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Continuous versus intermittent moderate energy restriction for increased fat mass loss and fat free mass retention in adult athletes: protocol for a randomised controlled trial—the ICECAP trial (Intermittent versus Continuous Energy restriction Compared in an Athlete Population)

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ABSTRACT

Introduction Reducing fat mass (FM) while retaining fat free mass (FFM) is a common goal of athletes. Evidence suggests that some—but not all—forms of intermittent energy restriction (IER) may be superior to the conventional method of continuous energy restriction (CER) for people with excess body fat that are sedentary, by reducing some of the adaptive responses to ER. However, it is yet to be established whether this dietary approach is effective for athletes.

Methods and analysis A single-blind, parallel group, randomised controlled trial with a 1:1 allocation ratio is proposed. Sixty healthy athletes aged ≥18 years will be recruited from local sporting facilities and randomised to an intervention of either moderate CER (mCER) or moderate IER (mIER). Both interventions will consist of 12 weeks of moderate ER, plus 3 weeks in energy balance (EB). The mCER intervention will entail 12 weeks of continuous moderate ER, followed by 3 weeks in EB. The mIER intervention will entail 12 weeks of moderate ER, administered as 4×3 week blocks of moderate ER, interspersed with 3×1 week blocks of EB. The co-primary outcomes are changes in FM and FFM after 12 weeks of moderate ER. Secondary outcomes will be changes in FM and FFM at 15 weeks after intervention commencement, as well as muscle performance, physical activity, sleep quality, changes in resting energy expenditure, subjective drive to eat, circulating concentrations of appetite-regulating hormones, mood states and diet acceptability.

Trial registration ACTRN12618000638235p.

INTRODUCTION

Athletes, although not typically obese or over fat, may benefit from reducing body weight to be competitive in a target weight-class (eg, combat sports, weight lifting), weight-sensitive sports (eg, endurance events, ski jumping) or aesthetically judged sports (eg, gymnastics, bodybuilding). Within athletic populations, the most common nutritional strategy implemented to achieve desired body composition is continuous energy restriction (CER).[1 2] Specifically, CER involves reducing energy intake every day relative to weight maintenance energy requirements.[3] Thus, CER is sometimes referred to as 'daily energy (or caloric) restriction'. Despite being commonly used, CER is accompanied by a number of metabolic and endocrine responses that collectively tend to resist ongoing loss of weight and fat mass (FM), threaten retention of fat free mass (FFM) and predispose the individual to regain weight and FM on termination of CER, notably by increasing the drive to eat and by reducing energy expenditure.[4–9] Of athlete concern, combining CER with high training loads may negatively impact performance and induce losses of FFM, which includes lean tissues such as muscle.[10]

Given the shortcomings associated with CER, alternative effective forms of weight or FM reduction are of great interest. Intermittent energy restriction (IER) is one nutritional strategy that contrasts to the conventional approach of CER by alternating periods of ER with periods of greater energy intake (often referred to as 'refeed' periods) within the weight loss phase. IER protocols described in the literature differ considerably, with significant variation in the level of energy intake

prescribed during periods of ER and refeeding, as well as the duration of these periods.[11] During refeed periods, there may or may not be restrictions placed on energy intake.

While continuous and intermittent approaches to ER have both been shown to be effective facilitators of weight loss in adults with a Body Mass Index (BMI) in the overweight or obese range,[3 12 13] a long-standing question is whether or not IER yields benefits over CER. A systematic review of robust clinical studies suggested that IER in adults of normal weight or overweight likely provides equivalent cardiometabolic benefits to CER, as indicated by reduced risk factors for cardiometabolic disease.[14] Three other reviews have provided evidence for comparable reductions in insulin resistance, fasting circulating concentrations of insulin and similar improvements in glucose homeostasis between IER and CER.[3 15 16] With respect to the effect of these dietary interventions on weight and body composition, recent clinical trials[17 18] and several reviews[3 11 13 15 16 19] indicate that IER and CER are equally effective for achieving weight and FM loss in adults with overweight or obesity. One review suggested that IER may result in greater retention of FFM than CER in adults with overweight or obesity.[3] However, more recently, other systematic reviews[11 16] and a randomised controlled trial[20] concluded that IER and CER were comparable with respect to loss of FFM in similar populations. It is worth noting that the majority of studies mentioned above pertain to a specific form of IER known as 'intermittent fasting'. While intermittent fasting has been used to describe a number of different dietary interventions—including time-restricted feeding approaches—in the context of IER, intermittent fasting has been defined as severe restriction of energy intake on at least one but no greater than 7 days, followed by a period of increased energy intake, where restrictions may or may not be placed on the quantity of foods and beverages consumed.[15 16]

While most data to date consistently show no significant difference between intermittent fasting forms of IER and CER, IER protocols that implemented longer periods of ER and refeeds have shown mixed results, some of which are promising. These longer-form IER protocols involve ≥7 consecutive days of ER, alternated with periods of no prescribed ER or a lesser degree of prescribed ER. In one study in women with overweight or obesity, 1 week of ER (a prescribed deficit of 5500 kJ/day relative to energy requirements) alternated with 1 week where each participant followed their usual diet was compared with CER (5500 kJ prescribed ER per day) for 8 weeks.[12] Weight loss at 8 weeks was not significantly different between groups (mean±SD 2.0±1.9 kg for IER vs 3.2±2.1 kg for CER); however, it is noteworthy that the IER resulted in similar weight loss to CER with less time in ER (4 weeks vs 8 weeks). These findings suggest that this form of IER results in greater weight loss efficiency (weight lost per unit of ER) when compared with CER. A recent systematic review and meta-analysis evaluated five randomised controlled trials of longer-form IER interventions in comparison with CER for the treatment of overweight and obesity in adults.[13] That report demonstrated that while both long-form IER and CER resulted in significant weight loss, there was no significant difference between interventions in weight loss either at the end of the interventions (weighted mean difference −1.36 (95% CI −3.23 to 0.51) kg, p=0.15) or at follow-up, which ranged from 14 weeks to 12 months following completion of the interventions (weighted mean difference −0.82 (−3.76 to 2.11) kg, p=0.58).[13]

