Intermittent Fasting vs Continuous Caloric Restriction for Weight and Body Composition Changes in Humans

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Abstract

Background: Obesity and overweight are major health concerns in the UK and worldwide. Dietary restriction is an effective strategy for weight and fat loss and it is mainly implemented as daily Calorie Restriction (CR). However, continuous CR has consistently shown to be difficult to adhere. Intermittent Fasting (IF) protocols have been recently proposed as an alternative for traditional CR where compliance might be improved since caloric restriction is only required during certain times or days of the week, rather than every day. Even though both approaches are proven to be effective, it remains unknown which one produces greater changes in body weight and body composition.

Participants and Methods: Subjects (n = 14) were physically active, healthy non-obese (BMI < 29.9 kg/m2) males (n=4) and females (n=10) aged 20-30 that were randomly assigned to 5-week intervention programs that used either an Intermittent Fasting (IF) protocol of per iodised severe energy restriction (500 kcal/day for 2 days/week) or a traditional Calorie Restricted (CR) protocol (1200 kcal/day for 7 days/week). Body weight and body composition were assessed at baseline and at the end of the intervention.

Results: Participants in the IF protocol lost significantly more weight than did CR participants at the end of the 5-week program (0.8 ± 0.4 Kg versus 0.1 ± 0.6 Kg). Similarly, IF participants experienced significantly greater body fat reduction than did CR participants (1 ± 0.6 % versus 0.3 ± 0.7 %). However, even though participants did not report problems following the diet, researchers believe that subjects undergoing the CR intervention might have experienced adherence issues and could have unintentionally underestimated total food intake based on the results.

Conclusion: The IF dietary approach has achieved significant weight loss and body composition improvements, whereas the CR approach has not produced any significant changes in weight or body composition. Moreover, it is believed that the CR protocol has led to adherence problems.

Introduction

Obesity is currently considered a global pandemic; 2.8 million people die each year as a result of being overweight or obese as declared by the World Health Organization (WHO) [1]. In the UK it affects 25% of the population and the NHS has not succeeded at developing coherent policies that address obesity as a major cause of health and social care expenditure [2]. Thus, it is of great importance for the scientific community to identify and investigate effective nutritional interventions to fight obesity. Weight gain is considered a subsequent cause of excessive calorie intake [3], and Calorie Restriction (CR) defined as a reduction in energy intake without malnutrition [4,5], has been proven as an effective strategy to reduce adiposity in humans [6,7,8,9].

However, CR diets have traditionally shown notoriously low long-term success rates [10] and high attrition rates within the first weeks [11]; it has been estimated that only 20% of obese individuals are successful at long-term body fat reduction when defined as losing at least 10% of initial body weight and maintaining the loss for at least a year [12]. Therefore, there has

been an increased interest in developing more manageable long-term CR interventions as it is unlikely that constant CR will be widely adopted, mainly due to the difficulty in maintaining long-term low-calorie intake in modern society [3]. Intermittent Fasting (IF), a dietary approach where the frequency of food consumption is altered instead of limiting overall calorie intake has been recently proposed as an alternative to the classic model of CR [13,14].

Continuous Calorie Restriction

CR has been studied in animal models for almost a century, and even though the majority of the studies were aimed to investigate delays in aging and extensions in life span, consistent reductions in bodyweight are always observed: Osborne et al. found significant weight loss among other improved biomarkers of health in rats in 1917 [15], similarly, McCay et al. concluded in 1935 that controlled CR without causing malnutrition in rats compared with rats fed *ad libitum* effectively reduces body weight and also improves various other health markers [5]. Accordingly, subsequent studies have confirmed similar results attributed to CR in rodents [16,17,18] and also in rhesus monkeys [19].

CR in humans promotes weight loss and changes in body composition, and it has been associated with improvements of different markers for cardiovascular and metabolic health in both overweight [20,22] and non-overweight subjects [22,23]. As dietary intervention, CR is seen as a reduction of usually 20-40% of daily calorie requirements [18] while maintaining adequate nutrition over a certain period of time [24], which has been traditionally applied in humans in the form of either a Low-Calorie Diet (LCD) providing around 1000 to 1500 kcal/day [25,26,27,28] or a Very-Low- Calorie Diet (VLCD) providing <800 kcal/day [29,30, 31,32]. While at short-term the VLCDs appear to be superior for initiating changes in body composition, the long-term effects on sustained weight loss seem to be very similar for both CR interventions [29]. In fact, a meta-analysis of randomized trials comparing long-term efficacy of LCDs vs VLCDs conducted by Tsai and Wadden concluded that even though VLCDs lead to greater results at first, they do not produce greater long-term weight losses than LCDs [25].

The negative side effects reported on long-term CR for humans are similar to those observed in animals: perpetual hunger, reduced body temperature leading to cold intolerance, and diminished libido [33] while rare adverse effects reported on long-term VLCDs are mild postural light-headedness, fatigue, decreased bowel movements and constipation, electrolyte disturbances, dry skin and hair loss [34,35]. Another important drawback observed in long-term studies seems to be the adaptive decrease in Total Energy Expenditure (TEE) linked to prolonged periods of CR seen in Biosphere experiments [36,37,38].

Intermittent Fasting

Even though some researchers support the feasibility of long-term CR [39], adherence to the recommended CR diets remains an issue for the majority of the population in the long term [40]. Another major drawback of CR is that, according to Johnstone, subjects following both LCD and VLCD diets tend to regain all of the weight lost one year after their initiation of the diet [41]. It has been hypothesized that the reported beneficial effects from CR on body composition and other health biomarkers can be mimicked by alternating periods of short term fasting with periods of refeeding, without deliberately altering the total caloric intake [42,43,44].

