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Effect of intermittent versus continuous energy restriction on weight loss, maintenance and cardiometabolic risk: A randomized 1-year trial

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Abstract *Background & aims:* Long-term adherence to conventional weight-loss diets is limited while intermittent fasting has risen in popularity. We compared the effects of intermittent versus continuous energy restriction on weight loss, maintenance and cardiometabolic risk factors in adults with abdominal obesity and ≥1 additional component of metabolic syndrome.
Methods & results: In total 112 participants (men [50%] and women [50%]) aged 21–70 years with BMI 30–45 kg/m^2 (mean 35.2 [SD 3.7]) were randomized to intermittent or continuous energy restriction. A 6-month weight-loss phase including 10 visits with dieticians was followed by a 6-month maintenance phase without additional face-to-face counselling. The intermittent energy restriction group was advised to consume 400/600 kcal (female/male) on two non-consecutive days. Based on dietary records both groups reduced energy intake by ~26–28%. Weight loss was similar among participants in the intermittent and continuous energy restriction groups (8.0 kg [SD 6.5] versus 9.0 kg [SD 7.1]; p = 0.6). There were favorable improvements in waist circumference, blood pressure, triglycerides and HDL-cholesterol with no difference between groups. Weight regain was minimal and similar between the intermittent and continuous energy restriction groups (1.1 kg [SD 3.8] versus 0.4 kg [SD 4.0]; p = 0.6). Intermittent restriction participants reported higher hunger scores than continuous restriction participants on a subjective numeric rating scale (4.7 [SD 2.2] vs 3.6 [SD 2.2]; p = 0.002).
Conclusions: Both intermittent and continuous energy restriction resulted in similar weight loss, maintenance and improvements in cardiovascular risk factors after one year. However, feelings of hunger may be more pronounced during intermittent energy restriction.
Trial registration: www.clinicaltrials.gov NCT02480504.

Introduction

Obesity has reached epidemic proportions worldwide requiring new approaches [1]. Energy restriction to achieve and maintain a healthy body weight is a cornerstone in the treatment of obesity and concomitant cardiometabolic risk factors, several of which are part of metabolic syndrome [2,3]. Most recommendations support

Acronyms: BMI, body mass index; TG, triglycerides; CRP, C-reactive protein; RMR, resting metabolic rate; PAL, physical activity level; IPAQ-SF, International Physical Activity Questionnaire-Short form; TDEE, total daily energy expenditure.

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the use of continuous energy restriction with a consistent daily reduction in energy intake. However, many patients find it difficult to adhere to weight-loss diets given changes in neurobiological pathways favoring weight regain [4]. Recently the notion that intermittent energy restriction may improve dietary adherence has achieved popularity. Intermittent energy restriction typically involves periods of very restricted energy intake or "fasting" interspersed with *ad libitum* energy intake. This implies that strict adherence is only needed some days a week. The most studied intermittent energy reduction approaches include two days of energy restriction per week [5] or alternate day fasting [6–9]. On "fasting" days, the dieter typically reduces energy intake to ~500 kcal/day.

Some data supports the feasibility and even potential physiological benefits of intermittent energy restriction [6,7]. Findings from short-term studies indicate that participants lose 3–7% of body weight after two to three months of alternate-day fasting with improvements in cardiometabolic risks [7–9]. The MATADOR study, a randomized trial of obese men examined a less common variant of intermittent energy restriction that alternated two-week-cycles of moderate energy restriction and energy balance [10]. This study showed greater weight and fat loss with intermittent than with continuous energy restriction. Two recent meta-analyses summarized the effects of intermittent energy restriction in intervention studies [11,12]. Both analyses concluded that neither intermittent nor continuous energy restriction was superior to the other in respect to weight loss. The investigators called for larger long-term trials in order to understand the impact of intermittent energy restriction on weight loss and cardiometabolic risk factors.

Individuals with metabolic syndrome, a clustering of risk factors (circulating triglycerides [TG], glucose, HDL-cholesterol, blood pressure and abdominal obesity), are at high risk of type 2 diabetes and coronary heart disease. Moderate weight loss improves all aspects of metabolic syndrome [13]. Whether intermittent fasting is effective for weight loss and improvements in cardiometabolic risk in such a high risk population is relevant to clinical practice. Thus, we conducted a 1-year, randomized controlled clinical trial to compare the effects of intermittent energy restriction versus continuous energy restriction on weight loss, maintenance and cardiometabolic risk factors in men and women with abdominal obesity and at least one additional component of metabolic syndrome.