Recently, however, two new randomised controlled trials—not included in the above systematic review and meta-analysis—found that some long-form IER protocols can result in greater FM loss with equivalent retention of FFM when compared with CER and can also attenuate the adaptive response to ER, at least with respect to the reduction of resting energy expenditure (REE). In one of the trials, a 6-week diet involving CER (prescribed energy intake of 45% of routine energy intake) was compared with a 6-week diet involving IER that cycled 11 days of ER (prescribed energy intake of 55% of routine energy intake) with 3 days of ad libitum feeding in 74 women with obesity.[20] There was significantly greater weight loss at 4 weeks after completion of the diet in women in the IER than in the CER group (mean±SEM was 5.8±1.2 vs 3.4%±1.4% of initial body weight, respectively). Moreover, REE was maintained at significantly higher levels in the IER than in the CER group at 6 weeks (p<0.05). The benefit of adopting a longer-form IER protocol over CER is further supported by a randomised controlled trial comparing 16 weeks of CER (prescribed energy intake of 67% of weight maintenance energy requirements) with 16 weeks of ER applied intermittently as 8×2 week blocks of ER (prescribed energy intake of 67% of weight maintenance energy requirements) alternating with 7×2 week blocks of energy balance (EB; where energy intake is matched to energy requirements for weight maintenance) in 51 men with obesity.[21] Significantly greater losses of weight and FM as well as lesser compensatory reductions in REE were observed in the IER compared with the CER group (weight loss mean±SD 14.1±5.6 vs 9.1±2.9 kg; FM loss mean±SD 12.3±4.8 vs 8.0±4.2 kg; change in REE mean±SD −360±500 vs −750±500 kJ/day). Furthermore, FFM loss was similar in both groups despite greater FM loss in the IER group. On the basis of the findings of these two trials, we hypothesise that longer-form IER may result in better body composition change for athletes than CER.

Interestingly, while IER has not been investigated in randomised controlled trials in individuals with a healthy body composition and active, such as athletes, there is evidence of athletes already adopting this dietary strategy.[10 22–24] However, athletes typically use a form of IER that is different from that which is normally used in clinical trials, namely intermittent fasting.[10] This is because severe ER—such as the severe ER used in intermittent fasting protocols—has been associated with

adverse health and performance outcomes in adult athletes, including reductions in muscle strength, reflexes and glycogen stores, and increased risk of injury due to fatigue.[10 25–27] Severe ER has also been shown to induce greater FFM losses than moderate ER, at least in lean individuals.[28] As such, athletes typically favour dietary interventions involving moderate ER,[26] which can arguably be defined as a prescribed energy intake of no less than 65% of weight maintenance energy requirements.[29] In a recent series of in-depth interviews, bodybuilders commonly reported the implementation of refeed days during pre-contest weight loss interventions, achieved primarily through elevating carbohydrate consumption.[24] Positive effects of this practice were also described, including enhanced training performance and mental recovery (which participants attributed to perceived increases in muscle glycogen storage), and a perceived prevention of further adaptive downgrades in energy expenditure. However, it is unknown how participants were able to subjectively perceive increases in muscle glycogen storage or prevention of adaptive downgrades in energy expenditure. Some participants also reported better fat loss and muscle retention when employing refeed periods during pre-contest weight loss interventions, compared with interventions without refeeds.

Due to the absence of research in the realm of IER applicable to athletes, there is a lack of consensus among coaches and nutritionists on how to successfully employ IER in the field, with many IER protocols for athletes based on anecdotal evidence alone. The development of evidence-based dietary recommendations for athletes is important, as the use of untested dietary strategies may be ineffective and may lead athletes to depend on more rapid weight loss techniques close to competition that could compromise performance and aesthetics.[1 30] We thus aim to provide an evidence-based IER protocol for athletes by investigating IER in a cohort of resistance-trained athletes, using a macronutrient profile thought to maximise retention of FFM and performance during ER.

The purpose of this paper is to detail the protocol (ACTRN12618000638235p) for a randomised controlled trial that compares CER involving moderate ER (mCER) with IER involving moderate ER (mIER) on FM loss and FFM retention in adult athletes. Our primary hypothesis is that compared with mCER, mIER will result in greater FM loss, with equivalent or greater retention of FFM, in adult athletes at the end of 12 weeks of ER. Secondary hypotheses are that athletes undergoing mIER will have greater retention of muscle performance, physical activity and REE, less drive to eat, better mood and will find the diet more acceptable than mCER.

METHODS AND ANALYSIS

Participants

Sixty athletes (see sample size calculations below) aged ≥18 years who have participated in regular resistance exercise for the previous 6 months or more will be recruited for this randomised controlled trial. Online and hard copy advertisements will be displayed across social media websites, and at local sports facilities, respectively. Publicity about the trial will also be solicited via press releases to local television, radio and print media. Interested prospective participants will be invited to contact the lead investigator (JJP) via e-mail, and in response they will be emailed a soft copy of a document outlining the Information for Participants, as well as an invitation to complete an online screening questionnaire to determine eligibility. Prospective participants will not be informed of the selection criteria for the trial prior to this step in order to help prevent them from tailoring their responses to the online screening questionnaire. All prospective participants who pass the online screening will be invited to the University of Western Australia Exercise Physiology Laboratory for a face-to-face screening appointment. At this appointment, they will be invited to sign an informed consent form and will be assessed against all inclusion and exclusion criteria listed below. Prospective participants who meet these selection criteria will have their baseline body composition assessed (described below), and—for women of reproductive age—a urinary pregnancy test will precede body composition assessment.