IF programs for weight loss in obese and non-obese subjects have been recently classified as Whole Day Fasting (WDF), Daily IF (DIF) and Alternate Day Fasting (ADF), each form of IF utilises different periods of feeding and fasting [45] (Table 1). They are currently gaining popularity in the lay press and among research scientists [46], common models are the 5:2 diet (an ADF protocol of 500 kcal/day two days per week) and the 18:8 diet (a DIF protocol of no calories during 16 hr and an eight-hr feeding window over a 24-hr period) [46]. DIF protocols like the 18:8 diet have been supported by some research such as the crossover study conducted by Kahleova et al. which found that daily small feeding windows (two meals per day skipping dinner) produced significantly greater weight reduction than grazing (six smaller meals per day) [47] and other studies that found similar results on weight loss [13,48,49] however, the 5:2 model seems to be more popular at the moment and it is more utilised in research [50,51,52,53].

IF protocol	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
ADF	*Ad libitum*	25% kcal	*Ad libitum*	25% kcal	*Ad libitum*	25% kcal	*Ad libitum*
DIF	16-20 h fasting / 4-8 h feeding	16-20 h fasting / 4-8 h feeding	16-20 h fasting / 4-8 h feeding	16-20 h fasting / 4-8 h feeding	16-20 h fasting / 4-8 h feeding	16-20 h fasting / 4-8 h feeding	16-20 h fasting / 4-8 h feeding
WDF	*Ad libitum*	*Ad libitum*	*Ad libitum*	24-h fast	*Ad libitum*	*Ad libitum*	24-h fast
ADF = Alternate Day Fasting, DIF = Daily Intermittent Fasting, WDF = Whole Day Fasting							

Table 1: Examples of weekly food intake schedules of different categories of IF protocols.

IF has been widely studied in animal models, most often in the form of Every-Other-Day feeding (EOD), where they have no food for 24 hr and *Ad Libitum* (AL) access to food during the next 24 hr [54]. In many rodent species, mice managed to compensate for the calorie deficit created during the fasting days by increasing their calorie intake on the AL feeding days [55], over a two-day period, they kept their total caloric intake at the same level as in mice fed an *ad libitum* diet. In human trials seeking to replicate the effects reported in rodent studies, IF in the form of ADF has consistently shown significant reductions of body weight in only three weeks [56,57]. In studies where participants underwent modified versions of ADF similar to the 5:2 models, most trials found weight reductions in all of the participants [58], although some researchers found significant weight decreases in obese subjects [59,60], while bodyweight was maintained in lean individuals [61,62].

Common Misconceptions and Potential Adverse Effects from IF

Decreased Metabolic Rate

It is widely believed that IF leads to decreases in human metabolism and that multiple small meals cause the opposite effect increasing the overall energy expenditure due to the Thermic Effect of Food (TEF) [63], but the research on metabolic rate is remarkably conclusive: TEF is dependent on the total caloric intake and changes with macronutrient variability and not meal frequency [64,65, 66,67]. Webber and Macdonald studied the metabolic effects of fasting for 12, 36 and 72 h in 29 participants and found no changes in their metabolic rate [68]. Heilbronn et al. demonstrated that ADF does not affect resting metabolic rates in healthy males and females [56]. Gjedsted et al. examined the effects of 72 h fast on 10 lean men, at the end of trial the subject's energy expenditure was found to be unchanged from the initial measurements [69]. Similar data has been found regarding continuous CR diets; no decreases in metabolic rates were found after a 12-week trial that examined the effects of a VLCD of 800 kcal/day on subjects undergoing resistance training [70], the same results were found in another study where 30 female subjects underwent a 72h severe CR intervention [71].

Low Blood Glucose Levels

It is commonly believed that IF can cause pathologically low levels of blood glucose in non-diabetic subjects, however, research shows that in healthy subjects short-term fasting periods of up to 24 h do not lead to hypoglycaemia [72]. In fact, no data has been found where subjects undergoing IF interventions reported glucose levels below 3.6 mmol/L. Alken et al. studied individuals that reported a history of hypoglycaemic episodes and compared them to subjects that have never experienced any form of hypoglycaemia. Both groups completed a 24 h fast while their glucose levels

were monitored and none of the participants showed any periods of hypoglycaemia, although the group that had a history of hypoglycaemia reported periods of 'feeling hypoglycaemic' even though their blood glucose was at normal levels [73], the study concluded that despite reported 'hypoglycaemic sensations', in the absence of metabolic disease, the ability to maintain blood glucose levels within the normal range does not seem to be affected by short periods of fasting. Award et al. concluded that blood glucose levels are kept in the normal range after a 24 h fast mainly because the liver can store enough glycogen; in fact, they found that fasting for 24 h only decreased 57% of the liver glycogen stores in healthy individuals that were not engaged in vigorous exercise [74].

Increased Hunger

It is widely accepted that eating smaller meals frequently as opposed to restricting feeding frequency helps reduce hunger perception in humans [75,76,77]. Such assumption has linked IF interventions with a possible increment of feelings of hunger, which is indeed a major limiting factor for adherence and compliance in most dietary interventions. However, perceived hunger appears to be highly subjective [78,79] as food ingestion seems to be modulated by both peripheral and central signals [80], suggesting that feelings of hunger are greatly dependent on the individual's preferred feeding pattern [81]. Studies on starvation have shown decreased feelings of hunger: Duncan conducted a 14-day fast experiment in obese patients who were only allowed to consume water and non-caloric beverages. The intervention caused great reductions of body weight but did not cause increased perceived hunger sensations, demonstrating that prolonged fasts might have a hunger suppressing effect [82], although the results might not transfer to the short duration fasting periods of IF protocols. Heilbronn et al. studied the perception of hunger and fullness in 18 males and females that followed an ADF IF protocol during 22 days and found that subjects reported increased feelings hunger on fasting days [56]. However, Johnson et conducted a similar study where 10 obese subjects underwent an eight-week ADF intervention and hunger perception did not increase significantly from baseline during the trial period [60].