Methods

Participants

Men and women aged 21–70 years with body mass index (BMI) 30–45.0 kg/m^2 were recruited from August 1, 2015 to April 30, 2016, through advertisement in newspaper and on the face-book page of Oslo University Hospital as well as from patient referrals to the Section of Preventive Cardiology, Department of Endocrinology, Morbid Obesity and Preventive Medicine.

Inclusion criteria included waist circumference ≥94/80 cm (men/women) and ≥1 additional metabolic syndrome component: circulating levels of TG ≥ 1.7 mmol/l, HDL cholesterol ≤1.0/1.3 (men/women), blood pressure ≥130/85 mmHg or use of antihypertensive drugs or fasting glucose ≥5.6 mmol/l, and weight stability within ±3 kg during the last three months. Exclusion criteria were diabetes if treated with insulin or incretin analogues, bariatric surgery, use of anti-obesity drugs or other drugs affecting body weight, eating disorder, or psychiatric illness, or alcohol or drug abuse that could contribute to difficulties with study procedures.

The study was approved by the local Regional Ethics Committee, and conducted according to the Declaration of Helsinki. All participants provided written informed consent before enrolling in the study. The study was registered at www.clinicaltrials.gov NCT02480504.

Randomization

Participants were randomized in a 1:1 ratio to an intermittent or continuous energy restriction group. Block randomization was performed by a stratified sampling procedure by sex and BMI grouped as 30 to <35 kg/m^2 and 35–45 kg/m^2. A statistician prepared a computer-generated random number list. The project leader (TS) opened numbered and sealed envelopes consecutively with no exception. Researchers and participants were not blinded to the intervention group.

Study design

We conducted the trial between August 2015 and April 2017 at the outpatient clinic of the Section of Preventive Cardiology. Total trial duration was one year consisting of a 6-month weight-loss phase and a 6-month maintenance phase with a pre-planned weigh-in at 12 months. Inclusion and exclusion criteria were applied at the screening visit. At the randomization visit participants were assigned to intermittent energy restriction with two days of fasting/week or to continuous energy restriction. Dietary intake and adherence were assessed at baseline and after three months with a 7-day food record analyzed using a diet tool produced by the Norwegian Directorate of Health [14]. Follow-up visits were scheduled at biweekly intervals up to eight weeks, and thereafter monthly up to six months for a total of 10 visits. During the maintenance phase no face-to-face counselling was given, but if requested by the participant, one or two follow-up phone calls or e-mails were conducted. Participants in both groups were encouraged to monitor body weight weekly and to record food intake for personal guidance for at least one week during the maintenance phase. The final visit was at 12 months.

Dietary interventions

We estimated baseline energy requirements using the Mifflin formula [15], and multiplied baseline energy

requirements with physical activity level (PAL) estimated according to self-reported physical activity to calculate the total daily energy expenditure (TDEE). Participants in the intermittent energy restriction group were advised to consume 400/600 (female/male) on each of two non-consecutive days a week and to consume food as usual the remaining five days a week. Participants in the continuous energy restriction group were advised to reduce their energy intake evenly seven days a week so the total weekly energy reduction was equivalent in both groups. The energy intake for participants in this group was based on the calculation of total weekly energy expenditure and its reduction if the participant fasted two days a week: Energy expenditure per week (TDEE x 7) minus total reduction in energy intake per week (TDEE minus 400/600 kcal [female/male] x 2)/7.

Both groups received individualized dietary plans including educational materials and individual counselling sessions. All participants were encouraged to follow the general principles of a Mediterranean type diet (30–35% fat, ~20% protein and 45–50% carbohydrates, mostly unrefined) emphasizing more vegetables, fruits, legumes, fish, poultry, nuts, fermented dairy products, and olive oil and restricting processed meats, red meat and sweets. Participants in the intermittent energy restriction group were recommended fasting on Mondays and Thursdays, but were given the opportunity to adapt this from week to week, as long as they had at least one "normal" day between the fasting days. They received menus that recommended ~50 g protein/day from chicken breast, lean meat, lean fish, fat free yoghurt, cottage cheese, egg or legumes and vegetables to increase satiety on fasting days. The participants in the intermittent energy group were given the choice of consuming one meal providing 400/600 kcal (women/men) or splitting their assigned energy for the day into two snacks of 200/300 kcal (woman/men) or three snacks 100/150 kcal (woman/men).