Inclusion and exclusion criteria

- Aged ≥18 years.
- Completed ≥2 resistance exercise sessions per week for the previous 6 months or more.
- Not currently on any weight loss programme.
- Willing to comply with a dietary weight loss intervention for ~5 months, involving weight loss for ~3–4 months and weight stability for ~1–2 months.
- Willing to comply with trial procedures for the duration of the trial, such as self-monitoring energy intake for ~5 months and attending our research facility for measurement of outcomes.
- The participant expects that their personal training regimen and dietary supplementation will be consistent during the ~5 months of the dietary weight loss intervention.
- Have access to a smart phone with internet and email access.
- Live within the Perth metropolitan region and be able to transport by car to and from the University of Western Australia.
- Have a set of body weight scales (with adequate precision and accuracy) at home.
- No tobacco use.
- No use of growth hormone or glucocorticoid or anabolic steroid products within the previous 6 months.
- Not pregnant or desiring to become pregnant during the trial.
- Predicted postintervention body fat percentage >5% for men or >12% for women.

The minimum amount of resistance exercise required for inclusion was selected in line with a previous publication that investigated weight loss in athletes.[31] This criterion is important, as accumulated data suggest that resistance exercise may increase weight loss and reduce the loss of FFM during ER in adolescents and adults with overweight or obesity,[32–36] and is more effective than aerobic exercise for retention of FFM and REE during ER.[37] Furthermore, resistance exercise with a concomitant high protein intake during ER has been shown to prevent the expected reductions in FFM in elite male and female athletes, and in amateur female athletes.[25 38] We are recruiting only participants with a consistent training schedule for the next ~5 months because shifting phases of training during the dietary intervention, such as moving from 'transition' to 'competition' phases, can result in drastic changes in daily physical activity energy expenditure and therefore energy requirements for weight maintenance. In such a situation, it would be difficult to determine whether body weight changes were due to the intervention or due to changes in training energy expenditure.

Following body composition assessment at the face-to-face screening appointment (described below), prospective participants with a calculated, predicted postintervention body fat percentage below the above thresholds will be excluded from the trial as a precautionary measure. Extreme low levels of body fat, such as <5% for men or <12% for women, are known to negatively impact health status.[39 40] This exclusion criterion has been applied in athlete weight loss trials elsewhere.[25]

Sample size

Sample size for this trial was calculated based on our co-primary outcomes of changes in FM and FFM because loss of FM and retention of FFM during weight loss are equally important to athletes. Given that athletes often go to great lengths for a 1%–2% improvement in performance, we predict that a 1 kg difference in FM loss (~1.5% of body weight) between dietary interventions would be considered practically significant for this population. Using the variance in FM loss observed among healthy male athletes 18 to 40 years old participating in regular resistance exercise and following a high-protein hypoenergetic diet (SD=0.9 kg),[31] we calculate that 42 people (21 per group) would be required to detect (two-tailed) a 1 kg difference in FM loss between diet groups with a statistical power of 0.9 (α=0.025). Additionally, a non-inferiority test for changes in FFM will be performed to determine if mIER is equivalent or superior to mCER in this respect. We selected a non-inferiority limit of 0.75 kg in FFM, as we predict that less than 0.75 kg greater retention of FFM in the mIER group compared with the mCER group would not be considered by athletes to be practically significant. Using previously-reported variance of FFM loss in the population described above (SD=0.8 kg),[31] we calculated that in order to show that there is no true difference in FFM change between diet groups, 48 people (24 per group) would be required to be 90% certain that the lower boundary of the one-sided 97.5% CI will be above the limit of −0.75 kg. Allowing for ~20% dropout during the intervention, we plan to recruit 60 participants.

Randomisation

Randomisation will be performed after completion of the face-to-face screening so that prospective participants meet all selection criteria. A computer-generated randomisation process will be used to assign participants, with a 1:1 allocation ratio, to either the mCER or mIER intervention (see interventions described below). To minimise confounding variance, participants will be stratified by sex and sport, using permuted blocks of random sizes. The block sizes will not be disclosed to investigators administering the intervention to ensure allocation concealment. To avoid bias, randomisation will be undertaken by an investigator who has not had contact with participants before randomisation and who is not involved in implementation of the dietary interventions.

Blinding/masking

Participants will not be informed of group assignment, but perfect blinding (also known as masking) is not feasible and discussion about the different diets is highly possible, particularly among participants in the same sporting team. With this considered, the two interventions will be referred to as the '1.2 diet' (mCER) and the '1.6 diet' (mIER), averting the possibility that participants will perceive one diet as being superior to the other. This strategy will also help to reduce the risk of athletes reviewing the body of literature surrounding CER versus IER. Participants will be informed that the primary purpose of the trial is to ascertain whether two different weight loss diets, shown previously to be equally effective in overweight populations, cause different body composition and performance outcomes in athletes. Due to the nature of the intervention, investigators involved with administrating the dietary intervention cannot be blinded to allocation.

Pre-energy restriction phase

The full trial timeline (detailed in figure 1) shows the three phases of the trial: pre-energy restriction (pre-ER), energy restriction (ER) and post-energy restriction (post-ER).

The pre-ER phase consists of training participants how to use a diet log over 1 week as described below, followed by a 4-week period of weight maintenance during which they will amend their energy intake so as to comply with the dietary prescription described in table 1. A 4-week weight maintenance phase was applied successfully in a previously published randomised controlled trial comparing IER with CER.[21] Participant compliance with our dietary prescriptions will be assessed, with the participants who cannot comply with these prescriptions being excluded from the study and replaced.

