekten av et raskt vekttap sammenlignet med å gå ned i vekt på en mer langsom måte, med fokus på hvilke effekter hastigheten har for de kompensatoriske mekanismene. Vi vil også undersøke hvilke konsekvenser hastigheten har for kroppssammensetning (muskelvev, fettvev).

Motivasjon er også viktig når man skal endre kostholdsvaner. Vi ønsker å kartlegge hvorfor deltakerne i studien ønsker å endre kostholdsvaner, og hva som gjør at de klarer å opprettholde et sunt kosthold.

### Hva innebærer studien?

I studien vil halvparten av deltakerne trekkes ut (ved loddtrekning) til å følge en diett som skal gi et raskt vekttap (fire ukers vektnedgang), mens den andre halvparten får diett med hensikt å gi et mer langsomt vekttap (i løpet av åtte uker). Vi tar sikte på å oppnå 10 % vekttap ved å begrense kaloriinnholdet i føden i varierende grad.

Gruppen som trekkes ut til rask vektreduksjon skal spise et variert utvalg av diettprodukter (shakes, smoothies, supper) og litt grønnsaker tilsvarende et daglig energiinntak på 550 kcal (kvinner) og 660 kcal (menn) i fire uker. Den andre gruppen som skal ha et mer langsomt vekttap og får en diett sammensatt av måltidserstatninger/diettprodukter (smoothies og barer) og vanlig mat tilsvarende et daglig energiinntak på 1200 kcal (kvinner) og 1500 kcal(menn) i åtte uker.

Det vil være ukentlig oppfølging av ernæringsfysiolog ved NTNU som gjennomgår kostdagboken og evt bivirkninger. Veiing inngår som en del av dette. Gruppen med raskt vekttap vil også måtte avgi urinprøve. Etter vektreduksjonsperioden vil alle få time hos ernæringsfysiolog for å få en diett bestående av normalkost som vil hjelpe de til å opprettholde vekttapet.

Undersøkelsene i studien er stort sett de samme uansett hvilken diettgruppe du trekkes ut til og innebærer blodprøver, målinger av energibehov, fysisk aktivitet, kroppssammensetning, treningseffektivitet og motivasjon før og etter intervensjon. Et spørreskjema vil også bli brukt til å kartlegge søvnkvalitet.

**Mulige fordeler og ulemper**
Fordelen med å delta kan være at man går ned i vekt og oppnår bedre helse. Behandlingen anses ikke som risikabel, men kan innebære forbigående bivirkninger (du kan leser mer i kapittel A). Undersøkelsene innebærer blodprøvetaking.

**Hva skjer med prøvene og informasjonen om deg?**
Prøvene tatt av deg og informasjonen som registreres om deg skal kun brukes slik som beskrevet i hensikten med studien. Alle opplysningene og prøvene vil bli behandlet uten navn og fødselsnummer eller andre direkte gjenkjennende opplysninger. En kode knytter deg til dine opplysninger og prøver gjennom en navneliste. Det er kun autorisert personell knyttet til prosjektet som har adgang til navnelisten og som kan finne tilbake til deg. Det vil ikke være mulig å identifisere deg i resultatene av studien når disse publiseres.

**Frivillig deltakelse**
Det er frivillig å delta i studien. Du kan når som helst og uten å oppgi noen grunn trekke ditt samtykke til å delta i studien. Dette vil ikke få konsekvenser for din videre behandling. Dersom du ønsker å delta, undertegner du samtykkeerklæringen på siste side. Dersom du senere ønsker å trekke deg eller har spørsmål til studien, kan du kontakte studiekoordinator Catia Martins på telefon 72825358.

Studien er godkjent av Regional etisk komité for medisinsk og helsefaglig forskningsetikk, REK Midt-Norge.