To date, research on the effects of IF on perceived hunger is limited, and even though there seems to be a greater amount of data on hunger and feeding frequency, it is not conclusive and studies frequently find conflictive results. Speechly et al. studied different feeding frequencies and the relationship between hunger and subsequent food intake in obese men. Participants were fed 33% of their daily calorie requirement in either one single meal or five meals before being allowed to eat *ad libitum*. The single meal group consumed 27% more calories when given the *ad libitum* meal [83]. The same setup has been used in lean individuals finding similar results, researchers concluded that when the dietary load was spread into equal amounts and consumed evenly through the

day, appetite control was enhanced [84].

Contrary to the common believe, some studies suggest that more frequent meals throughout the day lead to increased hunger levels: Smeets and Westerterp-Plantenga conducted a randomised crossover study where 14 females were given either two or three meals per day in a respiration chamber for measurements of energy expenditure and substrate oxidation. They concluded that in healthy, non-obese women, decreasing the feeding frequency sustains satiety [85]. Similarly, Munsters and Saris investigated the effects of meal frequency in 12 healthy males that randomly received two isoenergetic diets with either three or 12 meals a day. The low-frequency diet increased satiety and reduced hunger ratings compared to the high-frequency one [86]. Ohkawara et al. found similar results in a randomized cross-over study that compared the effects of consuming three vs six meals in 15 lean male and female subjects; They found no difference in fullness, but hunger and "desire to eat" were greater during six compared to three meals [87]. Very recently, Perrigue et al. conducted a randomized crossover intervention trial in 12 healthy males and females to examine the effects of high vs low feeding frequency on self-reported appetite and found the same results, concluding that frequent meals do not help to decrease overall appetite when compared to restricted feeding frequency [88].

Increased Stress

Fasting research in animal models have shown that ADF forms of fasting can increase adrenocorticotropic hormone and cortisol levels in rodents [89,90], which has led to the assumption that IF produces the same effects in humans [91]. However, research shows that the controlled stress response from IF interventions in humans seems to be different from the one by uncontrolled physiological and psychological stress seen in rat studies, and the possible increased stress in humans might be a necessary factor for initiating molecular resistance for larger stressors that can promote beneficial effects [16]. In fact, short periods of increased cortisol secretion such as the ones seen during some IF interventions can enhance fatty acid oxidation, while more prolonged cortisol increases can have negative effects such as causing vulnerability to immunosuppression, and to autoimmune related and metabolic disorders [92]. Most research on fasting show little or no changes in cortisol levels in response to short periods of fasting: Soeters et al. conducted a crossover study where lean healthy subjects underwent two weeks of an ADF fasting protocol of 36 hours fasts and found no negative effects on cortisol levels [62]. Similar interventions have found the same results after fasting periods of up to 24 hours [93] and even after 72 hours of total calorie deprivation [94], although 72 hours of fasting has been shown to increase cortisol levels in very lean females [95]. Research shows that sustained periods of fasting can indeed lead to significant

increments of cortisol levels in humans; Bergendahl et al. found that five days of fasting caused a 1.8-fold increase in the 24-hour endogenous cortisol production rate in non-obese healthy [96], but the duration of the fasted stage of normal IF protocols do not exceed 24 hours.

Loss of Lean Mass

It is commonly believed that it is important to have a steady stream of amino acids available to avoid muscle catabolism, and it has been hypothesised that IF can lead to depleted liver glycogen stores in humans, increasing proteolysis and flux of amino acids from skeletal muscle for hepatic de novo gluconeogenesis [42]. However, research does not seem to suggest that short periods of fasting of up to 24 hours can deplete hepatic glycogen stores in healthy individuals [74], and caloric deprivation of up to 40 hours does not appear to stimulate a significant catabolic effect or amino-acid breakdown [97]. Fasting increases ketone body concentrations [60] which have been shown to have an anti-catabolic effect and also provide a non-glucose energy substrate for the body decreasing the need for protein-derived substrates for gluconeogenetic conversion [98,99]. Soeters et al. conducted a crossover study where eight healthy subjects underwent a two weeks ADF IF protocol and a two week of a standard diet and they found no significant loss of lean mass [62]. Gjedsted et al. also suggest that fasting for up to 72 hours does not correlate with an increased breakdown in the muscle and it does not slow down muscle protein synthesis in healthy individuals [94].

It is important to mention that the majority of the literature on the preservation of muscle mass during calorie deprivation or reduction involve some form of resistance or anaerobic exercise: Bryner et al. studied male and female subjects consuming 800kcal/day during a 12-week intervention that participated in resistance exercise three days a week. Researchers found that all participants were able to maintain their fat free mass [70]. Another study conducted in 1999 studied obese males over a 16-week period controlling their caloric intake by reducing their daily intake by 1000 calories per day. Researchers found that whilst the participants attended a weight training programme three times a week, they were able to lose over 20 pounds of body fat and still maintain all muscle mass [100]. Janssen et al. carried out a similar study into 38 obese women who had reduced their calorie intake for 16 weeks and participated in weight training three times a week. The findings also showed that the participants were able to maintain their muscle mass [101]. Cchomentowski et al. looked into 29 males and females between the age of 60 and 75 who had dieted for 4 months. The results underline that the group that did not participate in exercise had over 4% decrease in lean body mass, whereas those who had participated in exercising had no significant decrease in lean mass.

Rationale for the Present Study

From the current body of research, IF appears to produce similar effects to continuous CR, being able to reduce body weight and adipose tissue in normal-weight, overweight, and obese individuals [45], although it has been speculated that the calorie deficit from the fasting periods could precede weight gain due to over-eating during the *ad libitum* feeding days, which is something that has been seen in some rodent species [55]. Most animal research shows a number of positive effects IF on weight and fat distribution [102], however, scientific evidence for the benefits of IF in humans is often extrapolated from the mentioned animal trials, based on observational data, or derived from experimental studies with inadequate sample sizes [44,103]. To date, there is a scarce number of studies in healthy non-obese individuals comparing IF with CR and there is currently no data comparing IF with CR in normal-weight subjects [104]. Further studies comparing IF vs CR for weight loss and body composition changes in normal-weight populations will likely add valuable data to the available knowledge, as more research is needed to establish the effectiveness of one method over the other.