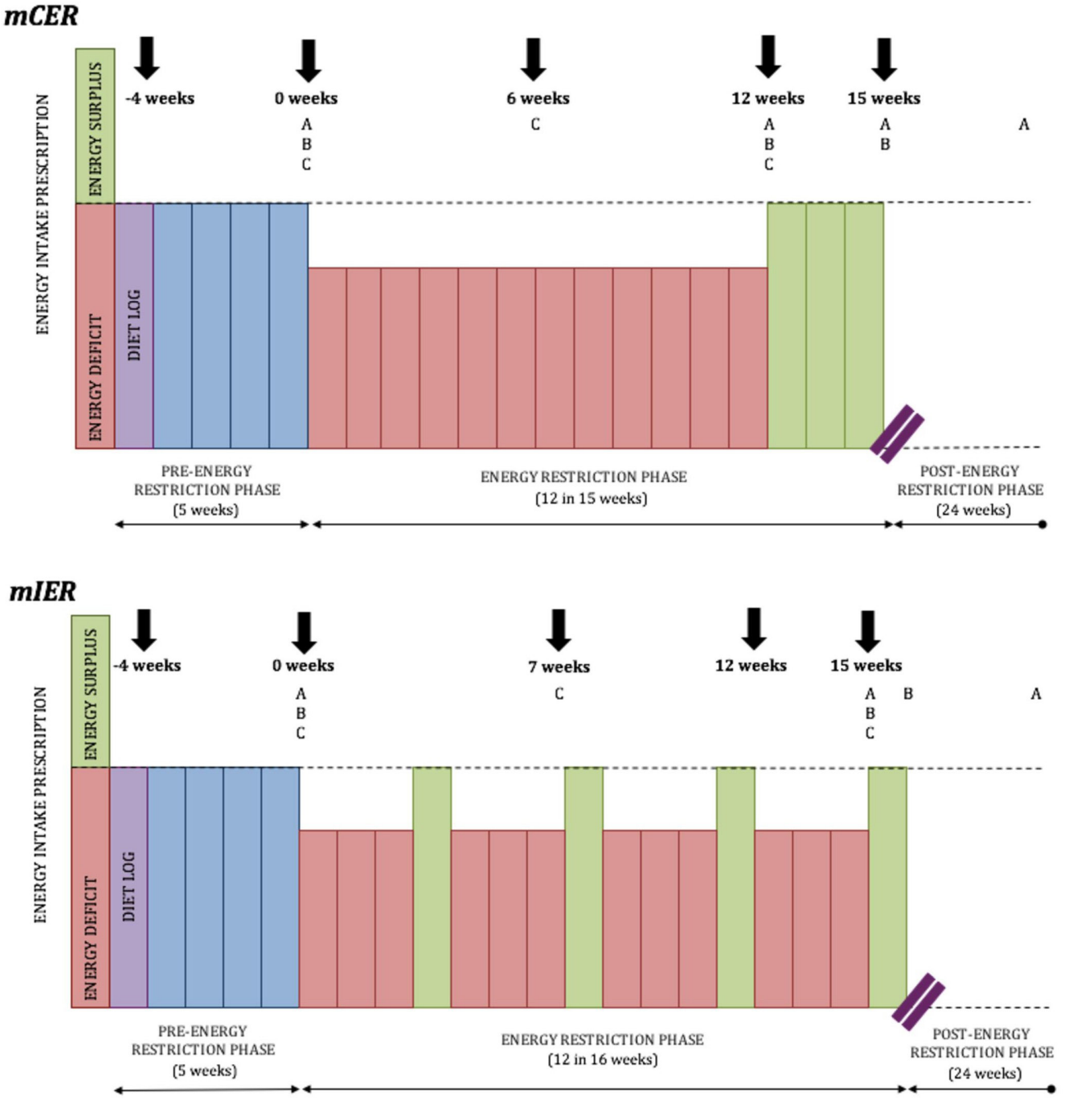

Figure 1 Trial design. (A) Fat mass (FM), fat free mass (FFM) and body weight measured at 0, 12 and 15 weeks in continuous moderate energy restriction (mCER), and at 0 and 15 weeks in intermittent moderate energy restriction (mIER), and at 6 months after 12 weeks of moderate ER in both groups. (B) Muscle performance (strength and endurance), resting energy expenditure, subjective drive to eat, and plasma leptin, peptide YY and ghrelin levels measured in the fasting state at 0, 12 and 15 weeks in mCER and at 0, 15 and 16 weeks in mIER. (C) Mood states, diet acceptability, physical activity and sleep quality (by self-report questionnaires and three-dimensional wrist accelerometers) measured at 0, 6 and 12 weeks in mCER and at 0, 7 and 15 weeks in mIER.

Diet log training

Once accepted into the trial and randomised, participants will be trained to use a popular kilojoule (kJ) and macronutrient tracking mobile application, MyFitnessPal (Under Armour, Baltimore, Maryland, USA). This application was previously validated for assessing

Table 1 Summary of weight loss targets and dietary prescription

Weight loss target or diet component	Pre-energy restriction phase	Energy restriction periods (during energy restriction phase)	Refeed periods (during energy restriction phase)
Weekly weight loss (% of body weight at week 0)	0%	0.7%	0%
Protein (g per kg of absolute body weight at week 0)	2.3	2.3	2.3
Fat (% of total energy, or g)	20% (Minimum 0.5 g/kg of absolute body weight at week 0)	20% (Minimum 0.5 g/er kg of absolute body weight at week 0)	Same absolute weight as in energy restriction periods
Carbohydrate (% of total energy)	Remaining	Remaining	Remaining

dietary intakes compared with weighed food records[41] and was shown to be effective for the implementation of dietary advice among people who are ready to self-monitor energy intake.[42 43] Participants will then record their usual food and drink intake with MyFitnessPal for 7 days as a means of ensuring proficiency in use of the application and to allow potential hurdles to be addressed with the investigator (JJP) before beginning the 4-week period of weight maintenance. While 3-day to 4-day food monitoring periods are usually recommended for individuals in the general population,[44] extending the length of the food diary from 3 to 7 days was shown to significantly improve energy and macronutrient intake estimates in a population of athletes.[45] Given that athletes are typically highly motivated and have experience with recording other components of their training programme, many researchers and clinicians prefer to implement 7-day food diaries for athletes,[46] as it is reasonable to expect a high degree of compliance and quality of recorded food data. To develop useful habits for later in the study, participants will be asked to record their body weight at home on a flat and hard surface, in a fasted state after emptying their bladder, every morning of the diet log (see outcome measures below). Participants' scales will have been checked for precision and accuracy in our research facility during the face-to-face screening appointment prior to commencement of the diet log.