The continuous energy reduction group received meal plans with suggestions for breakfast, lunch, dinner and snacks in line with their individualized energy recommendations.

In addition to dietary counselling both groups were similarly counselled in cognitive behavioral methods to improve compliance. All the participants were advised about factors shown to improve weight loss maintenance [16]. These factors included planning meals and activity schedules, improving step-wise problem-solving-skills to handle barriers and stronger stimulus control to minimize overeating and to create positive cues for healthy eating, homework exercises regarding high-risk situations for overeating, distinguishing between hunger and cravings and individualized consultations of 30 and 60 min at each follow-up. They were encouraged to maintain a consistent eating pattern, to focus on how to maintain life-style changes, to be satisfied with achieved weight loss and to have confidence in their ability to maintain weight-loss without professional help.

Clinical and laboratory procedures

Body weight was measured following a 10-h fast using the same calibrated digital scale to the nearest 0.1 kg. Waist circumference was measured at the approximate midpoint between the lower margin of the last palpable rib and the top of the iliac crest, and hip circumference around the widest portion of the buttocks [17]. Blood pressure was measured after the participant rested quietly in a sitting position for at least 5 min alone in a quiet room. The mean of three measurements spaced 1 min apart was calculated at screening, baseline, three, six and 12 months. Ratings of well-being, hunger and overeating were measured at three, six and 12 months with a subjective Visual Analogue Scale with a numeric rating from 1 (to a small degree) to 10 (to a very high degree).

Blood samples were obtained following a minimum of a 10-h fast. Analyses of blood samples were performed at Oslo University Hospital Clinical Chemistry Laboratory. Lipids were measured using enzymatic colorimetric methods (Cobas 8000 c 702, Roche Diagnostics, Manheim Germany), while apolipoprotein B was determined using an immunoturbidimetric method (Cobas c501, Roche Diagnostics, Manheim Germany). Serum glucose was measured using hexokinase (Cobas 8000 c702, Roche Diagnostics, Mannerheim Germany). HbA1c was measured using ion-exchange quantitative high performance liquid chromatography (D-100® from Bio-Rad Laboratories, Hercules, CA, USA), C-reactive protein (CRP) was determined with a particle enhanced turbidimetric assay (Cobas 8000 c702, Roche Diagnostics, Manheim Germany).

Energy expenditure

All participants were instructed not to change their physical activity habits throughout the trial to avoid potential confounding. They filled out the self-administered International Physical Activity Questionnaire – Short form (IPAQ-SF) at baseline and after three months. A subgroup consisting of the first 24 participants wore an accelerometer (Actigraph® monitor, GT3X+) for seven consecutive days at baseline and after three months. A valid registration was defined as a minimum of four out of seven days of ≥10 h of monitor wear [18]. The IPAQ-SF calculates and reports physical activity in MET min/wk and we converted accelerometer data into MET min/wk. For the calculation of weekly activity the sum of valid days was adjusted by the number of valid days and multiplied by seven. To classify physical activity into different intensities, we used the cut-off point proposed by Freedson et al. categorizing moderate activity as counts between 1952 and 5724, >5725 counts as vigorous activity and <1952 as light activity [19]. Data were then converted into minutes spent in moderate-intensity (3.00–5.99 METs, 1952–5724 counts per minute) or vigorous activity (≥6.00 METs, ≥ 5725 counts per minute) [19]. The MET score per minute (MET-min) for a day was computed with the following formula: 8 × minutes spent in vigorous activity + 4 × minutes spent in moderate-

intensity activity. We measured resting metabolic rate (RMR) in this sub-group at baseline and after three months by indirect calorimetry, using standard reference method procedures [20].

Outcome measures

The primary endpoint was change in body weight after one year. Secondary outcomes were changes in weight after six months and waist circumference, blood pressure, and other cardiometabolic risk factors after six months and one year. Measurements were not blinded, but data entry was done by assistants who were blinded to study group.