Aim

To compare the short term (5 weeks) effects on weight and body composition of the popular IF protocol 5:2 against a conventional CR diet in healthy non-obese individuals.

Objectives

The objectives of this study are to: (i) compare the effectiveness of IF with continuous CR for weight loss; (ii) compare the effectiveness of IF with continuous CR for changes in body composition.

Hypothesis

It has been hypothesised that IF and CR protocols will both lead to short-term weight loss and body composition changes in healthy non-obese individuals. However, subjects on the IF diet might compensate for the calorie deficit created during the fasting periods by increasing their calorie intake on the *ad libitum* feeding days, as seen in animal models [39]. This would make the CR protocol more effective for weight loss and body composition changes.

Methods

Subjects

Fourteen physically active, non-obese (BMI < 29.9 kg/m²) healthy males (n=4) and females (n=10) aged 20-30 years and primarily Caucasian that have been recruited at the Peckham Pulse Healthy Living Centre, 10 Melon Rd, London SE15 5QN. Participants' measurements have been taken at baseline and upon completion of the trial at Haymerle School's Gym, Haymerle Road, Peckham London SE15 6SY.

Participants have been required to be non-smokers, not dieting before the trial or losing weight and have regular menstrual cycles; they were required not to consume high intakes of alcohol (>28 units per week) and not be diagnosed with diabetes, cardiovascular disease or cancer.

Approval was obtained from the St Mary's University, Twickenham ethics sub-committee. Prior to the study initiation, each participant was provided with a Consent Form and Information Sheet (Appendices 1 and 2).

- **Appendix 1** - Participant Information Sheet

Participant Information Sheet

Participant Information Sheet	
Section A: The Research Project	Section B: Your participation in the Research Project

1. Title of project: Intermittent Fasting vs continuous Caloric Restriction for weight and body composition changes in humans.
2. Purpose: To compare the short-term effects on weight and body composition of the popular IF protocol 5:2 against a conventional CR diet in healthy non-obese individuals.
3. I would like to invite you to participate in this study to help improve your dietary knowledge and practices.
4. The organiser of this research project is German Pertusa Molina.
5. The information collected will be kept confidentially on an encrypted disc accessible only by the organiser of the study. Information will be presented anonymously in the final report. Participants will be referred to by a number, not by name nor initials.
6. Contact for further information: german.healtheducation@gmail.com
	1. You have been invited to take part as you are a non-obese healthy male or female aged 20-30 years non-smoker, not currently dieting or losing weight and having regular menstrual cycles, you do not consume high intakes of alcohol (>28 units per week) or phyto-oestrogens, and you have not been diagnosed withdiabetes, cardiovascular disease or cancer.
	2. You may decline to take part in the project
	3. You may withdraw from the project at any time by completing the withdrawal form at the bottom of the consent form and returning it to:german.healtheducation@gmail.com
	4. If you agree to take part in the project:
	
	   • Your weight will be measured on calibrated digital scales and body fat percentage will be assessed using a standardised 4-site skinfold protocol at baseline and after the fifth week.
	   • You will be asked to undergo a strict dietary program (either an IF or a CR protocol) during five weeks.
	5. No risks to participation in the project other than possible feelings of hunger at certain points have been identified
	6. Agreement to participate in this research should not compromise your legal rights if something goes wrong.
	7. There are no special precautions you must take before, during or after the research project.
	8. The information collected will kept confidentially on an encrypted disc accessible only by the organizer and supervisor of the study. Information will be presented anonymously in the final report.
	9. The anticipated benefits of taking part in the study will likely be weight loss and sub-cutaneous body fat reduction.
	10. You will need to undergo a five-week dietary intervention.
	11. Your participation in the project will be kept confidential at all times. Details of your identity will not be shared. Participants will be referred to by a number, not by name nor initials

You Will be Given a Copy of this Form to Keep Together with a Copy Of your Consent Form

• **Appendix 2** - Participant Consent Form

Name of Participant: _____

Title of the project: **Intermittent Fasting vs continuous Caloric Restriction for weight and body composition changes in humans**

Main investigator and contact details: German Pertusa Molina - german.healtheducation@gmail.com

Members of the research team: German Pertusa Molina

1. I agree to take part in the above research. I have read the Participant Information Sheet which is attached to this form. I understand what my role will be in this research, and all my questions have been answered to my satisfaction.
2. I understand that I am free to withdraw from the research at any time, for any reason and without prejudice.
3. I have been informed that the confidentiality of the information I provide will be safeguarded.
4. I am free to ask any questions at any time before and during the study.
5. I have been provided with a copy of this form and the Participant Information Sheet.

Data Protection: I agree to the University processing personal data which I have supplied. I agree to the processing of such data for any purposes connected with the Research Project as outlined to me.

Name of participant (print)……………………………………………………………………..
Signed………………..……………… Date………………………….........

If you wish to withdraw from the research, please complete the form below and return to the main investigator named above.

Title of Project: **Intermittent Fasting vs continuous Caloric Restriction for weight and body composition changes in humans**

I WISH TO WITHDRAW FROM THIS STUDY
Name: _____
Signed: _____ Date: _____

Design

Randomized comparison of the participants divided in two groups: (i) IF group - Periodised severe energy restriction (500 kcal/day for 2 days/week) and (ii) CR group - Continuous caloric restriction (1200 kcal/day for 7 days/week) observed over a period of five weeks. The IF protocol has been based on previous studies on the common version of 5:2 IF diet which generally involve severe caloric restriction (75 - 90% restriction of energy needs or an intake of 200 - 500 kcal/day) on non-consecutive 2 days per week [53,]. The CR protocol has been based on a recent systematic review and meta-analysis of randomized controlled trials that classified LCDs as diets where total calorie intake is <1200 kcal/day [105].

