Continuous vs intermittent dieting for fat loss and fat-free mass retention in resistance-trained adults: the ICECAP trial

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Abstract

Introduction: Can intermittent energy restriction (IER) improve fat loss and fat-free mass retention compared with continuous energy restriction (CER) in resistance-trained adults?

Methods: Sixty-one adults (32 women) with mean (SD) age 28.7 (6.5) years, body weight 77.2 (16.1) kg and body fat 25.5 (6.1)% were randomized to 12 weeks of (1) 4 x 3-weeks of moderate (m) energy restriction interspersed with 3 x 1-weeks of energy balance (mIER; n=30; 15 weeks total), or (2) 12 weeks of continuous moderate energy restriction (mCER; n=31). Analyses of all outcome measures were by intention-to-treat.

Results: After accounting for baseline differences, mIER did not result in lower fat mass or body weight, or greater fat-free mass, compared to mCER after energy restriction. Mean (and 97.5% confidence interval, CI) for fat mass at the end of mIER versus mCER was 15.3 (12.5 to 18.0) kg versus 18.0 (14.3 to 21.7) kg (P=0.321), for fat-free mass was 56.7 (51.5 to 61.9) kg versus 56.7 (51.4 to 62.0) kg (P=0.309), and for body weight (with 95% CI) was 72.1 (66.4 to 77.9) versus 74.6 (69.3 to 80.0) (P=0.283). There were no differences between interventions in muscle strength or endurance or in resting energy expenditure, leptin, testosterone, insulin like growth factor-1, free 3,3′,5-triiodothyronine or active ghrelin, nor in sleep, muscle dysmorphia or eating disorder behaviours. However, participants in mIER exhibited lower hunger (P=0.002) and desire to eat (P=0.014) compared to those in mCER, and greater satisfaction (P=0.016) and peptide YY (P=0.034).

Conclusions: Similar fat loss and fat-free mass retention are achieved with mIER and mCER during 12 weeks of energy restriction; however, mIER is associated with reduced appetite.

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Key words: WEIGHT LOSS, DIET, FAT LOSS, ATHLETES, DIET BREAKS, CALORIC RESTRICTION

Introduction

While most athletes do not have a body mass index (BMI) in the overweight or obese range, many regularly undergo periods of energy restriction in an attempt to reduce fat mass while concurrently striving to maintain fat-free mass (1-5). They do so for a variety of biomechanical, locomotive, aesthetic and competitive reasons, including to reach a target weight class (6-8). Recently, intermittent energy restriction (IER) has become a popular means of weight and fat reduction (7, 9). IER contrasts with conventional continuous energy restriction (CER) methods of weight and fat reduction, as it involves interrupting periods of energy restriction (where energy intake is reduced to below weight maintenance requirements) with periods of greater energy intake (to weight maintenance requirements or above). These periods of greater energy intake are often referred to as 'diet breaks' or 'refeeds' (7).

Intermittent energy restriction protocols have been implemented using moderate or severe energy restriction. Moderate and severe energy restrictions may be defined as restrictions in energy intake of up to 35% or exceeding 65%, respectively, relative to weight maintenance requirements (10). Compared to CER, IER protocols using periods of moderate energy restriction in adults with overweight or obesity have been shown in two randomised controlled trials – one in men and the other in women – to result in superior weight and fat loss and greater retention of resting energy expenditure (REE) (11, 12), albeit these benefits were not shown in all trials in adults with overweight or obesity (13, 14). Recently, we proposed (7, 15) that IER using energy restriction combined with diet breaks that achieve energy balance (as opposed to energy restriction or energy excess) may offer a more effective option than CER for body composition management, including among athletes, by normalising – or at least attenuating – some of the adaptive responses to energy restriction through deliberate periods of energy balance. This approach is akin to periodisation in exercise programs, whereby training volume is progressively overloaded to stimulate adaptation, before being alternated with a deload period to offset accumulated fatigue and the negative side effects associated with high chronic training volumes (16).

In adult men with obesity, an IER protocol alternating 2-week periods of moderate energy restriction with 2-week periods of energy balance (diet breaks) was superior to CER for weight loss, fat loss, and retention of REE (11). While this IER protocol was effective in adult men with obesity, we proposed (17) that it may not be acceptable to athletes due to the almost two-fold greater time requirement in the IER intervention, compared to CER. We thus suggested that an appropriate IER protocol for athletes would be to combine 3-week periods of moderate energy restriction with 1-week periods of energy balance (diet breaks), so as to reduce the frequency and duration of the diet breaks, as well as the overall length of the intervention (17). The purpose of the trial reported in the current paper is to test the effect of this IER protocol on fat mass and fat-free mass in resistance-trained adults. The trial is named ICECAP (Intermittent versus Continuous Energy restriction Compared in a resistance-trained Adult Population). We hypothesised that, compared with moderate CER (mCER), moderate IER (mIER) will result in lower fat mass, with equivalent or greater fat-free mass at the end of 12 weeks of energy restriction. Additionally, following on from the positive effects reported in a resistance-trained population as a result of periods of energy balance during weight loss (including maintenance of energy expenditure, enhanced training performance and improved mental recovery) (18), we hypothesised that those undergoing mIER will have higher REE, superior muscle strength and endurance, less mood disturbance and less drive to eat than those undergoing mCER.

Materials and methods

The full protocol for this randomized controlled trial has been published previously (17), and a summary of the protocol is provided below and in **Figure 1** for readers' convenience.

Eligibility criteria for participants

Eligible participants were men and women aged 18-54 years not currently involved in any weight loss program, who had participated in regular resistance exercise (≥ 2 sessions per week) for ≥ 6 months prior to participation in this trial, and who were proficient (or willing to become proficient) in the use of a kilojoule (kJ) and macronutrient-tracking mobile application, MyFitnessPal (Under Armour, Baltimore, Maryland, USA). This application was previously validated for assessing dietary intakes compared with weighed food records, and was shown to be effective for the implementation of dietary advice among people who are ready to self-monitor energy intake (19-21). The participants were also required to expect that their training regimen would be consistent during the dietary weight loss intervention. These attributes were the key eligibility criteria for the trial, and full inclusion and exclusion criteria have been published previously (17).

Determination of weight maintenance energy requirements

Once participants provided written informed consent and were recruited into the trial, they were instructed to follow a diet that provided ~100% of energy requirements for weight maintenance for 4 weeks (Figure 1). As per our previously-published methodology (17), participants were told that if they gained or lost weight consecutively for 3 days, they should contact the lead researcher (JJP) for an amended diet prescription to maintain weight stability. Weight maintenance energy requirements were initially estimated for each participant using a sequential series of prediction equations that take into consideration age, sex, body size and physical activity level, as described previously (22). In addition to a prescribed energy intake, participants were also provided with specific macronutrient targets for input to MyFitnessPal (dietary composition detailed below). For the entire duration of the trial, participants were instructed to weigh what they consumed every day using a food scale to help ensure accurate portion sizes, and they were encouraged to record *all* food and drink intake (including any deviations from targets) in MyFitnessPal every day. During each day of the trial, participants submitted their morning body weight measurement as well as a copy of their MyFitnessPal food diary into an online form for review by the lead researcher (JJP). At the end of each week of the trial, participants received emailed feedback, including personalised help and encouragement.