Weight maintenance

After the 1-week diet log, all participants will be instructed to follow a diet that provides ~100% of weight maintenance energy requirements for 4 weeks (dietary composition detailed in table 1). Weight maintenance energy requirements will be 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.[47] Participants will be asked to continue recording their body weight every morning at home, as well as their daily food and beverage intake (for estimation of energy and macronutrient intake). As per previously published methodology,[21] if weight is gained or lost consecutively for 3 days, participants will be instructed to contact the lead researcher (JJP) in which case they will be provided with an amended diet prescription to maintain weight stability. The purpose of this 4-week period is to help ensure that all participants are weight stable on commencement of ER and to allow accurate determination of each athlete's energy requirements for weight maintenance.

Energy restriction phase

After the 5-week pre-ER phase (comprising 1 week for the diet log training and the 4-week weight maintenance period), both groups will undertake 12 weeks of moderate ER. ER will be delivered as either[1] mCER (12 weeks of continuous moderate ER) or[2] mIER (12 weeks of moderate ER), administered as 4×3 week blocks of moderate ER interspersed with 3×1 week blocks of EB (15 weeks total), as shown in figure 1. The 3-week blocks of ER to be used in the mIER intervention were chosen based on previous findings,[48] which demonstrated consistent weight loss for 3 weeks in non-athlete men of healthy weight undergoing ER. As mentioned in the Introduction section, an IER intervention that cycled 2 weeks of moderate ER with 2 weeks of EB was superior to CER involving moderate ER in men with obesity, in terms of weight and FM loss after 12 (and also 16) weeks of ER.[21] However, a caveat of that particular IER model for athletes is the considerably greater absolute time required for the intervention (30 weeks for IER vs 16 weeks for CER) despite both interventions involving equal time in ER. Typically, athletes will reduce weight for competition over 8–16 weeks,[26] implying that the aforementioned IER protocol[21] may seem unattractive to athletes by significantly extending the duration of the weight loss phase. An IER intervention that uses periods of EB that are less frequent and of shorter duration than the previously published IER intervention[21] (hence reducing the time required for the intervention) would likely increase the appeal of IER to the athletic community. While a shorter intervention duration is important to athletes, it is however also important that periods of EB implemented during IER are not too short as available research suggests that reversal of some of the adaptive responses to ER may require 7 to 14 days in EB, at least in adults with a BMI in the overweight or obese range.[49 50] Consequently, we have chosen to employ 1-week periods

of EB during our mIER protocol, administered after every 3 weeks of moderate ER.

Based on published recommendations for athletes,[25] participants exposed to moderate ER in both groups will have a moderate weekly weight loss target of 0.7% of their pre-ER body weight. For example, a participant weighing 80 kg will lose approximately 6.7 kg of body weight (approximately 0.56 kg per week) after 12 weeks of moderate ER. As ER-induced reductions in REE are expected,[48] the participants who achieve a weekly weight loss of <0.5% of their pre-ER body weight will have the daily energy intake of their prescribed diet reduced by 5% to help keep participants at approximately the same rate of weight loss throughout the study, which is in keeping with a method commonly used by athletes to amend energy intake during weight loss interventions. Of note, weekly weight loss will be calculated via week-to-week changes in average daily body weight over 7 days, to account for daily body weight fluctuations.[51]

In line with previously published methodology,[25] energy intake for each participant during the ER phase will be calculated under the assumption that the oxidation of 1 g of mixed tissue liberates ~29 kJ of energy. Thus, for example, a participant weighing 80 kg will need to reduce weekly energy intake by ~16 240 kJ (560 g×29 kJ/g) below weight maintenance energy requirements to achieve his or her weekly weight loss target of 0.56 kg (0.7% of body weight). Participants in both groups will be instructed to split the weekly energy deficit evenly across the week. In the above example, this would correspond to an ~2320 kJ (16 240 kJ÷7 days) energy deficit every day. During each period of EB, prescribed energy intake will be based on weight maintenance energy requirements determined in the pre-ER phase (during the 4-week weight maintenance period) as described above, and adjusted to take into account any changes in body mass.

Weekly review

In each week of the pre-ER and ER phases, participants will submit their past seven daily body weight measurements into an online form for review by an investigator (JJP). Participants will also submit online copies of their training diary and MyFitnessPal food diary for the week. Following weekly submissions, participants will receive email feedback by an investigator (JJP) including personalised help and encouragement, in keeping with a method commonly used by coaches administering weight-loss interventions remotely.[52] Depending on weekly progress, the diet prescription may be adjusted as described above.

Post-energy restriction phase

After a 6-month free-living period at the end of ER (the post-ER phase), during which time there will not be any scheduled dietary support from the research team, athletes will come back to the laboratory for a follow-up assessment as outlined in figure 1.