**Ytterligere informasjon om studien finnes i kapittel *A*** – *utdypende forklaringom hva studien innebærer.*
**Ytterligere informasjon om personvern og forsikring finnes i kapittel B** – *Personvern, økonomi og forsikring.*

**Samtykkeerklæring følger etter kapittel B.**

Kapittel A – Utdypende forklaring om hva studien innebærer

**Kriterier for deltakelse**

De som kan delta i denne studien må:

1. ha BMI mellom 30 og 45 kg/m$^2$,
2. være vektstabil i de siste 3 måneder (< 2kg variasjon)
3. være frisk
4. være inaktive (det vil si, som ikke trener/mosjonerer regelmessig)

De med melkeintoleranse kan ikke delta i studien siden slankeprodukter som skal benyttes i studien inneholder melk.

**Undersøkelser (før og etter vektreduksjon og i uke 13):**

- Dag 1: Du møter fastende (10 timer faste og uten å ha mosjonert eller inntatt alkohol siste døgn). Du ville bli bedt om en urinprøve. Etterpå, du ville få en kanyle i blodåren for blodprøvetaking. Deretter får du en standardisert frokost. Etter måltidet og i de følgende tre timene vil det bli tatt en serie blodprøver for å måle kostens effekt på appetitthormonene. Du må også fylle ut et spørreskjema angående appetitt. I slutten vil vi måle treningseffektivitet og oksygenopptak ved sykling med ulik motstand (cirka 40 min). Totalt vil dette ta cirka 3,5 timer.

- Dag 2: Du møter opp fastende (10 timer faste) for følgende undersøkelser: Høyde, vekt og hofte/midjemål, hvilestoffskiftet (liggende med en plasthette i ca 30min) og undersøkelse av kroppsmassesammensetning (10 min). Totalt vil dette ta cirka 1 time.

I perioder av studien må du gå med et spesielt armbånd som registrerer din fysiske aktivitet. Varighet er en uke. Dette skjer på tre tidspunkt: Før diettstart, midtveis, og i siste uke av dietten.

Du vil også bli bedt om å fylle ut to korte spørreskjema annenhver uke fra du starter i prosjektet (opp til fem ganger totalt). Spørsmålene dreier seg om hvorfor du vil legge om til et sunnere og mer kalorifattig kosthold, og om opprettholdelse av et sunnere kosthold.

**Mulig ubehag/bivirkninger**

Rask vektreduksjon kan ha flere forbigående bivirkninger. Omfanget av disse varierer fra person til person. Mens noen ikke vil få noen symptomer i det hele tatt, vil andre oppleve ganske plagsomme bivirkninger. Mulige bivirkninger er:

- slapphet
- svimmelhet
- forstoppelse
- hårtap
- tørr hud
- neglene kan bli sprø
- kvalme
- diaré
- forstyrret menstruasjonssyklus
- økt kuldefornemmelse

**Studiedeltakerens ansvar**
Det er studiedeltakerens ansvar å møte til avtalt tid.

**Kompensasjon**
Det gies ingen honorar for å delta i studien, men du vil få diettproduktene gratis. Vi kan dessverre ikke gi kompensasjon for reiseutgifter.

# Kapittel B - Personvern, økonomi og forsikring

## Personvern
Opplysninger som registreres om deg er konfidensielle. Ingen utenforstående forskere vil ha tilgang til dataene.

**Biobank**
Det biologiske materialet som blir tatt vil bli lagret i den spesifikke forskningsbiobanken "Speed of
Weight Loss" ved Institutt for Kreftforskning og Molekylær Medisin (NTNU). Materialet vil bli
analysert for ulike metabolitter/hormoner som er involvert i appetittregulering. Professor Magne
Børset er ansvarshavende for denne forskningsbiobanken. Det biologiske materialet kan bare brukes
etter godkjenning fra Regional komité for medisinsk og helsefaglig forskningsetikk (REK).

**Rett til innsyn og sletting av opplysninger om deg og sletting av prøver**
Hvis du sier ja til å delta i studien, har du rett til å få innsyn i hvilke opplysninger som er registrert om deg. Du har videre rett til å få korrigert eventuelle feil i de opplysningene vi har registrert. Dersom du trekker deg fra studien, kan du kreve å få slettet innsamlede prøver og opplysninger, med mindre opplysningene allerede er inngått i analyser eller brukt i vitenskapelige publikasjoner.

**Økonomi**
Studien og biobanken er finansiert gjennom forskningsmidler fra ”Fundacao Ciencia e Tecnologia” (Det portugisiske forskningsrådet).
Allevo, en slankekostprodusent, vil gi alle slankeprodukter.