Energy restriction interventions

After the 4-week weight maintenance diet, both groups undertook 12 weeks of moderate energy restriction. Energy restriction was delivered as either (1) mIER: 4 x 3-week blocks of moderate energy restriction interspersed with 3 x 1-week blocks of energy balance (15 weeks total), or (2) mCER: 12 weeks of continuous moderate energy restriction, as shown in Figure 1 (17). These regimens were designed to cause moderate weekly weight losses of 0.7% of the participants' pre-intervention body weight during time in energy restriction, with the assumption that the oxidation of 1 g of mixed tissue liberates ~29 kJ of energy (3). The weekly body weight loss target of 0.7% was selected following published recommendations on rates of weight loss for athletes (3). To account for reductions in REE due to energy restriction/weight loss, participants who achieved a weekly weight loss of < 0.5% of their preenergy restriction body weight had their prescribed energy intake reduced by 5% to help keep them at approximately the same desired rate of weight loss throughout the study. To account for the potential for participants in one intervention to require a greater number of energy intake reductions to achieve the same magnitude of weight loss as participants in the other intervention, the diets were assessed not only by examining the magnitude of weight loss, but also by comparing the drop in energy intake between groups across the trial. Weekly weight losses were calculated via week-to-week changes in average daily body weight (measured and self-reported by participants at home) over 7 days. During the 1-week blocks of energy balance in the mIER group, participants were prescribed a diet that provided ~100% of weight maintenance requirements, based on the energy requirements determined in the 4-week weight maintenance phase, and adjusted to take into account the aforementioned reductions in REE due to energy restriction/weight loss. In addition to an individualised kJ intake prescription, each participant was provided with targets for daily dietary protein, carbohydrate and fat intake as alluded to above (details below), with meal frequency, meal timing and foods/drinks consumed to meet energy and macronutrient targets at the discretion of each participant.

Dietary composition

Participants were instructed to consume 2.3 g of protein per kg of absolute body mass daily, and 20% of energy intake was allocated to dietary fat, with the remaining energy intake allocated to carbohydrate. During the diet breaks in energy balance, participants in the mIER group were instructed to adjust the macronutrient targets in the kJ and macronutrient tracking mobile application so as to consume the same amount of protein and fat (in grams) as prescribed for energy restriction, with the increase in energy intake being totally derived from increased carbohydrate intake. The rationale underlying the dietary interventions have been published previously (17).

Outcome measures

Figure 1 summarizes the outcome measures for this trial and the time points at which they were collected. Additionally, the methods for the collection of data have been published previously in our protocol paper (17). Note that our published protocol lists 2 additional time points for which outcomes are not in this paper: 16 weeks and 39 weeks. At the 16-week time point, we collected data from participants in the mIER, but not in the mCER intervention, as per our original published protocol (17). The purpose of that 16-week time point was to determine the effects of a 1-week diet break in mIER on the variables investigated here. This will be the topic of a separate paper. For the 39-week time point, we decided not to collect that data after observing that 6 of the first 8 participants who completed the energy restriction intervention wanted to transition to a period of positive energy balance to facilitate muscle gain, as opposed to attempting to maintain their reduced weight and fat mass. The following descriptions of our outcome measures provide an overall summary of the methods, as well as details about the methods that were either not included in or were altered from the published protocol (17), as well as the rationale for any alterations.

For all outcome measurements conducted in our laboratory, participants were instructed to consume 600 mL of plain water upon waking (and nil by mouth until after testing was complete), and to come to the laboratory by car, between the hours of 0600 and 0900, having refrained from all exercise, food and fluids (other than water), caffeine, alcohol or other drugs (recreational, over-the-counter or prescribed, excluding regular medications that had been taken for >6 months) for the previous 12 hours.

Self-reported energy intake, weight, and adherence

Daily self-reported energy intake was obtained from data entered into the smartphone application that participants were instructed to use throughout the 15-week interventions. For the collection of self-reported weight data, the participants were asked to measure their weight at home, and record it in the aforementioned smartphone application on a daily basis. Adherence was defined as a daily self-reported energy intake within 800 kJ of the prescribed daily energy intake on > 90% of days during the mIER and mCER interventions.

Weight, fat mass, fat-free mass, and REE

As detailed in our published protocol (17), body weight was measured in the laboratory using an electronic calibrated scale, whereas fat mass and fat-free mass were determined by whole-body dual-energy X-ray absorptiometry (DXA) scans (Lunar iDXA, GE Healthcare, Chicago, Illinois, USA) by qualified investigators. As mentioned above, participants were given specific instructions about exercise and the ingestion of food, fluids, alcohol, caffeine and all other drugs (recreational, over-the-counter or prescribed, with the exception of regular medication as defined above) in the 12 hours prior to the DXA scans, as a means of standardizing test conditions for all participants. During the DXA scan, participants lay supine on the scanning table with their arms at their sides. DXA scans were conducted in accordance with the procedure outlined in the manufacturer's manual and analysed using the enCORE Software Platform (version 17, GE Healthcare). The DXA scanning machine was serviced annually, subject to regular quality assurance testing, and calibrated on each day of use. REE was calculated from measurements of oxygen consumption and carbon dioxide production under the same pre-testing instructions listed for DXA above, using an Ametek metabolic cart system (S-3A/I oxygen and CD-3A carbon dioxide analysers) designed for measurement of energy expenditure during exercise and at rest (AEI Technologies, Berwyn, Pennsylvania, USA), with participants asked to adopt a supine position in a darkened and quiet room, breathing through a respiratory valve with a nose clip in place for a continuous 30-minute resting period. The average 1-minute value calculated from the data collected during the final 10 minutes of the 30-minute resting period was used for analysis.

Physical activity

Physical activity was assessed using a triaxial accelerometer placed on the wrist of participants (Actigraph, Pensacola, Florida, USA). During collection periods, accelerometers were worn by participants for 24 hours per day for 7 consecutive days, only being taken off for showering or other water-based activities. Data was analysed via the Actilife software (Version 6.13.3), which provided estimates for daily steps, physical activity exergy expenditure, and time spent in sedentary and vigorous activity. The settings in the Actilife software used were the Troiano default settings, with sample rate set at 30 Hz, with data collected using 60-second epochs. Non-wear time was defined as at least 60 minutes of zero activity counts. The cut-points (in activity counts per minute) for intensity of activity were <2860 for sedentary activity, and >3941 for vigorous activity. This data was collected from a subset of participants (n = 12, with n = 7 from mIER and n = 5 from mCER), due to reduced access to accelerometers at the time this trial was conducted.

Sleep

Sleep quality and sleepiness were assessed with validated surveys (the Pittsburgh Sleep Quality Index (23) and the Epworth Sleepiness Scale (24)).

Muscle performance

Muscle strength and endurance were determined using an isokinetic dynamometer (Biodex Medical Systems, Shirley, New York, USA) as per our published protocol (17). Following a standardised warmup, muscle flexion and extension strength at the knee (which assesses strength of the hamstrings and quadriceps muscles of the leg, respectively), and at the elbow (which assesses strength of the biceps and triceps muscles of the arm, respectively) were assessed during a maximum-effort 3-repetition set (peak torque; power; total work) at a speed of 60 degrees per second, while muscle endurance at the knee (hamstrings and quadriceps) and elbow (biceps and triceps) were assessed using a maximum-effort 25-repetition set (total work; work during last third of 25-repetition set) at a speed of 240 degrees per second. To allow for recovery, muscle endurance tests were performed 5 minutes following muscle strength tests. Muscle performance testing was scheduled as the last outcome measurement for the morning in our laboratory, to avoid potential interference on other outcome measures, in particular the measurement of REE.

Psychological outcomes

Profile of Mood States survey and diet acceptability: as stated in our original published protocol (17), we intended to measure mood states and diet acceptability via the Profile of Mood States survey (POMS 24) and the custom-made Process Evaluation survey, respectively. However, instead of using POMS 24, we used the abbreviated version of the Profile of Mood States (ie, POMS A), as this tool has been validated in a trained population (25). Diet acceptability was determined via both the assessment of self-reported dietary adherence and participant dropout, as these measures arguably provide a more accurate depiction of diet acceptability than the aforementioned Process Evaluation survey. Moreover, we also added the following psychological measurements to the trial (listed below), to provide a broader evaluation of the psychological consequences of energy restriction. The psychological measures were administered as online surveys using Qualtrics (Qualtrics, Utah, United States).