Dietary composition

In addition to an individualised kilojoule intake prescription, each participant will be provided with targets for daily dietary protein, carbohydrate and fat intake. Prior to commencement of each week of the pre-ER and ER phases, participants will be provided with all dietary targets via email for input to MyFitnessPal on their personal mobile devices. They will be instructed to weigh what they consume using a food scale to help ensure accurate portion sizes, and will be encouraged to record *all* food and drink intake (including any deviations from targets) in MyFitnessPal for the duration of the pre-ER and ER phases (~5 months). For occasions where tracking is likely to be inaccurate or not possible (eg, birthday dinner events, anniversaries), participants will be encouraged to continue to report their intake by estimating portion sizes and meal macronutrient content to their best ability using the MyFitnessPal food and beverage database. Meal frequency, meal timing and foods/drinks consumed to meet these energy and macronutrient targets will be at the discretion of each participant. However, participants will be provided with a number of low-energy-dense meal and snack ideas to assist with compliance. In addition, all athletes will be provided with a list of common foods or beverages that are rich in protein, carbohydrate or fat, with accompanying nutritional information. This list may be of particular benefit to athletes with limited nutritional knowledge, by providing a number of common food and beverage options that the athlete might choose to consume to help meet daily macronutrient targets.

Previous literature recommends a dietary protein intake of 1.2–2.2 g/kg of absolute body mass for athletes with an energy intake at or above EB to facilitate favourable adaptations from training.[53–55] However, a recent systematic review[30] suggests that a protein intake ranging from 2.3 to 3.1 g/kg of FFM (which equates to approximately 2.0–2.6 g/kg of absolute body mass for an 80 kg athlete with 15% body fat) may be more appropriate for retention of FFM in athletes undergoing ER with concurrent resistance exercise. In another review, it was suggested that 1.8–2.7 g/kg of absolute body mass was optimal for athletes training under hypocaloric conditions.[56] In line with these recommendations, and previously published methodology,[31] athletes will be instructed to consume 2.3 g of protein per kilogram of absolute body mass daily in order to minimise FFM losses during ER. Protein targets are expressed in terms of absolute body weight as opposed to FFM, to allow results from the trial to be used more widely by athletes (eg, including those without access to accurate measurement of FFM).

In terms of dietary fat intake, dietary recommendations for athletes typically maintain an adequate but lower end intake, while emphasising carbohydrate intake to fuel performance.[30] Thus, in keeping with previous recommendations,[57] and as previously published,[25] 20% of energy intake will be allocated

to dietary fat in both groups unless this equates to an intake below 0.5 g of dietary fat per kilogram of absolute body mass, in which case 0.5 g/kg of body mass will be prescribed. The implementation of a dietary fat minimum is to avoid very low intake of dietary fat in participants with lower energy expenditures, which could present safety and palatability concerns. Remaining energy intake will be allocated to carbohydrate to support training demands.

During the pre-ER phase (the weight maintenance period), participants will also be instructed to consume 2.3 g of protein per kilogram of absolute body mass and to allocate 20% of energy intake to dietary fat, with the remainder being assigned to carbohydrate. During time in EB during the ER phase (refeeds), athletes will be instructed to adjust MyFitnessPal macronutrient targets so as to consume the same amount of protein and fat (in grams) as prescribed during ER, with the increase in energy intake being totally derived from increased carbohydrate intake. Our rationale for this strategy is that—although yet to be confirmed—it seems wise for an athlete to place emphasis on increasing intake of carbohydrate during refeed periods, as opposed to increasing protein or fat. This is because elevated levels of leptin following carbohydrate feeding have been shown to stimulate REE and to suppress the drive to eat,[58 59] which would be expected to lead to greater efficiency of weight and FM loss, and easier diet adherence. Greater carbohydrate availability during refeed periods may also result in more pronounced anabolic responses when mIER is applied in concert with resistance exercise through the insulin-mediated activation of anabolic signalling pathways, potentially reducing FFM losses during ER.[60 61]

Training and supplementation

Participants will be instructed to continue their sport-specific and resistance training schedule without significant deviation from the pre-ER phase, recording all training activity in a training diary, including the type of training, intensity and duration. Furthermore, participants will be instructed to remain as consistent as possible throughout the trial with respect to any dietary supplementation they may be taking, recording any changes. This is important because some supplements—such as creatine—can induce changes in total body water and body mass.[62]

OVERVIEW OF OUTCOME MEASURES

The outcomes for the trial and the time points for measurement are shown in figure 1.

Co-primary outcomes

- Change in…
  - FM (kg) and
  - FFM (in kg)

  … from 0 weeks to after 12 weeks of moderate ER (which corresponds to 12 weeks in mCER and 15 weeks in mIER).

Secondary outcomes

- Change in body weight (kg) from 0 weeks to after 12 weeks of moderate ER (which corresponds to 12 weeks in mCER and 15 weeks in mIER).
- Change in…
  - FM (kg),
  - FFM (kg) and
  - Body weight (kg)

  … from 0 weeks to 15 weeks and

  … from 0 weeks to 24 weeks after completing 12 weeks of moderate ER.
- Change in…
  - Muscle performance (strength and endurance as determined by isokinetic dynamometry),
  - REE,
  - subjective drive to eat (by self-report questionnaire), and
  - Plasma levels of appetite-regulating hormones (leptin, peptide YY and ghrelin)

  … from 0 weeks to after 12 weeks of moderate ER (which corresponds to 12 weeks in mCER and 15 weeks in mIER),

  … from 0 to 15 weeks and

  … from 0 weeks to 16 weeks in mIER only. The rationale for including this time point (after 4×3 week blocks of moderate ER and 4×1 week blocks of EB) is to allow within-group comparison of these outcomes during energy *restriction* and during energy *balance*. We hypothesise that ER-induced changes in these outcomes may be recovered or partially recovered once EB is restored.
- Change in…
  - Mood states (by self-report questionnaire),
  - Diet acceptability (by self-report questionnaire),
  - Physical activity (by self-report questionnaire and three-dimensional wrist accelerometer analysis) and
  - Sleep quality (by self-report questionnaire and three-dimensional wrist accelerometer analysis)

  … from 0 weeks to after 6 weeks of moderate ER (which corresponds to 6 weeks in mCER and 7 weeks in mIER) and

  … from 0 weeks to after 12 weeks of moderate ER (which corresponds to 12 weeks in mCER and 15 weeks in mIER).