Since heavier subjects were considered likely to lose weight and adipose tissue faster than leaner individuals [106], it was considered that starting BMI may confound the rate of weight loss during the trial. A Randomized Block Design has been used where BMI is the blocking variable; Block one clusters participants with lower BMI scores (BMI = 18-22 kg/m^2) and block two clusters higher scores (BMI = 23-30 kg/m^2). For equal allocation, odd participant numbers have been assigned to the CR dieting group and even participant numbers have been assigned to the IF dieting group.

The length of the intervention has been based on Barnosky's review of the scientific literature on IF which concludes that significant fat loss can be seen from the third week [50], CR interventions also tend to be studied during periods of around five weeks [28,29,53] as the weight reduction normally appears to be significant after the fourth week.

Weight and body composition have been assessed at baseline and after the fifth week. The anthropometric assessment for body composition consisted in the 4-site skinfold Jackson and Pollock equations where the skinfold sites are abdominal, triceps, thigh and suprailiac to calculate the % of sub-cutaneous body fat [107] (Appendix 3), as they are widely used in research and highly effective in non-obese populations [108]. Weight have been assessed with a Salter digital scale and skinfolds have been taken using a Harpenden (HRP) caliper [109,110].

- **Appendix 3** - Jackson and Pollock anthropometric equations for body composition

Males (107) 4-Site Skinfold Equation for calculating % body fat	Females 4-Site Skinfold Equation for calculating % body fat
% Body Fat = (0.29288 x sum of skinfolds) - (0.0005 x square of the sum of skinfolds) + (0.15845 x age) - 5.76377, where the skinfold sites (measured in mm) are abdominal, triceps, thigh and suprailiac.	**% Body Fat** = (0.29669 x sum of skinfolds) - (0.00043 x square of the sum of skinfolds) + (0.02963 x age) + 1.4072, where the skinfold sites (measured in mm) are abdominal, triceps, thigh and suprailiac.

During the initial session of anthropometric measurements both groups of participants received detailed information regarding the dietary intervention and were able to ask questions to the main investigator. Both groups received examples of weekly meal plans (Appendices 4 and 5).

- **Appendix 4** - IF group 5:2 protocol

IF group 5:2 protocol

The 5:2 Intermittent Fasting protocol requires that you consume only 500 calories a day during two non-consecutive days a week and eat unconstrainedly the other five days of the week. It is very important that you leave at least one or two days of *ad libitum* eating between your weekly fasting days.

Remember to drink plenty of water throughout your fasting days. You can drink tea and coffee during your fasts, but you cannot add sugar, milk or cream, which contain calories. Use artificial sweeteners for flavour if you like. Avoid the coffee drinks in coffee shops if you are not sure whether they contain some type of syrup, milk product or sugary add-in.

Example 1 of meal plan for fasting day:	Example 2 of meal plan for fasting day:	Example 3 of meal plan for fasting day:
1. A breakfast of around 200 calories such as two scrambled eggs with a couple of slices of ham, water, green tea, or black coffee. 2. A lunch or dinner of small portion of lean beef grilled with broccoli, amounting to 300 calories.	1. A breakfast of around 200 calories such as one large banana and two cups of halves of strawberries, water, green tea, or black coffee. 2. A lunch or dinner of two small cod fillets, skin removed and 100 grams of cherry tomatoes with spices, amounting to 300 calories.	1. A breakfast of around 200 calories such as two cups of raspberries or blueberries with one boiled egg and water, green tea, or black coffee. 2. A lunch or dinner of two chicken breasts with a cup of grilled Brussel sprouts, amounting to 300 calories.

- **Appendix 5** - CR group protocol. Weekly meal plan - Approximate daily intake: 1200kcal

	Breakfast	Lunch	Diner	Snacks
Monday	2 hard-boiled eggs + 2 slices of lean sliced cooked ham 2 Rye crackers + 1 Coffee with Milk	Mixed Beans Mixed green salad (2 portions) + 1 spoonful vinaigrette + 2 rice crackers.	1 portion fillet of Cod (bake or sauté in 1tsp olive oil) with parsley sauce (2 table spoon). Mixed boiled vegetable + 1 small cup of brown rice	1 portion of mixed nuts (**AM**) 1 banana, 1 herbal tea (**PM**)
Tuesday	½ avocado + 2 strawberries + 1 spoonful of mixed nuts 1 green tea	Mixed vegetable omelette (3 eggs) 2 rye crackers + 1 green tea	Grilled beef steak 1 portion of rice +1 portion of vegetables	1 apple + 1 coffee (**AM**) 2 rice crackers (**PM**)
Wednesday	Scrambled eggs + ricotta cheese 1 rice breads + 1 coffee with milk	1 burgers 1 portion of mixed vegetables	1 breast of turkey in marinade 2 portions of salad + 2 rye crackers	1 pear (**AM**) 1 pear (**PM**)

Thursday	Tuna with lemon dressing 2 rye crackers + 1 green tea	2 pork skewers grilled ½ portion of salad + 1 portion ricotta cheese + 2 rye crackers	Trout with garlic lemon and pine nuts. 1 portion of rice + 1 portion of vegetables.	Olive and cheese (**AM**) 1 portion of mixed nuts (**PM**)
Friday	Scrambled eggs and ricotta cheese 2 rice crackers	1 stuffed pepper 1 stuffed tomato ½ portion salad	2 burgers 1 portion of vegetables + 1 portion of cottage cheese 2 rye crackers.	1 apple (**AM**) 2 rye crackers (**PM**)
Saturday	Smoked salmon 2 rye crackers + 1 black coffee	Vegetable soup 1 portion of salad + 2 rye crackers	3 pork skewers 1 portion of rice and 1 portion of vegetables	Olives and cheese (**AM**) Mixed nuts + 1 herbal tea (**PM**)
Sunday	Tuna and lemon dressing 2 rice breads + green tea	Shrimps in garlic ½ portion of salad + 1 portion of rice	Chicken breast 1 portion of salad 1 portion of vegetables + ricotta cheese	1 coffee + 1 banana (**AM**) 2 rye crackers + olives with cheese (**PM**)