Statistical analysis

We based the sample size calculation on a mean 4–5 kg (SD 4 kg) decrease in body weight after one year in both groups as shown in previous work [21]. For a non-inferiority trial with a clinically relevant difference of up to 2 kg between groups, power of 80% and one-sided alpha set at 0.05, 50 participants were needed for each group [22]. To take into account dropouts, we included 112 participants. Variables were normally distributed except for TG and CRP. Since the sample size was over 40, parametric tests were used [23]. Analyses followed the intent-to-treat principle with the last value carried forward for dropouts, with additional complementary analyses of the per protocol population (i.e. the population that completed all 12 months). These analyses did not differ substantially, and the intent-to-treat analyses are presented. A linear mixed model, repeated measure ANOVA was used for between-group comparisons. A paired sample t-test was used for within-group comparisons but these were considered secondary analyses and not primary results [24]. We did not adjust for the primary outcome variable (body weight) at baseline, as it did not differ between groups (data not shown). Data was analyzed using IBM SPSS Statistics for Windows version 21 (SPSS Inc., Chicago, IL). The significance level was assumed at $p < 0.05$.

Results

Study participants

As shown in the Consolidated Standards of Reporting Trials flow chart four dropouts occurred in the intermittent versus three in the continuous energy restriction group (Fig. 1). None of the participants withdrew due to difficulties adhering to the diet. Baseline characteristics as shown in Table 1 were similarly distributed between the two groups except for TG.

Study outcomes

Changes in body weight and cardiometabolic variables are reported in Table 2. Overall, weight loss was similar among participants in the intermittent versus continuous energy restriction group after one year (8.0 kg [SD 6.5] versus 9.0 kg [SD 7.1]; $p = 0.6$) as were changes in waist circumference (8.7 cm [SD 5.9] versus 9.6 cm [SD 6.3]; $p = 1.0$). Both groups maintained weight loss in the maintenance phase with no between group differences, but regain in weight within the intermittent energy restriction group was statistically significant (Table 2). In total 63% of the participants in the intermittent energy restriction group and 69% in the continuous energy restriction group achieved >5% weight loss (31.5% achieved >10% and 31.5% achieved 5–10% in the intermittent group, while 34.5% achieved >10% and 34.5% achieved 5–10% in the continuous group). There were no between group differences in changes in cardiometabolic risk factors (Table 3). Within-group improvements were observed in regard to blood pressure and concentrations of HDL-cholesterol, TG and HbA1c.

Adverse events

No serious adverse events were reported. In the continuous energy restriction group 3% reported dizziness, 5% mild headache and 2% mild nausea during the first four weeks, while 11% reported dizziness, 20% mild headache, 6% mild nausea and 2% temporary sleep disturbance in the same period in the intermittent energy group.

Energy intake, physical activity and resting metabolic rate

Participants reduced estimated energy intake by 28% (SD 18%) in the intermittent and 26% (SD 17%) in the continuous energy restriction group from baseline to three months ($p = 0.6$). Women in the intermittent energy restriction group reduced estimated energy intake from 2042 kcal/day (SD 415) to 1507 kcal/day (SD 374). The estimated reduction in women in the continuous restriction group was from 2104 kcal/day (SD 390) to 1463 kcal/day (SD 237) with no between group difference ($p = 0.4$). Men in the intermittent energy group reduced energy intake from 2482 kcal/day (SD 651) to 1694 kcal/day (SD 470). The reduction in men in the continuous restriction group was from 2475 kcal/day (SD 513) to 1837 kcal/day (SD 322), with no between group difference ($p = 0.2$).

The IPAQ-SF score and accelerometer score did not change from baseline to three months (eTable 1 in Supplement 1). RMR was reduced from baseline to three months, from 1917 kcal/day (SD 285) to 1824 kcal/day (SD 222) in the intermittent energy restriction group ($n = 12$) and from 1882 kcal/day (SD 253) to 1767 kcal/day (SD 236) in the continuous energy restriction group ($n = 12$) with no between-group difference ($p = 0.5$).

Feelings of hunger and well-being

Participants in the intermittent energy restriction group reported more hunger compared to participants in the continuous energy restriction group (Table 4).