  Measurement in the middle of the energy restriction phase—in addition to the end—will be important to show whether changes in these outcome measures increase in line with time spent in ER.

DETAILED METHODOLOGY OF OUTCOME MEASURES

Body composition and body weight

FM and FFM will be determined via a whole-body dual-energy X-ray absorptiometry (DXA) scan, performed using a Lunar iDXA machine (GE Healthcare, Chicago, Illinois, USA) by qualified investigators. During the scan, participants will lay supine on the scanning table with their arms at their sides. Scans will be conducted in

accordance with the procedure outlined in the manufacturer's manual and analysed using the enCORE Software Platform (V.17; GE Healthcare). The DXA machine will be serviced annually, subject to regular quality assurance testing, and calibrated on each day of use. Body weight for data analysis will be measured in the laboratory using a calibrated scale. FM, FFM and body weight will be measured at the timepoints denoted by the letter A in figure 1. Body weight will also be measured at home, every morning during the pre-ER and ER phases of the trial. At-home body weight measurement will be used for implementation of the dietary intervention and will not be used as an outcome for data analysis. Participants will be instructed to weigh themselves on waking without clothing, before eating or drinking, and with an empty bladder.

Muscle performance

A critical concern for athletes undergoing weight loss interventions is to minimise any possible performance decrements. Participants in this study cohort will likely come from a range of sporting disciplines, with each sport having different key performance outcome measures. Therefore, as a somewhat shared performance feature across a range of sports, we will monitor changes in muscle performance (strength and endurance), as shown by the letter B in figure 1. This will be determined by supervised strength and endurance tests using isokinetic dynamometry (Biodex Medical Systems, Shirley, New York, USA), the gold standard of muscle strength assessment.[63]

A recent meta-analysis of seven interventions that used isokinetic dynamometry to measure knee extensor strength in 108 participants with overweight or obesity observed a significant 7.5% decrease from baseline values following moderate ER-induced weight loss,[64] highlighting the potential performance implications of even moderate ER for athletes. Isokinetic dynamometry thus provides a viable, sensitive measure for strength assessment during moderate ER, at least in people with overweight and obesity. Following a standardised warm-up,[65] isokinetic flexion/extension strength at the elbow and knee will be assessed via peak torque during three maximum-effort repetitions at a speed of 60 degrees/s.[66]

Muscle endurance will be assessed via the total work and work performed during the last third of a maximum-effort 25-repetition set, at a speed of 240 degrees/s.[67] To allow for recovery, muscle endurance tests will be performed 5 min following muscle strength tests.

For muscle performance tests, participants will be instructed to come to the laboratory by car, and to refrain from all exercise, food and fluids (other than water), caffeine, alcohol or other drugs (excluding regular medications) for the previous 12 hours. The tests will be conducted before 12:00, to avoid excessively long periods without energy intake. Additionally, muscle performance testing will be scheduled as the last outcome measurement for the morning to avoid potential interference effects with other outcome measures, in particular measurement of REE.

Resting energy expenditure

For REE assessments, also denoted by the letter B in figure 1, participants will be provided with the same instructions for the preceding 12 hours as described above. They will be 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 min resting period. REE will be calculated by expired gas analysis during the latter stage of this period using a metabolic cart system (Ametek, Berwyn, Pennsylvania, USA).

Subjective drive to eat and plasma levels of appetite-regulating hormones

Also at the time points denoted by the letter B in figure 1, and still in the fasted state, athletes will have their subjective drive to eat evaluated using a self-report questionnaire based on previously published recommendations on how to measure appetite.[68 69] Participants will be asked to answer questions concerning their current drive to eat and their overall drive to eat during the past week. Then blood will be collected from participants into EDTA-containing tubes for subsequent measurement of fasted plasma levels of the appetite-regulating hormones leptin, peptide YY and ghrelin. Blood sampling will be scheduled after completion of the questionnaire to help reduce potential stress responses from blood collection that could affect the drive to eat. Leptin is a satiety signal known also for its stimulatory effect on metabolism.[70] Leptin is released predominantly by adipocytes and is regulated by long-term energy availability.[71] We are interested in leptin levels, as pharmacological administration of leptin has been demonstrated to reverse a number of adaptive responses to ER, notably reductions in REE, increased skeletal muscle work efficiency and reduced circulating levels of thyroid hormones.[70] Furthermore, there is evidence that leptin release is temporarily elevated following short-term overfeeding, being particularly sensitive to increased carbohydrate intake.[58 72] It is feasible that periods of EB during mIER—particularly when carbohydrate intake is elevated—may trigger leptin release, contributing to normalisation of REE[41] and decreased drive to eat, increasing efficiency of fat loss and enabling easier diet adherence. Peptide YY (PYY) is another satiety signal. It is released from the gastrointestinal tract in response to episodes of feeding, signalling shorter-term satiety.[73] In contrast to the appetite-supressing effects of leptin and PYY, ghrelin stimulates an increase in hunger. It is released from the gastrointestinal tract during periods of fasting.[74] Measurement of these appetite-regulating hormones provides a more objective insight into any potential differences between interventions in the biological drive to eat and compliments findings on measures of subjective drive to eat.