Analysis

Data from weight and body composition of the subjects have been analysed using the Statistical Package for Social Sciences (IBM 2015). Descriptive data and weight and body composition data at baseline and upon completion of the trial are presented as mean and standard deviation. Dependent (paired sample) t-tests were carried out to assess differences in weight and body composition before and after the intervention in both groups. Normality was assessed by Shapiro- Wilk's test and independent t-tests were carried out to examine weight loss and sub-cutaneous body fat reduction differences between each diet group (Appendix 6). The level of significance for all tests has been set at $p < 0.05$. Dependant variables: Weight (ratio), % body fat (ratio); Independent variables: Diet (nominal), gender (nominal), age (ratio).

- **Appendix 6** - Raw SPSS outputs

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
Age	14	21	30	26.86	2.77
Height	14	154	177	167.357	7.5916
Ethnicity	14	1	3	1.43	0.756
BMI	14	18.9	29.5	23.243	2.8667
IF.fat.post	7	15.4	34.7	21.114	8.1501
IF.fat.pre	7	16.1	35.9	22.086	8.1522
IF.weight.post	7	45.2	80.9	63.5	14.1481
IF.weight.pre	7	46.6	81	64.271	13.9962
CR.fat.post	7	12.2	27.3	20.186	5.6896
CR.fat.pre	7	13.5	28.1	20.486	5.6931
Diet	14	1	2	1.5	0.519
Gender	14	1	2	1.71	0.469
CR.weight.post	7	56.9	75	66.814	6.7812
Weight.pre	14	46.6	81	65.586	10.6936
CR.weight.pre	7	57.8	75.5	66.9	6.9169
Weight.post	14	45.2	80.9	65.157	10.7966
Fat.pre	14	13.5	35.9	21.286	6.806
Fat.loss	14	-0.9	2.3	0.636	0.7801
Fat.post	14	12.2	34.7	20.65	6.7698
Weight.loss	14	-1.1	1.4	0.464	0.6823
Valid N (listwise)				7	

Figure A1: Sample characteristics descriptive statistics.

Tests of Normality

	Diet	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
Weight.loss	CR	0.253	7	0.197	0.928	7	0.53
	IF	0.201	7	.200*	0.939	7	0.629
Fat.loss	CR	0.17	7	.200*	0.97	7	0.899
	IF	0.225	7	.200*	0.903	7	0.35
*. This is a lower bound of the true significance. a. Lilliefors Significance Correction							

Figure A2: Shapiro-Wilk's test output for normality of weight loss and sub-cutaneous body fat reduction differences.

Paired Samples Test

	Paired Difference					t	df	Sig. (2-tailed)
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
				Lower	Upper			
Pair 1 CR. weight pre - CR. weight post	0.0857	0.6669	0.2521	-0.5311	0.7025	0.34	6	0.745
Pair 2 CR. fat.pre - CR.fat.post	0.3	0.7724	0.292	-0.4144	1.0144	1.028	6	0.344
Pair 3 IF.weight.pre - IF.weight.post	0.7714	0.4348	0.1643	0.3693	1.1735	4.694	6	0.003
Pair 4 IF.fat.pre - IF.fat.post	0.9714	0.6775	0.2561	0.3448	1.598	3.793	6	0.009

Figure A3: Dependent (paired sample) t-test output for assessing weight and body fat differences.

Group Statistics

Diet	N	Mean	Std. Deviation	Std. Error Mean
Weight loss CR	7	0.086	0.6669	0.2521
IF	7	0.843	0.4791	0.1811
Fat loss CR	7	0.3	0.7724	0.292
IF	7	0.971	0.6775	0.2561

Figure A4: Weight and fat loss means + SD by group output.

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Low	High

Weight loss	Equal variances assumed	0.809	0.386	-2.44	12	-0.7571	0.3104	-1.4334	-0.0809	-0.0809
	Equal variances not assumed			-2.44	10.86	-0.7571	0.3104	-1.4411	-0.0732	-0.0732
Fat.loss	Equal variances assumed	0.269	0.614	-1.729	12	0.109	-0.6714	0.3884	-1.5176	0.1747
	Equal variances not assumed			-1.729	11.79	0.11	-0.6714	0.3884	-1.5192	0.1763

Figure A5: Levene's test for equality of variances and independent t-test for weight and fat loss differences.

Results

Descriptive characteristics of subjects at baseline are reported in (Table 2). All participants were of comparable age, height, BMI and were mainly Caucasian (Appendix 6).

	All participants (N = 14)	CR group (N = 7)	IF group (N = 7)
Age at start years	26.8 ± 2.7	27.5 ± 0.8	26.1 ± 1.2
Baseline BMI (kg/m²)	23.2 ± 2.8	23 ± 0.5	23.4 ± 1.5
Height (cm)	167.3 ± 7.5	170 ± 2.3	164.7 ± 3.1
Gender	10 females, 4 males	5 females, 2 males	5 females, 2 males
Ethnic origin:			
Caucasian	10	6	4
Black	2	0	2
Latino	2	1	1

Table 2: Sample characteristics descriptive statistics (means ± SD).

Table 3 shows the descriptive statistical analysis of the weight and body composition data obtained at baseline and upon completion of the intervention (Appendix 6).