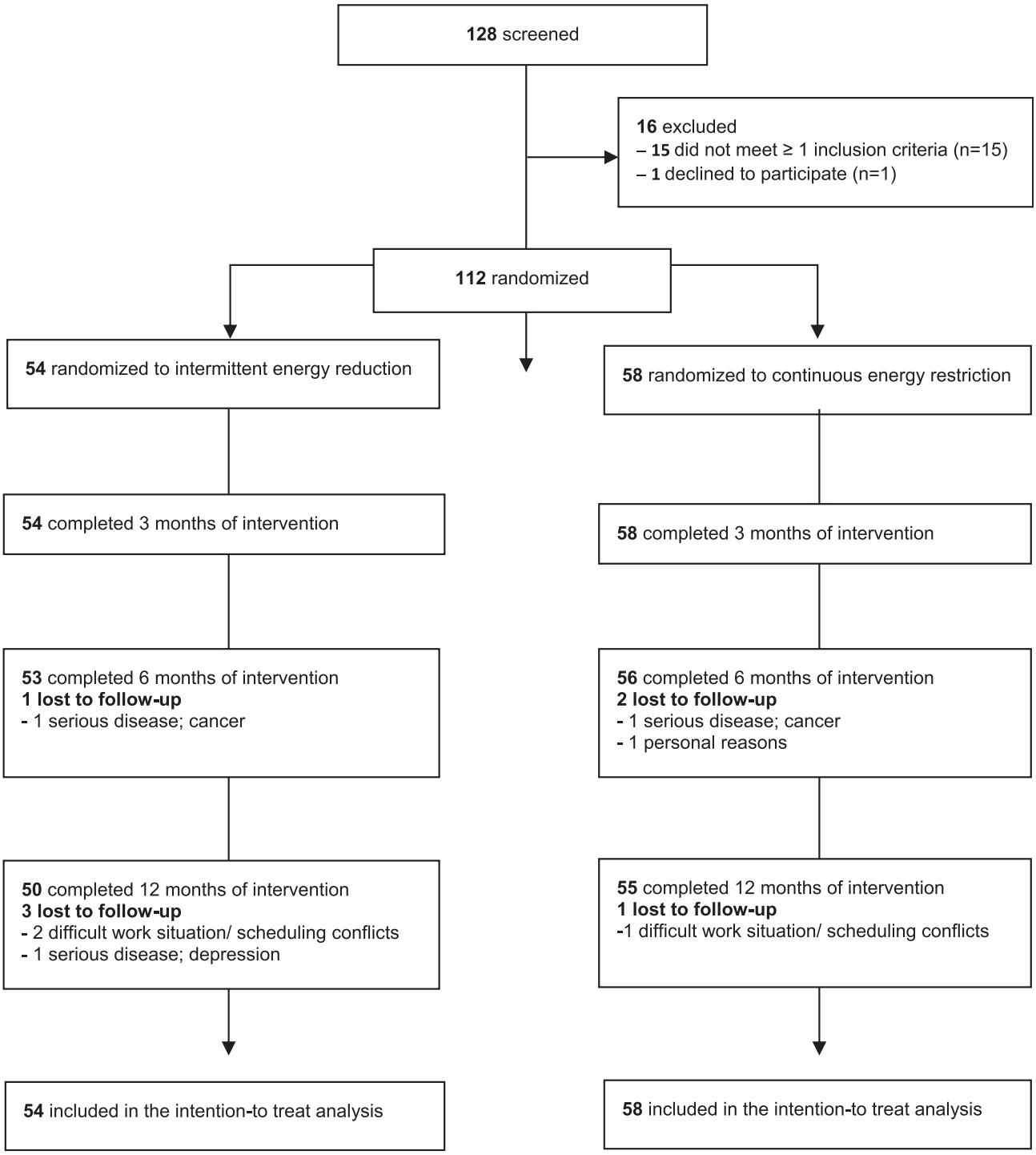

Figure 1 Consolidated Standards of Reporting Trials (CONSORT) flow diagram for participants' allocation into study arms.

Discussion

To our knowledge, this is the first randomized, controlled, long-term study of the 5:2 approach to intermittent fasting indicating that intermittent energy restriction is as effective, but not superior to continuous energy restriction at inducing clinically significant weight loss (2) and maintenance and improving cardiometabolic risk factors in free-living men and women with abdominal obesity and at least one additional component of metabolic syndrome. Both diets resulted in equivalent reduction in energy intake. The lack of change in physical activity indicates that the diet is the reason for the observed changes.