Muscle Dysmorphic Disorder Inventory (MDDI): The MDDI is a 13-item survey including questions pertaining to cognitions, emotions, and behaviours related to body image (26). Answers are provided on a 5-point Likert Scale to assess three diagnostic factors associated with muscle dysmorphia, namely drive for size, appearance intolerance, and functional impairment. The drive for size subscale consists of questions relating to thoughts of being smaller, less muscular, and weaker than desired. The appearance intolerance subscale consists of questions regarding negative beliefs about one's body and appearance anxiety. Finally, the functional impairment subscale consists of questions about behaviours relating to avoidance of social situations and negative emotions because of preoccupation with one's body.

Three-Factor Eating Questionnaire: This questionnaire is a 51-item questionnaire used to assess aspects of eating behaviour, namely cognitive restraint of eating, disinhibition, and behavioural consequences of hunger (27).

Eating Disorders Examination Questionnaire: This questionnaire provides a measure of the range and severity of eating disorder behaviours (28). Scores for dietary restraint, eating and weight/shape concerns are derived to assess eating disorder behaviours (ie, binge eating, very strict dieting, purging). We administered this questionnaire as per our previous publication (29).

Loss of Control Over Eating Scale: A significant feature of eating disorders is the experience of loss of control over eating, an issue addressed by this questionnaire (30).

Appetite

Initially, we intended to measure drive to eat by using questions pertaining to both current drive to eat as well as overall drive to eat during the past week, as detailed in our previously-published protocol (17). Instead, this study measured only the current drive to eat (in the fasting state), with a survey designed in line with previously-published guidelines on good practice in carrying out appetite research (31). This was considered to provide a more accurate assessment of any differences in appetite between groups, or any changes in appetite occurring as a result of the interventions. The survey consisted of 8 items, with questions pertaining to current feelings of hunger, desire to eat, the amount of food one feels one could eat (prospective consumption), satisfaction, fullness, as well as nausea, irritability, and alertness.

Hormones involved in the regulation of fat mass, fat-free mass, resting energy expenditure, and appetite

Blood was collected in the fasted state from a subset of participants (n = 17 for the mIER group and n = 16 for the mCER group). Approximately 1500 μL of blood was sampled from the median cubital vein into a 2 mL tube containing EDTA (Terumo Corporation, Tokyo, Japan). Whole blood was aliquoted (480 µL aliquots) into microtubes, with one microtube containing 20 µL of the protease inhibitor Pefabloc SC (Sigma-Aldrich, Missouri, United States), important for analysis of active ghrelin. All microtubes were centrifuged at 3000 x *g* for 10 minutes at 4°C within 30 minutes of collection. Following centrifugation, the plasma was transferred to plastic tubes and immediately stored at -80°C until further analysis. Samples were analysed for leptin, active ghrelin and peptide YY using the Milliplex metabolic panel kit (Merck, Massachusetts, United States), and read on a Luminex 200 instrument (Luminex, Texas, United States). The intra- and inter-assay coefficients of variation (respectively) were 5.5% and 13.4% for leptin, 2.5% and 5.5% for active ghrelin, and 6.8% and 9.6% for peptide YY. Samples were analysed for insulin like growth-factor-1, testosterone and free 3,3′,5-triiodothyronine in a single assay run using DiaSorin reagents (DiaSorin, Minnesota, United States) and the automated immunoassay instrument Liasion XL (Liasion Technologies, Georgia, United States). The intra-assay coefficients of variation for insulin like growth factor-1, testosterone and free 3,3′,5-triiodothyronine were 5.0%, 4.8% and 7.3%, respectively. The rationale for the hormones selected in our analysis has been described previously (17).

Statistical analyses

All outcome variables were analysed using intent-to-treat principles, with baseline values carried forward for any missing values. The intention-to-treat analyses include every participant who was randomized according to randomized treatment assignment, ignoring level of compliance, protocol deviations and withdrawals. In addition to intention-to-treat analyses, we also applied completers-only (per-protocol) analyses to 3 trial outcomes: our co-primary outcomes of fat mass and fat-free mass, as well as weight. The completers-only (per-protocol) analyses included only participants who completed the trial per-protocol, which was defined as completion of daily reporting of body weight and of energy and macronutrient intake in the smartphone/online diaries provided, and meeting all testing requirements up to and including week 12 of energy restriction. Completers-only (per-protocol) analyses were omitted for all other outcome variables given that overall attrition was less than 20%, and because completers-only analyses gave the same results as our intention-to-treat analyses for our co-primary outcomes and weight. We decided to analyse men and women together because it appears men and women respond similarly to an intermittent dieting protocol, such as the one we used in this trial. Case in point, women prescribed an intermittent dieting regime had less weight regain after the weight loss intervention and better maintained their resting energy expenditure compared to women prescribed a continuous dieting regime (12). Similarly, for men, one study showed that those prescribed an intermittent dieting regime also has less weight regain post diet and better maintained their restring energy expenditure, compared to those prescribed a continuous dieting regime (11), For all outcome variables, comparisons between groups were made at 15 weeks in mIER and 12 weeks in mCER (after equal time in energy restriction), as well as at 15 weeks in both groups (after equal absolute time). Since data for physical activity, sleep, psychological variables, and appetite were also collected at 6 weeks of energy restriction (occurring at 7 weeks in mIER and 6 weeks in mCER), these time points were also included in our analyses.

Statistical analysis was conducted on absolute values as opposed to change scores (as proposed in our published protocol) in light of literature on optimal analysis of data for randomized controlled trials (32). For this reason, between-group analyses were performed using analysis of covariance (ANCOVA), with group (mIER or mCER) as a fixed factor and the baseline value as a covariate. The assumption of equality of variances was assessed using Levene's test.

The assumption of the normality of residuals was checked using Q-Q plots. When these assumptions were violated, a Kruskal-Wallis test was performed instead of ANCOVA. All within-group comparisons were performed using repeated measures analysis of variance (ANOVA) with planned contrasts, whereby 12 and/or 15 weeks as well as 6 or 7 weeks for some outcomes were compared to baseline (week 0), with the exception of mIER for outcomes that were only measured at baseline and 15 weeks, in which case paired t-tests were used. Normality assumptions for paired t-tests were verified using a Shapiro-Wilk test. In the case of violation of the assumption of normal distribution of data, a Wilcoxon Signed Rank test was used instead of a paired t-test. To determine whether there were any differences between groups in dropout from the study and dietary adherence, a Chi-square test was used.

The co-primary outcomes of this trial were fat mass (kg) and fat-free mass (kg) after 12 weeks of energy restriction (occurring at 15 weeks in mIER and 12 weeks in mCER). The sample size for this trial was calculated as detailed previously (17), and was based on the co-primary outcomes of fat mass and fat-free mass, because loss of fat mass and retention of fat-free mass during weight loss are equally important to training adults. This trial was powered to detect a 1 kg difference in fat loss and a 0.75 kg difference in fat-free mass retention between groups. As actual dropout rate (12/61, 19.7%) was similar to our anticipated dropout rate of 20%, this trial was adequately powered to assess these co-primary outcomes. Given the examination of two co-primary outcomes, effects for fat mass and fat-free mass were considered significant at $P \leq 0.025$. Effects for all other outcome variables were considered significant at $P \leq 0.05$. Data are reported as means (with SDs) unless otherwise specified.