**Forsikring**
Studiedeltakerne omfattes av Norsk pasientskadeforsikring, jf. pasientskadelovens §1.

## Informasjon om utfallet av studien
Du er berettiget til å motta informasjon om utfallet av studien.

# Samtykke til deltakelse i studien

Jeg er villig til å delta i studien

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(Signert av prosjektdeltaker, dato)

Jeg bekrefter å ha gitt informasjon om studien

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# Appendix 2: Medical questionnaire

## Medisinsk spørreskjema

Kryss av alle aktuelle:

- ☐ Jeg har ingen tidligere/ nåværende historie med koronar hjertesykdom.
- ☐ Jeg har ingen tidligere/ nåværende historie med Type 1 eller Type 2 diabetes.
- ☐ Jeg har ingen tidligere/ nåværende historie med endokrin sykdom/ hormon forstyrrelse (eks. Hypo/ hyperthyroidisme)
- ☐ Jeg har ingen tidligere/ nåværende historie med lungesykdom.
- ☐ Jeg har ingen tidligere/ nåværende historie med nyresykdom.
- ☐ Jeg har ingen tidligere/ nåværende historie med anemi.
- ☐ Jeg har ingen tidligere/ nåværende historie med gallestein.
- ☐ Jeg har ikke laktose intoleranse (Intoleranse for melk).
- ☐ Jeg har ingen tidligere/ nåværende historie, eller er under behandling for depresjon og/ eller for annen psykisk lidelse.
- ☐ Jeg har ingen tidligere/ nåværende historie med spiseforstyrrelser, inkludert anoreksi og bulimi nervosa.
- ☐ Jeg har ingen tidligere/ nåværende historie med stoff eller alkohol misbruk de siste to årene.
- ☐ Jeg har ingen plan om noe kirurgisk inngrep, eller plan om deltakelse i noe annet forskningsprosjekt under perioden for dette studie.

Sign._____ Dato___/___/____

# Appendix 3: Interview

## Interview

Navn _____ Kode_____

Alder _____ Kjønn_____

Etnisitet _____

Røyker? _____

Har du kommet i overgangsalderen (mistet menstruasjon)? _____

Hvis ja, går du på noen hormonbehandling? _____

Bruker du noen form for prevensjonsmiddel? _____

Hvis ja, hvilken type?_____

Hvor lang er menstruasjonssyklusen din? _____ (dager)

Når var den 1. dagen i din forrige menstruasjonssyklus? ___/___ (dd/mm)

Går du på diet? _____

Prøver du for øyeblikket å gå ned i vekt? _____

Tidligere forsøkt å gå ned i vekt? _____ Hvordan?_____ Hvor mange ganger?_____

Hva var din maks vekt?_____ Når?_____

Har du gått opp/ned i vekt de siste tre mnd.?_____ Hvor mye?_____

Rapportert vekt_____ høyde_____ BMI_____

Kontakt informasjon:

Telefon arbeid_____

Mobil _____

Email _____

## Trenings historie

Vennligst oppgi hvilke av de følgende aktivitetene / sportene, eller andre hvis ikke oppført, har du deltatt i løpet av de siste tre månedene.

Bruk følgende for beskrivelse:

***Varighet***: I minutter og timer

***Hyppighet:*** Daglig
Ukentlig
Månedlig

***Intensitet:*** **Lav -** ingen tungpustenhet, svette eller økt hjertefrekvens.
**Moderat** – lett trening, litt andpusten og svettende, hjertefrekvens økt slik at pulsen kjennes.
**Høy** – hard fysisk trening, andpusten, kraftig svetting og økt hjertefrekvens.

| Type aktivitet | Varighet | Hyppighet | Intensitet |
|---|---|---|---|
| Gå | | | |
| Gå tur med hund | | | |
| Jogge | | | |
| Sykle | | | |
| Svømme | | | |
| Lag idrett (fotball/håndball) | | | |
| Dans | | | |
| Annet, spesifiser:<br>a)<br>b)<br>c) | | | |

# Appendix 4: Flowchart