Most previous studies of intermittent fasting were limited to short intervention periods [9]. The 1-year follow-up period in the current study covered both

Table 1 Baseline characteristics and cardiometabolic risk factors according to assignment to intermittent or continuous energy restriction. Mean (SD) values are shown.

	Intermittent	Continuous
Subjects, n	54	58
Females, n (%)	26 (48.1)	30 (51.7)
Age, years	49.9 (10.1)	47.5 (11.6)
Education attained		
Primary school, n (%)	2 (4)	3 (5)
High school, n (%)	15 (28)	21 (36)
College/university, n (%)	37 (69)	34 (59)
Smokers, n (%)	4 (7)	3 (5)
Body weight, kg	108.6 (16.3)	107.5 (16.1)
BMI, kg/m^2	35.1 (3.9)	35.3 (3.5)
Waist circumference, cm	116 (10)	116 (10)
Females	111 (8)	113 (8)
Males	121 (10)	121 (10)
Hip circumference, cm	115 (9)	116 (7)
Females	118 (9)	118 (7)
Males	113 (8)	114 (7)
Antidiabetic drugs, n (%)	1 (2)	4 (7)
Antihypertensive drugs, n (%)	20 (37)	23 (40)
Statins, n (%)	10 (19)	8 (14)
Cardiometabolic risk factors		
Systolic blood pressure, mmHg	129 (13)	128 (13)
Diastolic blood pressure, mmHg	88 (8)	86 (9)
Heart rate/minute	69 (11)	68 (8)
Total cholesterol, mmol/L	4.97 (0.90)	5.09 (0.87)
HDL-cholesterol, mmol/L	1.21 (0.34)	1.17 (0.25)
Females	1.27 (0.36)	1.22 (0.25)
Males	1.17 (0.32)	1.12 (0.24)
LDL-cholesterol, mmol/L	3.26 (0.83)	3.45 (0.84)
Triglycerides, mmol/L*	1.84 (0.83)	1.55 (0.68)
Apolipoprotein B, g/L	1.04 (0,22)[a]	1.09 (0.23)[a]
Glucose, mmol/L	5.8 (1.2)	5.7 (0.7)
HbA1c, %	5.6 (0.7)[a]	5.5 (0.5)
C-reactive protein, mg/L	3.2 (3.0)[a]	4.2 (3.8)[a]

*$p<0.05$ between groups.
[a] Missing for one subject.

weight loss and six months of weight maintenance. Regardless of the type of diet chosen, weight maintenance after six months or so of energy restriction is not achieved by most dieters [25]. In the current study, though no face-to-face counselling was scheduled during the maintenance phase, both groups complied with their dietary plan as shown by their maintained weight loss. This could be ascribed to the frequency of follow-up during the weight loss phase, the pre-planned weigh-in after 12 months, cognitive behavioral counselling and efforts made at the six month visit to prepare participants for maintenance (described in the methods section) as recommended in obesity treatment guidelines [2,26].

Participants in the current trial were at high risk for adverse health conditions, given the presence of at least two metabolic syndrome components in addition to all grades of obesity. This group has been less well represented in previous long-term trials [11,12,27] yet are a primary target for obesity treatment and intervention [2]. All components of metabolic syndrome were improved in both groups (waist circumference, blood pressure, lipids and glycemia) and the improvements remained stable in the weight maintenance phase (though HbA1c was not measured at 12 months). The improvement in HbA1c after six months reflects postprandial glucose regulation, while fasting glucose concentrations were not changed despite significant weight loss.

We found that the participants in the intermittent energy restriction group reported stronger feelings of hunger throughout the study and numerically more adverse events and larger weight regain than in the continuous energy restriction group. Earlier studies have reported unchanged, increased and decreased hunger following intermittent energy restriction [28]. While a previous study of 12 weeks did not find differences in subjective appetite ratings or appetite-regulating hormones between intermittent and continuous energy restriction [29], increased feeling of hunger may limit long-term adherence. Further research should examine whether intermittent dieting affects appetite hormones unfavorably in long-time studies, and if behavioral traits influence individual tolerability of intermittent energy restriction.