Mood states

ER may cause worse mood, heightened irritability, increased fatigue and difficulties concentrating in some people.[75] Therefore, mood states will be evaluated via completion of the Profile of Mood States (POMS-24), which has been applied successfully in athlete populations.[76] Completion of the POMS-24 is relevant to non-clinical populations, by detecting potential improvements in mood within the normal range.[77] Responses will be analysed to obtain scores for each of the six mood states (anger, confusion, depression, fatigue, tension and vigour), and Total Mood Disturbance will also be determined. Measurements will be completed as denoted by the letter C in figure 1, which involves measurement at the start, middle and end of the ER phase.

Diet acceptability

Also evaluated as denoted by the letter C in figure 1 will be diet acceptability. To this end, we will evaluate athlete perception of their assigned intervention via completion of a custom-made Process Evaluation Questionnaire. As another indicator of diet acceptability, we will also compare dropout rates and compliance with requested behaviours (eg, completion of MyFitnessPal diaries) between groups.

Physical activity and sleep

Previous research has demonstrated reduced physical activity in humans undergoing ER.[78–81] To detect potential behavioural compensatory responses during the ER phase and to explore possible differences between interventions, physical activity will be monitored using three-dimensional wrist accelerometers (Actigraph, Pensacola, Florida, USA) to generate estimates for average daily physical activity at intervals across the trial, as denoted by the letter C in figure 1. During collection periods, accelerometers will be worn for 24 hours per day for seven consecutive days. Seven-day monitoring periods have been routinely used in studies monitoring physical activity as they provide a sufficient number of days to achieve intraclass correlations of more than 80% in most populations, while also providing the ability to sample behaviour on both weekdays and weekend days.[82] Additionally, participants will complete daily training diaries to detect potential changes in training load across the trial.

Sleep patterns were shown to be significantly altered by ER, by increasing sleep-onset latency and decreasing slow-wave sleep in women with a BMI in the overweight range.[83] Sleep curtailment may compromise the efficacy of a dietary intervention using moderate ER by decreasing the fraction of weight lost as FM and increasing the loss of FFM, as illustrated in adults with overweight.[84] Furthermore, in a narrative review, it was suggested that reduced sleep might disrupt appetite hormone regulation.[85] In athletes—as reviewed previously—exercise performance seems to be negatively affected during periods of sleep deprivation, specifically endurance efforts and repeated exercise bouts.[86] Additionally, it has been suggested that sleep loss could potentially impact physiological responses to exercise and hinder muscular recovery.[86] Therefore, accelerometer data will also be analysed for a quantitative assessment of sleep, evaluated via average total sleep time duration and activity levels during sleep, as published previously.[87–89] Sleep will also be monitored qualitatively by completion of the Pittsburgh Sleep Quality Index,[90] the most frequently cited index for evaluating sleep quality and quantity, and the Epworth Sleepiness Scale.[91] Participants will be instructed to collect accelerometers from our research facility 1 week prior to the time points designated by the letter C on figure 1, returning them 1 week later for analysis after completing a 7-day monitoring period.

DATA STORAGE, VALIDATION AND ANALYSES

All data in this trial will be collected electronically. Statistical analyses will be performed using two data sets: the intention-to-treat set, with all participants included regardless of completion or protocol adherence; and the *per protocol* set, with all participants that meet all trial requirements up to and including week 12 of moderate ER. All analyses will be performed using SPSS statistical software (for Windows, 2015 edition; IBM, North Castle, New York, USA). For any outcome measures missing for participants who withdraw from the trial or who miss assessments, modern imputation techniques will be applied in intention-to-treat analyses. This will be accomplished by the generation of repeated imputations using predictive models based on the majority of participants with complete data. Data cleaning will take place by a series of logical checks on all data. Discrepant values will be crosschecked with the electronic source data documents, and data amendments made if necessary. All study-related hard-copy information (signed consent forms) will be stored securely at the University of Western Australia in locked filing cabinets in areas with limited access. Electronic databases will be secured with password-protected access systems.

ETHICS AND DISSEMINATION

This study has been approved by the Human Research Ethics Committee at the University of Western Australia. As mentioned above, written informed consent will be obtained from each eligible participant prior to study inclusion. Trial results will be submitted to a peer-reviewed scientific journal for publication and released to the media following publication. No data relating to individuals will be identified in these publications.

DEFINITION OF END OF TRIAL

End of trial is defined as after the 24-week follow-up, where the last measurement is taken from the last participant, and the last participant undergoing the trial has been debriefed on their personalised key data. The timeframe for the debriefing period is expected to be up to 4 weeks following the final laboratory visit.

DISCUSSION

Athletes from different sports may have many reasons for wanting to reduce body weight or body fat, and there is a need to evaluate novel dietary strategies that may allow this population to better achieve desired body weight or composition while not jeopardising health or performance outcomes. While recent findings suggest that some IER models—in comparison to CER—may reduce compensatory responses to ER, in turn, improving weight loss or fat loss (or efficiency thereof) in people with obesity,[20 21] it has yet to be determined whether this strategy is effective for athletes. Hence, this dietary approach merits further research attention to explore whether the recruitment of athletes, implementation of exercise and the optimisation of macronutrient intake could influence results achieved with IER. Outcomes of this trial will serve to extend our understanding of IER strategies and also potentially broaden application of IER to people who are healthy and active.

Contributors JJP and AS conceived of the study and developed the trial protocol and wrote this manuscript. All authors contributed to refinement of the trial protocol and approved the final manuscript.

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Competing interests AS is the author of *The Don't Go Hungry Diet* (Bantam, Australia and New Zealand, 2007) and *Don't Go Hungry For Life* (Bantam, Australia and New Zealand, 2011). She has also received payment from Eli Lilly, the Pharmacy Guild of Australia, Novo Nordisk, the Dietitians Association of Australia, Shoalhaven Family Medical Centres and the Pharmaceutical Society of Australia for presentation at conferences, and has received consulting fees from Nestlé Health Science since 2016.

Patient consent Not required.

Ethics approval Human Research Ethics Committee at The University of Western Australia (RA/4/20/4340).

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