Ethics approval

This study was approved by the Human Research Ethics Committee at the University of Western Australia (RA/4/20/4340).

Consent

Written informed consent was obtained from each eligible participant prior to study inclusion. Participants also signed informed consent regarding publication of their data.

Results

All outcomes measured before, during and/or after the mIER and mCER interventions are presented in **Table 1 (Supplementary Data File)**.

Participant details, attrition rate and adherence

Participants were recruited between August 2018 and July 2019, and 61 participants were randomized to the trial (**Figure 2**). Of the 61 participants, 29 (47.5%) were male and 32 (52.5%) were female. Participants had a mean (SD) age of 28.7 (6.5) years, a mean (SD) weight of 77.2 (16.1) kg, and a mean (SD) body fat percentage of 25.5 (6.1)%, with 22.4 (7.3)% in men and 30.0 (6.1)% in women. At baseline (0 weeks), there were no apparent differences between groups in percent of male and female participants, age, weight, body fat percentage, or the primary outcome variables of fat mass and fat-free mass (Table 1, Supplementary Data File). Most (55 of 61, or 90.2%) of the participants were engaged in competitive sports. Overall, 49 of 61, or 80.3%, of participants completed the 15-week intervention, with 26 of 30, or 86.7%, in mIER versus 23 of 31, or 74.2%, in mCER. There were half as many participants discontinuing the trial in mIER compared with mCER (4 versus 8 participants, which corresponds to 13.3% and 25.8% attrition, respectively), albeit this difference was not statistically significant (P = 0.220). Of the 26 participants that completed the 15-week mIER intervention, 23, or 88.5%, were adherent as per our definition of adherence outlined in the Materials and methods section, whereas of the 23 participants that completed the 15-week mCER intervention, 18, or 78.3%, were adherent, with no significant difference between groups. If we assume that participants who discontinued the trial did *not* adhere to the intervention, then 23 of 30, or 76.7%, in the mIER group were adherent, versus 18 of 31, or 58.1%, in the mCER group, also with no significant difference between groups. Results were similar when examining adherence during the 12 weeks of energy restriction only, with 22 of 26, or 84.6%, and 19 of 23, or 82.6%, of participants meeting our definition of adherence in mIER and mCER, respectively (22 of 30, or 73.3%, and 19 of 31, or 61.3%, in mIER and mCER, respectively, when assuming that people who discontinued the trial were not adherent), with no significant difference between groups.

Self-reported energy intake and weight

During the 12 weeks of energy restriction (which in mIER was from weeks 0 to 3, 4 to 7, 8 to 11 and 12 to 15, and which in mCER was from weeks 0 to 12, Figure 3), mean overall self-reported energy intake was 6880 kJ per day, which is an average of 3560 kJ per day lower than self-reported energy intake at week 0, with no significant difference between groups (Figure 3A and Table 1, Supplementary Data File). In keeping with this energy intake being less than energy requirements, self-reported weight decreased by an overall average of 0.37 kg per week over the 12 weeks of energy restriction, with no difference between groups (Figure 3B, Table

1, Supplementary Data File). The mIER group also appeared to adhere to the instructions for diet breaks. Indeed, during weeks 3 to 4, 7 to 8 and 11 to 12, energy intake in the mIER group was approximately 2260 kJ per day greater than during energy restriction (indicated by shaded vertical bars in Figure 3A, Table 1, Supplementary Data File). Despite this increase, energy intake was still an average of 1610 kJ per day less than at week 0. However, consistent with a state of energy balance during diet breaks is the observation of negligible average changes in self-reported weight (~0.09 kg) during the week-long diet breaks (indicated by shaded vertical bars in Figure 3B, Table 1, Supplementary Data File). When weight was measured in our laboratory at the end of 12 and/or 15 weeks, both groups were found to weigh significantly less than they did at baseline (week 0), consistent with the approximately 80% dietary adherence among completers in both groups, with no significant difference between groups after 12 weeks of energy restriction, which was at 15 weeks in mIER and at 12 weeks in mCER (Figure 3C, Table 1, Supplementary Data File). However, participants in the mIER intervention did weigh significantly less than those in the mCER intervention when the groups were compared at the end of 15 weeks (Figure 3C, Table 1, Supplementary Data File).

Fat mass, fat-free mass, resting energy expenditure, and hormonal regulators thereof

There was no significant difference between groups (mIER and mCER) in our co-primary outcomes of fat mass (in kg) or fat-free mass (in kg) after 12 weeks of energy restriction, which corresponds to 15 weeks in the mIER intervention and 12 weeks in the mCER intervention (Figure 3D and 3G, Table 1, Supplementary Data File). Even when we compared the groups after an equivalent absolute timeframe (15 weeks), there was no difference between groups in these co-primary outcomes. Moreover, there were still no differences in the absolute weight of fat mass or fat-free mass between groups when we compared only the subset of participants from each group who completed all intervention requirements up to and including week 15 (completers-only / per-protocol analyses, data not shown).

In keeping with the lack of difference in absolute fat mass between groups, there were also no significant differences between groups in relative fat mass (fat mass as a percent of body weight, Figure 3E, Table 1, Supplementary Data File) or fasting plasma concentrations of leptin (Figure 3F, Table 1, Supplementary Data File), which is highly correlated with fat mass (33). Consistent with the lack of difference in fat-free mass between groups (Figure 3G, Table 1, Supplementary Data File), there were no significant differences between groups in fasting circulating concentrations of insulin like growth factor-1 (Figure 3H, Table 1, Supplementary Data File) or testosterone (Figure 3I, Table 1, Supplementary Data File), which are major regulators of fat-free mass (34). Moreover, resting energy expenditure (which is predominantly determined by fat-free mass (35)), and fasting circulating concentrations of free 3,3′,5-triiodothyronine (a major modulator of resting energy expenditure (36)), were not significantly different between the two interventions (Figure 3J and 3K, Table 1, Supplementary Data File).

Despite the lack of difference between groups in our co-primary outcomes and related variables, both interventions were associated with significant reductions from baseline (week 0) in weight, absolute and relative fat mass, and leptin, insulin like growth factor-1, resting energy expenditure and free 3,3′,5-triiodothyronine (Figure 3, Table 1, Supplementary Data File). The only variables from Figure 3 that were not significantly decreased from baseline in both interventions were fat-free mass and testosterone, where the reductions from baseline were only seen in mIER and mCER, respectively (Figure 3G and 3I, Table 1, Supplementary Data

File). However, it must be emphasised that a difference from baseline in one group but not the other does not constitute a difference between groups (37, 38).

Physical activity

All participants reported full compliance to the instructions for wearing the accelerometers during the 7-day collection period. In general, none of the components of physical activity changed from baseline (week 0) in either intervention, with the exception of physical activity energy expenditure, which fell transiently with mIER, but not with mCER, after 6 (but not after 12) weeks of energy restriction (Table 1, Supplementary Data File). There were no significant differences in physical activity levels between interventions, except for a transiently greater time in sedentary activity in the mIER versus the mCER intervention after 6 (but not after 12) weeks of energy restriction (Table 1, Supplementary Data File).

Sleep

The Epworth sleepiness scale scores increased in response to both interventions, but did not differ between interventions after 12 weeks of energy restriction (Table 1, Supplementary Data File). The Pittsburgh sleep quality index score was not affected by either of the interventions (Table 1, Supplementary Data File).