In the present study participants in the intermittent energy group were given the choice of consuming one

Table 2 Changes in body weight and circumferences at baseline, three months and six months and changes in the maintenance phase between six and 12 months according to assignment to intermittent or continuous energy restriction. Mean (SD) values are shown.

Outcome variable	Baseline	3 months	6 months	P-value between groups[a]	Changes 6–12 months	P-value between groups[a]
Weight, kg						
Intermittent	108.6 (16.3)	−7.1 (3.7)	−9.1 (5.0)**		+1.1 (3.8)*	
Continuous	107.5 (16.1)	−7.4 (3.8)	−9.4 (5.3)**	0.9	+0.4 (4.0)	0.6
BMI, kg/m^2						
Intermittent	35.1 (3.9)	−2.3 (1.1)	−3.0 (1.6)**		+0.3 (1.2)*	
Continuous	35.3 (3.5)	−2.5 (1.3)	−3.2 (1.9)**	1.0	+0.1 (1.3)	0.4
Waist circumference, cm						
Intermittent	116 (10.3)	−6.9 (3.6)	−8.0 (5.6)**		0 (4)	
Continuous	116 (9.5)	- 7.8 (4.3)	−9.2 (5.4)**	1.0	0 (5)	0.9
Hip circumference, cm						
Intermittent	115 (8.8)	−5.0 (2.5)	−6.8 (4.6)**		0 (4)	
Continuous	116 (7.1)	−5.3 (3.3)	−7.5 (5.9)**	0.8	0 (4)	0.9

*Paired sample t-test within groups, p-value < 0.05.
**Paired sample t-test within groups, p-value < 0.01.
[a] Repeated measures ANOVA, mixed model.

Table 3 Changes in cardiometabolic risk factors at three, six and 12 months according to assignment to intermittent or continuous energy restriction. Mean (SD) values are shown.

Outcome variable	Baseline	3 months	6 months	12 months	P-value between groups[a]
Systolic BP, mmHg					
Intermittent	129 (13.4)	- 6.4 (12.6)	−4.9 (14.1)	−1.9 (12.3)	
Continuous	128 (13.2)	- 5.0 (10.6)	−5.8 (10.7)	−3.6 (11.8)*	0.6
Diastolic BP, mmHg					
Intermittent	88 (8.1)	- 6.4 (8.0)	−5.8 (7.5)	−3.0 (7.3)**	
Continuous	86 (8.7)	- 4.8 (7.2)	−4.7 (7.4)	−2.9 (7.7)**	0.3
Heart rate/minute					
Intermittent	69 (10.9)	- 4.9 (10.3)	−2.7 (9.0)	−1.3 (8.7)	
Continuous	68 (10.8)	- 3.6 (6.5)	−1.5 (8.4)	−0.7 (9.4)	1.0
Total cholesterol, mmol/L					
Intermittent	4.97 (0.9)	−0.21 (0.5)	−0.16 (0.6)	0.07 (0.7)	
Continuous	5.09 (0.9)	−0.18 (0.7)	−0.07 (0.5)	0.17 (0.7)	0.3
HDL-cholesterol, mmol/L					
Intermittent	1.22 (0.3)	0.02 (0.1)	0.05 (0.2)	0.13 (0.2)**	
Continuous	1.17 (0.2)	−0.01 (0.1)	0.06 (0.1)	0.13 (0.6)*	0.6
LDL-cholesterol, mmol/L					
Intermittent	3.26 (0.8)	−0.19 (0.4)	−0.16 (0.4)	−0.03 (0.6)	
Continuous	3.45 (0.8)	−0.18 (0.6)	−0.07 (0.5)	0.08 (0.6)	0.1
TG, mmol/L					
Intermittent	1.84 (0.8)	−0.39 (0.7)	−0.35 (0.7)	−0.31 (0.8)**	
Continuous	1.55 (0.7)	−0.19 (0.8)	−0.36 (0.6)	−0.11 (0.7)*	0.1
Apo B, g/L					
Intermittent	1.04 (0.2)	−0.04 (0.1)	−0.06 (0.1)	−0.04 (0.2)	
Continuous	1.09 (0.2)	−0.04 (0.2)	−0.04 (0.2)	0.00 (0.2)	0.1
Glucose, mmol/L					
Intermittent	5.8 (1.2)	−0.3 (0.7)	−0.2 (0.9)	−0.2 (1.2)	
Continuous	5.7 (0.7)	−0.3 (0.5)	−0.2 (0.6)	0.0 (0.4)	0.7
HbA1c, percentage[b]					
Intermittent	5.6 (0.7)		−0.3 (0.5)**		
Continuous	5.5 (0.5)		−0.2 (0.4)**		0.2
CRP, mg/L[b]					
Intermittent	3.2 (3.0)		0.5 (4.0)		
Continuous	4.2 (3.8)		−0.8 (3.9)		0.6