	All participants (N = 14)	CR group (N = 7)	IF group (N = 7)
Baseline weight (Kg)	65.5 ± 10.6	66.9 ± 6.9	64.2 ± 13.9
Baseline body fat (%)	21.2 ± 6.8	20.4 ± 5.6	22.1 ± 8.1
Final weight (Kg)	65.1 ± 10.7	66.8 ± 6.7	63.5 ± 14.1
Final body fat (%)	20.6 ± 6.7	20.1 ± 5.6	21.1 ± 8.1

Table 3: Weight and body composition descriptive statistics (means ± SD).

A dependent (paired sample) t-test was carried out to assess whether there is a significant difference between weight before and after the intervention in both dieting groups. The t-test revealed that the IF protocol had produced a statistically significant change in bodyweight (t = 4.69, p < 0.05) but the CR protocol had not produced a statically significant change in bodyweight (t = 0.34, p > 0.05) (Table 4) (Appendix 6) (Figure 1).

Dietary protocol	Baseline weight (Kg)	Final weight (Kg)
CR	66.9 ± 6.9	66.8 ± 6.7
IF	64.2 ± 13.9	63.5 ± 14.1*
(*= p <0,05) Statistically significant weight difference after intervention		

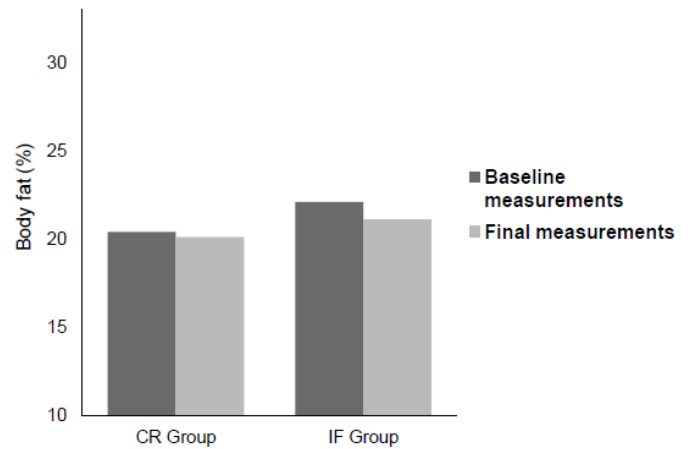Table 4: Bodyweight before and after the intervention in both groups (means ± SD).
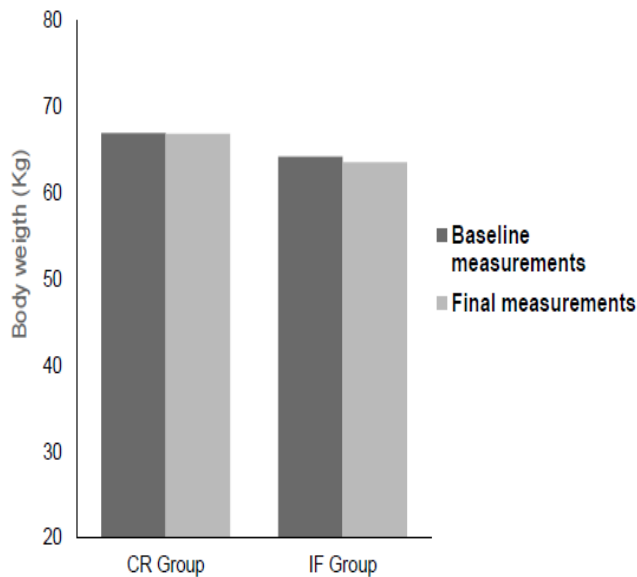
Figure 1: Mean body weight at baseline and upon completion of the intervention in both groups (error bars represent + 1 SD).

A dependent (paired sample) t-test was carried out to assess whether there is a significant difference between % of body fat before and after the intervention in both dieting groups. The t-test revealed that the IF protocol had produced a statistically significant change in % of body fat (t = 3.7, p < 0.05), the CR protocol had not produced a statically significant change in % of body fat (t = 1.02, p > 0.05) (Table 5) (Appendix 6) (Figure 2).

Dietary protocol	Baseline body fat (%)	Final body fat (%)
CR	20.4 ± 5.6	20.1 ± 5.6
IF	22.1 ± 8.1	21.1 ± 8.1*
(*= p <0,05) Statistically significant body fat difference after intervention		

Table 5: Sub-cutaneous body fat percentage before and after the intervention in both groups (means ± SD).

Figure 2: Mean body fat at baseline and upon completion of the intervention in both groups (error bars represent + 1 SD).

Weight loss differences within each diet group have been calculated (initial weight minus weight after intervention); Sub-cutaneous body fat reduction differences within each diet group have been calculated (initial sub-cutaneous body fat minus sub-cutaneous body fat after intervention). Weight loss and sub-cutaneous body fat reduction differences in the IF group have been compared against weight loss and sub-cutaneous body fat reduction in the CR group. The differences were normally distributed within each diet group, as assessed by Shapiro-Wilk's test (p > 0.05) (Appendix 6).

An independent t-test was carried out to determine whether the weight loss and sub-cutaneous body fat reduction differences between each diet group were statistically significant. Levene's Test for Equality of Variances revealed that equal variance could be assumed for weight loss (F = 0.80, p > 0.05) and body fat reduction (F = 0.26, p > 0.05) (Appendix 6). The independent t-test revealed that the IF protocol had produced statistically significant greater weight loss (0.8 ± 0.4 kg) and body fat reduction (1 ± 0.6 %) compared to the CR protocol (0.1 ± 0.6 kg for weight loss) (t = -2.4, p > 0.05) and (0.3 ± 0.7 % body fat reduction) (t = -1.7, p > 0.05).

Dietary protocol	Weight loss (Kg)	Body fat reduction (%)
CR	0.1 ± 0.6	0.3 ± 0.7
IF	0.8 ± 0.4*	1 ± 0.6*
(*= p <0,05) Statistically significant weight and body fat differences between groups		

Table 6: Weight loss and sub-cutaneous body fat reduction differences (means ± SD).