Muscle performance

There were no significant differences between interventions for any of the markers of muscle strength (peak torque, power, and total work during the maximum-effort 3-repetition set) or endurance (total work during the maximum-effort 25-repetition set, and work during the last third of the maximum-effort 25-repetition set) in the legs (hamstrings, quadriceps) or arms (biceps, triceps) (Table 1, Supplementary Data File). In general, a number of indicators of leg (but not arm) muscle strength increased from baseline, while a number of indicators of muscle endurance decreased from baseline, in mCER but not in mIER (Table 1, Supplementary Data File). Again, changes from baseline in one group but not the other does not mean that the two groups are different from each other (37, 38). Overall, the results suggest that neither dietary approach is superior for supporting muscle performance during energy restriction.

Psychological outcomes

There was a tendency for psychological disruption to increase during both interventions, with indicators of mood disturbance (from the POMS A), muscle dysmorphia, cognitive restraint, behavioural consequences of hunger (from the Three-Factor Eating Questionnaire), concern regarding eating, and restraint (from the Eating Disorders Examination Questionnaire) increasing from baseline in both groups. Of all the psychological variables that we measured (mood disturbance, muscle dysmorphia, eating disorder psychology, and loss of control over eating), there were no significant differences between interventions at any time point (Table 1, Supplementary Data File).

Appetite and hormonal regulators thereof

The only other variables that differed between the two interventions at the end of energy restriction were appetite sensations and fasting plasma concentrations of peptide YY (a regulator of satiety (39)). Specifically, participants in mIER experienced significantly less drive to eat than those in mCER after 12 weeks of energy restriction, as indicated by significantly lower measures of hunger and desire to eat (but not prospective consumption), as well as significantly greater measures of satisfaction (but not fullness) (Figure 4A to 4E, Table 1 in the Supplementary Data File) and significantly higher plasma concentrations of the satiety hormone peptide YY (Table 1 in the Supplementary Data File). Despite the significantly lower levels of hunger and desire to eat in mIER compared to mCER, this was not reflected by a difference in fasting plasma concentrations of active ghrelin (a modulator of hunger (40)) between interventions for any time point (Table 1 in the Supplementary Data File). The other variables measured during assessment of appetite sensations (irritability, alertness, and nausea) showed no significant differences between the two intervention groups (Table 1 in the Supplementary Data File).

When comparing appetite sensations to baseline (week 0), participants in mIER exhibited no significant changes in hunger, desire to eat, prospective consumption or satisfaction over the course of the intervention, albeit there was a significant decrease in fullness after 12 weeks of energy restriction (Figure 4, Table 1 in the Supplementary Data File). In contrast, those in mCER showed significant increases from baseline in hunger, desire to eat and prospective consumption, with significant decreases from baseline in satisfaction and fullness, after 6 and/or 12 weeks of energy restriction (Figure 4, Table 1 in the Supplementary Data File). Interestingly, the mCER but not the mIER group exhibited significant increases from baseline in irritability and nausea and a significant decrease in alertness (Table 1 in the Supplementary Data File), suggesting that the increased drive to eat may have been distracting to participants in the mCER intervention.

Discussion

This study shows that in resistance-trained adults, intermittent energy restriction delivered as alternating 3-week periods of moderate energy restriction and 1-week 'diet breaks' (ie, mIER) for a total of 15 weeks (12 weeks in energy restriction), does not result in lower fat mass or greater fat-free mass compared to 12 weeks of continuous moderate energy restriction (mCER). Participants in the mIER group did however achieve a 1.3-kg lower weight than those in the mCER group when both groups were compared at the end of 15 weeks. This magnitude of weight difference could be practically significant for trained adults involved in weight class sports (eg, boxing, powerlifting), but not for most resistance-trained adults who are usually primarily concerned with the composition of weight loss (ie, loss of fat mass with concomitant retention of fat-free mass) as opposed to absolute weight loss (7). There were no differences between interventions in REE, plasma concentrations of hormones that regulate fat mass, fat-free mass, and REE (ie, leptin, insulin like growth factor-1, testosterone and free 3,3′,5-triiodothyronine), physical activity levels, sleep, muscle performance, and components of psychology ie, mood, muscle dysmorphia and eating disorders). However, participants in mIER exhibited significantly less drive to eat than those in mCER, as indicated by significantly lower sensations of hunger and desire to eat, and significantly greater sensation of satisfaction and fasting circulating concentrations of the appetite-suppressing hormone peptide YY. While adherence to the dietary energy prescription was high in both groups (approximately 80%), dropout from the mIER intervention was about two-fold less than dropout from the mCER intervention (13.3% versus 25.8%, albeit the difference was not statistically significant), suggesting that participants found mIER easier to adhere to than mCER. Thus, while the same loss of fat mass and the same retention of fat-free mass was achieved with mIER compared to mCER in resistance-trained adults, mIER achieved these results with less drive to eat, albeit with a 25% longer intervention duration.

These findings in resistance-trained adults contrast with two previous trials in adults with overweight or obesity, in which CER was compared to IER using moderate energy restriction (ie, not intermittent fasting) alternating with 2-week diet breaks in adult men (the MATADOR study) (11) or 3-day refeeds in adult women (12). The IER interventions in both trials led to superior loss of weight and fat, and superior retention of REE, compared to CER. Our contrasting observation that resistance-trained adult men and women did not respond to IER with lower fat mass compared to CER could be related to differences in dietary composition between studies, but also the possibility that IER facilitates greater compliance than CER to prescribed energy intake in people with overweight or obesity, but not in training adults such as competitive athletes, who are typically compliant despite difficult interventions, thanks to their unusually-high levels of mental toughness, resiliency, and self-discipline (41). To exemplify this latter point, the MATADOR study reported a significantly greater retention of REE, by ~390 kJ per day, in the IER compared to the CER group, yet this difference in REE between groups is unlikely to explain the approximately 4.8 kg weight loss difference between groups over the 16 weeks of energy restriction (11). Our interpretation is based on calculations that an extra 4.8 kg of weight loss over 16 weeks would require an additional 1242 kJ restriction per day, but 1242 kJ per day is over three times greater than the approximately 390 kJ per day higher REE in IER versus CER. Thus, a reasonable hypothesis is that the superior loss of fat mass observed with IER compared to CER in adults with overweight or obesity is partially attributed to greater adherence to prescribed energy intake. In our study, however, we observed no significant difference in adherence between participants in mIER versus mCER, and adherence was generally high (approximately 80%), despite the significantly greater drive to eat in mCER versus mIER. Thus, it is possible that while people with overweight or obesity in IER interventions may have experienced lower hunger and greater satisfaction leading to greater dietary compliance and subsequently greater loss of fat mass compared to those in CER interventions, the mCER group in the current trial likely adhered to the protocol regardless, due to the trained nature of the cohort (42).

A recently-published randomised controlled trial by Campbell et al also investigated an IER protocol (compared with CER) in resistance-trained adults (43). Their IER protocol alternated (for a total of 7 weeks) 5 days of moderate energy restriction with 2-day refeeds achieving energy balance. The authors conducted a completers-only (per-protocol) analysis of the 27 participants who remained in the trial and complied with the intervention (of the 58 participants originally recruited), and concluded that those in the IER group showed no difference from those in the CER group in loss of fat mass (like in the present trial), but (unlike the present trial) greater retention of fat-free mass, dry fat-free mass, and REE, compared to those in the CER group. However, in our statistical analysis (38) of the completers' data that was provided by the authors in the online supplementary material (43), we found, using ANCOVA with baseline values as a covariate (32), that the only statistically significant difference between groups (IER and CER) was in dry fat-free mass, and there were no differences between IER and CER in fat mass, fat-free mass or REE – similar to our findings. Thus, our current findings do not contradict the results observed using the aforementioned 2-day refeed protocol in resistance-trained adults. It is worthwhile noting that the trial by Campbell et al, like our trial, also recruited a mixed-sex cohort with lean body compositions. Considering that the two trials mentioned above investigating 2-week diet breaks in adult men (11) or 3-day refeeds in adult women (12) showed superior results with an IER approach compared to CER in adults with overweight or obesity, it is unlikely that the contrasting findings between our study and those previous studies (11, 12) were due to us examining a mixed-sex cohort, but were instead due to differences in the starting BMI or body composition of the cohorts. We therefore conclude that in resistance-trained adults, neither an IER protocol that alternates 3 weeks of moderate energy restriction with 1-week diet breaks (as in the current trial), nor an IER protocol that alternates 5 days of moderate energy restriction with 2-day refeeds (43), improves fat loss or retention of fat-free mass or REE.