*$p < 0.05$.
**Paired sample t-test within groups, p-value <0.001.
[a] Repeated measures ANOVA, mixed model.
[b] Not measured at 3 and 12 months.

Table 4 Ratings of well-being, hunger and overeating according to diet assignment on a numeric rating scale of 1 (to a small degree) to 10 (to a very high degree). Mean (SD) values are shown.

Outcome variable	3 months	6 months	12 months	P-value between groups[a]
I feel that the diet is easy to follow				
Intermittent[c]	7.9 (1.7)	7.5 (2.4)	6.8 (2.5)	
Continuous[b]	7.8 (1.6)	7.7 (1.8)	7.2 (2.0)	0.6
I feel well while following the diet				
Intermittent[c]	8.3 (1.4)	7.7 (2.4)	7.4 (2.6)	
Continuous[b]	8.5 (1.4)	8.4 (3.3)	8.0 (1.8)	0.1
I plan to continue to follow the diet				
Intermittent[c]	8.7 (1.2)	8.4 (1.6)	7.4 (2.6)	
Continuous[b]	8.8 (1.0)	8.6 (1.1)	8.3 (1.4)	0.1
I have often felt hungry while on the diet				
Intermittent[c]	4.7 (2.4)	4.7 (2.3)	4.7 (2.2)	
Continuous[b]	3.8 (2.1)	3.6 (2.1)	3.7 (2.2)	0.002
I have overeaten since the last follow up				
Intermittent[c]	3.5 (2.3)	3.8 (2.6)	3.7 (2.4)	
Continuous[b]	3.3 (2.2)	3.4 (2.2)	3.7 (2.4)	0.6

[a] Repeated measures ANOVA, mixed model.
[b] Missing for two subjects.
[c] Missing for three subjects.

meal a day or split their assigned energy for the day into small meals/snacks. These choices could improve long-term compliance. In contrast, in a previous one-year trial alternate-day fasting participants were assigned one meal a day at lunch-time and the drop-out-rate was higher in the alternate-day-fasting group (38%) than in the daily calorie restriction group (29%) [27]. Furthermore, more participants in the alternate-day group withdrew owing to dissatisfaction with the diet. More study may clarify which form of intermittent energy restriction seems to be most satisfactory in the long term.

The main strength is the generalizability of the results due to high retention rates in both groups and inclusion of similar proportions of men as women. Drop-out-rates of 5–7% are unusual in long-term weight management studies. The low drop-out-rate might be due to intensive lifestyle intervention given by trained dietitians during the first six months including individual counselling combining dietary advice and behavior therapy. Six to 12 months trials comparing intermittent versus continuous energy restriction generally show rates of over 20% [11,12,26].

The study had some limitations. Study visits were not scheduled according to fasting days among participants in the intermittent energy restriction group, to limit lack of compliance, as participants were allowed to vary the day of the week on which they fasted. While this may affect biochemical measurements like glucose and TG our

findings of no between-group differences are in line with results in other studies [5,11,27,28,30].

In conclusion, the results of this study show that middle aged men and women with abdominal obesity at cardiovascular risk, following an intermittent or continuous energy restriction achieved similar weight loss and improvements in cardiometabolic risk factors. Further long-term studies lasting for two years or more may help determine whether intermittent energy restriction, perhaps modified to ensure adherence, is sustainable in the long term, compared with continuous energy restriction.

Statement of author contributions to the manuscript

T.M.S, S.T and M.S designed the study; T.M.S. conducted the dietary counselling and project supervision; T.M.S. analyzed the data; and T.M.S. S.T and M.S. wrote the paper. S.T. had primary responsibility for the final content. All authors read and approved the final manuscript.

Conflict of interest

None.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.numecd.2018.03.009.

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