The lack of greater REE retention observed in the IER group in the current trial and in another recent trial (43) compared to CER, might be concerning for training adults, as it brings into question the commonly-held assumption that IER protocols (ie, the use of diet breaks or refeeds during energy restriction) prevent downgrades in REE ('metabolic rate' as it is commonly named) and/or even stimulates REE (8), leading to superior fat loss efficiency. It has been speculated that any physiological benefits provided by IER could be driven by a transient increase in circulating concentrations of leptin (7, 8), yet our findings dispute this notion by demonstrating no significant differences in the circulating concentrations of leptin between mIER and mCER at any time point.

There was a trend for overall psychological disruption in both groups during the trial. Specifically, we found increases in sleepiness, mood disturbance, muscle dysmorphia, cognitive restraint, behavioural consequences of hunger, and concerns about eating at the completion of 12 weeks of energy restriction in both groups, which aligns with previous research on trained adults undergoing energy restriction, exhibiting increased fatigue, difficulties concentrating, worsened mood and heightened irritability (7, 42, 44, 45). Furthermore, in a group of body builders post energy restriction, 81% of participants reported increases in anxiety, anger, food preoccupations and binge eating episodes (46). Thus, psychological disturbances appear to accompany energy restriction in resistance-trained adults, regardless of whether an intermittent or continuous approach is adopted. To minimise the prolongation of negative psychological outcomes, researchers have recommended a quantified, tapered energy surplus for resistance-trained adults to induce steady rather than rapid weight regain once the weight loss phase is complete (47). Given that by the end of the diet in the present trial (week 12 of energy restriction), eating psychology had deteriorated, as evidenced by significant changes in the behavioural consequences of hunger and in concern over eating, then resistance-trained adults could be at a greater risk of eating more and rapidly regaining weight after the diet. Thus, support and coaching (from coaches or otherwise) may be advisable to allow resistance-trained adults to transition back to regular eating behaviours following interventions for fat loss (48, 49).

Strengths of this randomized controlled trial include its design in line with SPIRIT guidelines (50), the fact that it was adequately powered for our co-primary outcomes of fat mass and fat-free mass, the high participant retention rate we achieved (80.3%, which is relatively high for a weight loss intervention (51)), and the examination of both sexes. Additionally, the inclusion of resistance-trained adults and the optimisation of macronutrition to support retention of fat-free mass (high protein intake) and exercise performance (lower fat and higher carbohydrate intake) during energy restriction (17, 52, 53) makes these findings particularly applicable to healthy, training adults, as most previous studies of IER versus CER were conducted in sedentary people with overweight or obesity, and trained individuals were required to extrapolate that data if they wanted to apply it to their own situation. However, of note, it is possible that the dietary composition used in this study could explain some of the discrepancies with research on intermittent energy restriction in individuals with overweight and obesity.

In addition to strengths, this study also has some limitations. Firstly, given the demanding requirements of the intervention, there was some attrition, despite being comparatively low for a weight loss intervention. While higher participant retention would have increased statistical power, our results did not differ between the intention-to-treat and completers-only (per-protocol) analyses. A second limitation was that physical activity accelerometers were used in a subset of 12 participants only, thus conclusions for physical activity levels between groups are not clear. Another limitation was the use of DXA assessment for the measurement of body composition. The use of DXA for this purpose has been criticised recently, with individual error rates as high as 8-10% (54, 55). However, DXA is generally accepted as an appropriate method for comparison of group means, with group error estimates between 2-3% (56). Of note, despite considerable advancement in body composition assessment methods, there is still no method of body fat assessment with error rates below 1% (56). DXA also has several advantages, namely speed and convenience, and measurements are minimally influenced by fluctuations in body water content (56). An additional limitation of the current trial is that the resistance training program that participants engaged in was not supervised. Changing training schedules or training style during the trial could impact on retention of fat-free mass, as well as potentially also causing changes in daily physical activity energy expenditure, making it difficult to discern whether any or differences or changes in body weight/fat mass were due to the intervention, or due to changes in training. To minimise the potential for this to occur, a key component of our eligibility criteria for participation was that the participant expected that their training regimen would be consistent during the duration of the weight loss intervention. It is also possible that as our primary outcome measures were taken after 15 weeks of contact in mIER and 12 weeks in mCER (ie, after 12 weeks of energy restriction in both groups), the extra 3 weeks of interactions with participants in the mIER group may have caused an effect independent of the dietary intervention. However, by incorporating a measurement time point at 15 weeks in both groups, this is controlled for, thereby further supporting our conclusions.

In conclusion, mIER and mCER are viable weight loss options for resistance-trained adults. While similar fat mass and fat-free mass were achieved after 12 weeks of energy restriction, mIER was attended by a lower drive to eat. Of course, this benefit of mIER must be weighed against the greater absolute time required in mIER to achieve the same amount of fat loss. Thus, if duration is not an issue, IER may be a preferable fat loss intervention for resistance-trained adults due to superior appetite management. However, if a certain body composition is required as soon as possible, CER is likely a more suitable choice, albeit CER may be harder to adhere to than IER as it is accompanied by a greater drive to eat.

Declarations

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Conflicts of interest

AS owns 50% of the shares in Zuman International, which receives royalties for books she has written about adult weight management and payments for presentations at industry conferences. She has also received presentation fees and travel reimbursements from Eli Lilly and Co, the Pharmacy Guild of Australia, Novo Nordisk, the Dietitians Association of Australia, Shoalhaven Family Medical Centres, the Pharmaceutical Society of Australia, and Metagenics, and served on the Nestlé Health Science Optifast VLCD advisory board from 2016 to 2018.

Availability of data and material

Data generated during and/or analysed during the current study are available upon request from the authors.

Author contributions

JJP led the drafting of the manuscript with mentoring and supervision by AS. JJP, ERH, PAF and AS conceived of the study. JJP coordinated the study, and with JO, CH and AS arranged study protocols. JJP and JK conducted the statistical analyses with input from AS. All authors read and approved the final manuscript.

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The authors declare that the results of this study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation. The results of this study do not constitute endorsement by ACSM.

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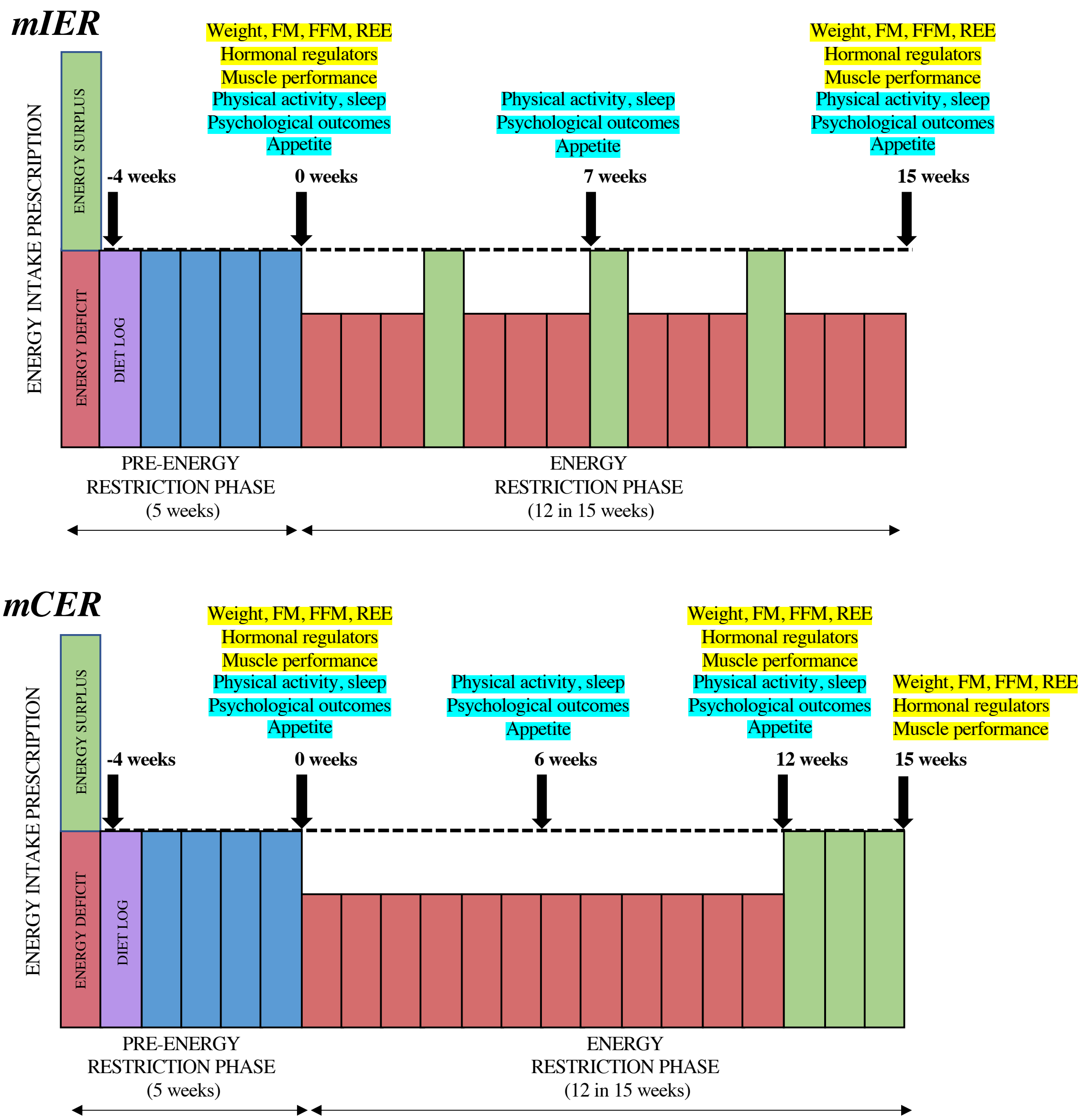

Figure 1. Summary of the protocol for the ICECAP randomized controlled trial
Measurements of body weight, fat mass (FM), fat-free mass (FFM), resting energy expenditure (REE), hormonal regulators of outcomes (ie, fasting plasma concentrations of leptin, insulin like growth factor-1, testosterone, free 3,3′,5-triiodothyronine), and muscle performance (strength and endurance) were made at baseline (0 weeks), at 15 weeks in mIER and 12 weeks in mCER (after equal time in energy restriction), and at 15 weeks in both groups (after equal absolute time). Physical activity (measured using 3-dimensional wrist accelerometers) and sleep (sleep quality and sleepiness, measured via surveys), psychological outcomes (mood disturbance, muscle dysmorphia, and eating disorder psychology, measured via surveys), and sensations of hunger, desire to eat, prospective consumption, satisfaction and fullness (measured using visual analogue scales in the fasting state) were additionally measured after 6 or 12 weeks of energy restriction (which are at 7 and 15 weeks in mIER due to the 1-week diet breaks taken after every 3 weeks of energy restriction).

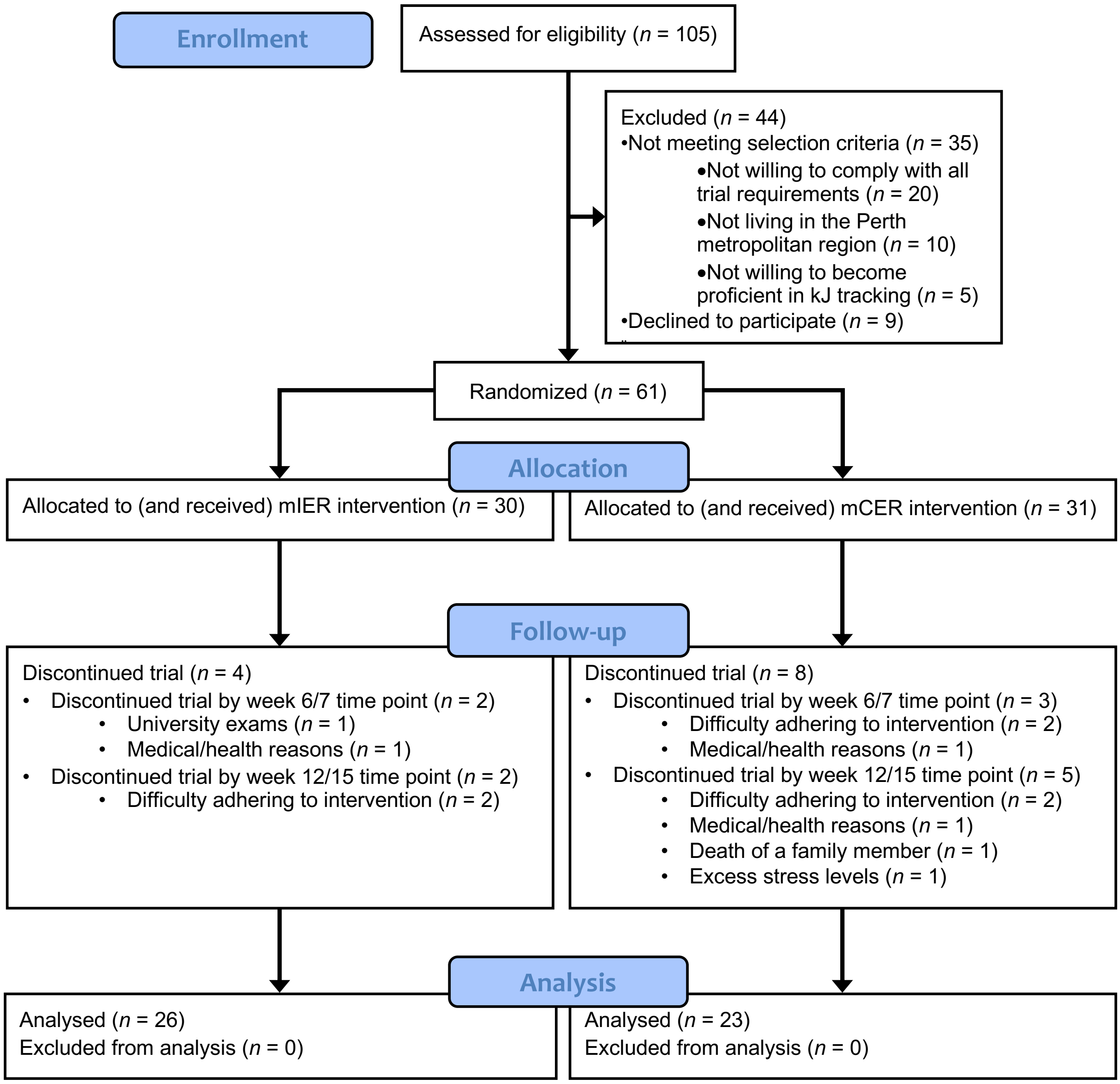

Figure 2. Flow of participants through the ICECAP Trial (Intermittent versus Continuous Energy restriction Compared in a resistance-trained Adult Population)

Both groups of resistance-trained adults undertook a 4-week weight maintenance diet followed by 12 weeks of moderate energy restriction. Energy restriction interventions were delivered as either (1) moderate intermittent energy restriction (mIER): 4 x 3-week blocks of moderate energy restriction interspersed with 3 x 1-week blocks of energy balance (15 weeks total), or (2) moderate continuous energy restriction (mCER): 12 weeks of continuous moderate energy restriction.

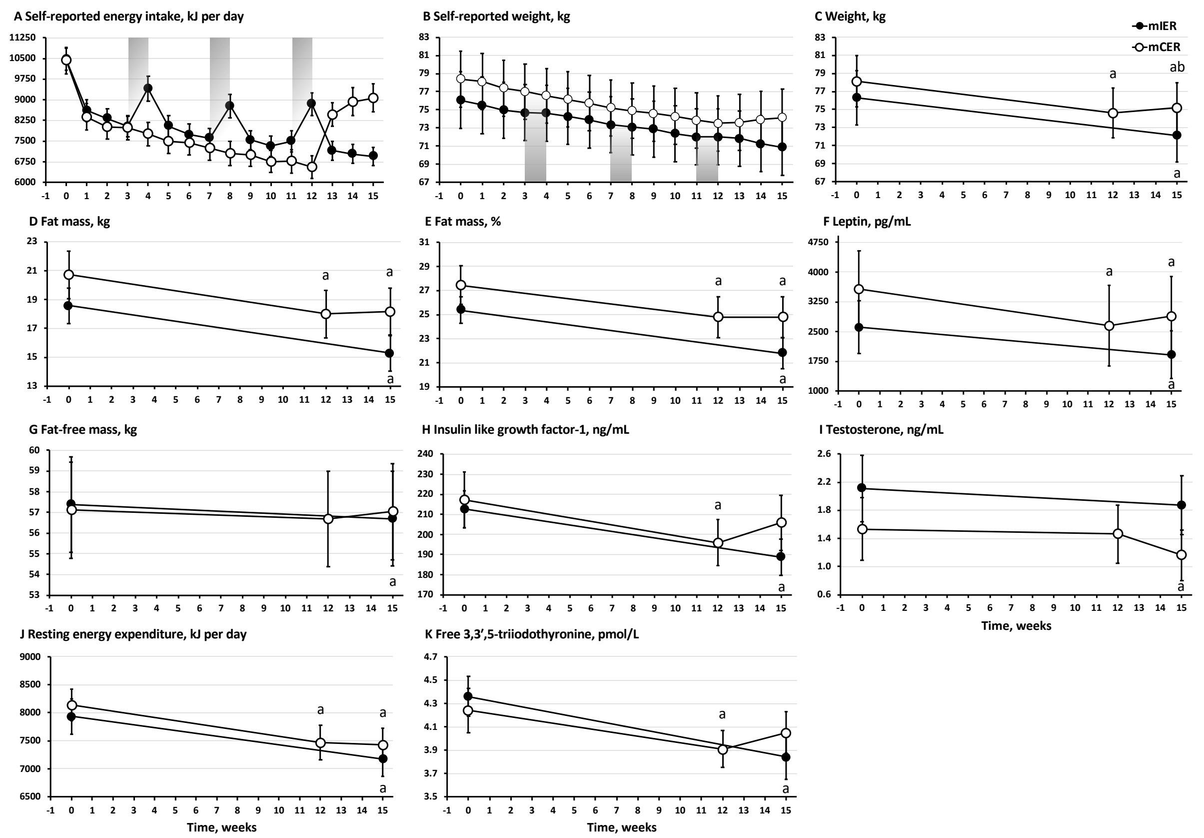

Figure 3. Effect of moderate intermittent energy restriction (mIER) versus moderate continuous energy restriction (mCER) on body composition in resistance-trained adults

(**3A-3B**) Self-reported energy intake (kJ/d) and self-reported body weight (kg) in mIER and mCER during 12 weeks of energy restriction and 3 weeks of energy balance. Shaded horizontal columns represent 'diet breaks' in the mIER group. (**3C-3K)** Comparisons between mIER and mCER in body weight (kg), fat mass (kg and % of body weight), plasma concentrations of leptin (pg/ml), fat-free mass (kg), plasma concentrations of insulin like growth factor-1 (ng/ml) and testosterone (ng/ml), resting energy expenditure (kJ/day), and free 3,3′,5-triiodothyronine (pmol/L), made at baseline (0 weeks), at 15 weeks in mIER and 12 weeks in mCER (after equal time in energy restriction), and at 15 weeks in both groups (after equal absolute time). Data are means ± SEM. a, significant difference compared to baseline, $p < 0.05$. b, significant difference between groups, $p < 0.025$ for the co-primary outcomes of fat mass and fat-free mass, $p < 0.05$ for all other outcome variables.

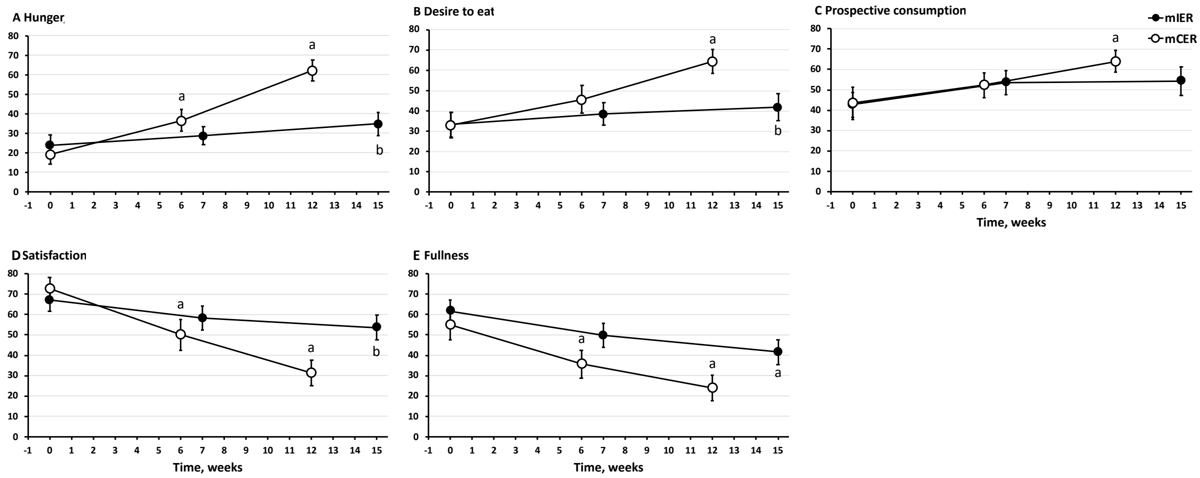

Figure 4. Drive to eat and satisfaction with moderate intermittent energy restriction (mIER) versus moderate continuous energy restriction (mCER) in resistance-trained adults

Sensations of **(4A)** hunger, **(4B)** desire to eat, **(4C)** prospective consumption, **(4D)** satisfaction and **(4E)** fullness, measured by visual analogue scales (in mm) in the fasting state after 6 or 12 weeks of energy restriction (which are at 7 and 15 weeks in mIER due to the 1-week diet breaks taken after every 3 weeks of energy restriction). Data are means ± SEM. a, significant difference compared to baseline, $p < 0.05$. b, significant difference between groups, $p < 0.05$.