Discussion

Main Findings

The aim of the study was to determine changes in weight and body composition between commons IF and CR protocols in healthy non-obese individuals over a five-week intervention. Even though it was initially hypothesised that the IF group could have compensated for the calorie deficit created during the fasting periods by increasing their calorie intake on the *ad libitum* feeding days, the IF dietary approach has achieved significant weight loss and body composition improvements, whereas the CR approach has not produced any significant changes in weight or body composition.

Comparison with Previous Literature

IF Results

The significant weight loss and body composition improvements achieved by the IF protocol appear to agree with most of the literature on IF. Previous studies have established that IF methods are known to be as effective as daily CR for weight reduction, body composition and weight control in humans [58]. It has been proven that as long as subjects undergoing IF interventions do not compensate by over-eating during the non-fasting periods, IF will always lead to reduced calorie intake [41, 50]. In line with our results for the IF group, most IF studies have found significant improvements on weight and body fat [57,59,60,61,111,112,113].

Our IF results for weight loss (0.8 ± 0.4) kg are not as strong as those found in similar trials of comparable duration: Johnson et al. conducted a 4-week ADF intervention and achieved 4kg of total weight loss [60], Eshghinia's first study found 4.7 ± 2.5kg of total weight loss after a similar 4-week ADF protocol [114] and achieved 6 ± 1.2kg after a 6-week ADF second study [113,118], Varady et al. achieved 5.6 ± 1kg with a similar ADF design, although the trial lasted 10 weeks [59]. According to these effects on body weight, our IF results for body fat reduction (1 ± 0.6) % are not as strong as those found in the above trials of comparable duration which reported changes in body composition: Eshghinia and Mohammadzadeh's study found a body fat reduction of 2.84 ± 0.2% and Varady's trial found a body fat declined of 2.9 ± 1% [59].

However, the mentioned trials utilised more severe forms of IF and often times participants were overweight or even obese, which may explain the weight loss differences compared to our study.

When examining other IF studies where researchers applied dissimilar fasting protocols to the present study, positive improvements are always found: Barnosky et al. conducted an IF vs CR for type 2 diabetes prevention study where they observed weight reductions of 0.25kg of body weight per week and also found

reductions of waist circumference on an IF regime with a 75% energy restriction during the 1-3 fasting days per week [50]. Heilbronn et al. conducted another interesting study where participants lost an average of 2.1kg total bodyweight after a 22-day ADF intervention despite given instructions to eat double their typical day's intake every feeding day [56]. Studies also looking at the effects of IF on different health markers such as decreased blood pressure, resting heart rates, glucose metabolism and cardiovascular health have consistently shown improvements after implementing IF protocols [4, 61,62]. More aggressive IF protocols are seen in the literature, such as the one utilised by Johnstone et al. where lean subjects underwent a 36 h fast that resulted in a negative energy balance of approximately 12 MJ; researchers found that participants lost an average of 1.3kg of total body weight [115], which matches the exact same amount of weight loss (1.3kg) found after a single 24 h fast in one of the early clinical studies on IF [116], although most of it was thought to be intramuscular glycogen and water. Again, most of these studies have examined overweight or obese participants. It is also important to mention that no IF protocols for weight loss recommending fasting periods over 24 h outside of a clinical setting have been found.

CR Results

Our CR results for both weight loss (0.1 ± 0.6) kg and body fat reduction (0.3 ± 0.7) % are statistically non-significant, data that do not seem to agree with the vast majority of the scientific literature. While research on CR in humans is still at an early stage [33], the effects on body weight and changes in body composition seem to be consistent in most studies: from early trials in humans concluding that CR is an effective strategy towards weight loss [117,118,119,120,121,122] to the current research that confirms a direct correlation between CR and body composition [123,124,125,126].

The positive correlation between CR and weight and body changes has been shown in short term trials of a similar duration to the present study where participants have experienced significant improvements: Stamets et al. examined the effects of CR intervention in obese women and after only 4 weeks of hypocaloric dieting participants experienced a weight reduction of 4.1 ± 1.7 kg [127], Norrelund et al. also conducted a 4 weeks trial on obese individuals where they examined the effects of a VLCD diet on protein breakdown [128], upon completion of the study participants reduced total body weight by 5% and body fat by 10%. Trials of longer duration have shown greater improvements for both weight and body composition: Haugaard et al. and Luscombe et al. utilised similar CR protocols during 8 weeks in obese and overweight participants, the first trial found an 8% body weight reduction and a 14% body loss [129], the second found the same percentage of weight loss and a 20% of body fat reduction [130]. The same trend is seen in long-term trials where the correlation

between CR and weight and body composition changes has also been well established, such as the coordinated multicentre study CALERIE (Comprehensive Assessment of Long Term Effects of Reducing Caloric Intake) in which healthy volunteers underwent the CR interventions for two years to test how practical and safe is a 25% CR diet in non-obese subjects, researchers found that participants lost an average of 10% of their body weight in the first year, and maintained the weight over the second year [131,132]. Even though the study did not focus solely on changes in body composition and weight, the results from the data collected are consistent with previous studies related to reductions in body weight and fat [133, 134,135]. Similarly, the Biosphere studies have demonstrated substantial weight loss in subjects after a low-calorie nutrient-dense diet intervention over two years [37,36]. Cross-sectional data on the effects of long-term CR in humans obtained from participants undergoing six years of CR also shows a dramatic reduction in body adiposity and Body Mass Index (BMI) [136,137] as well as improvements in other health markers seen in previous human and animal studies [39].

In previously mentioned studies such as the Biosphere trials researchers were able control participants' dietary intake in detail, other studies utilised either whole-body calorimeter measurements or a controlled environment for metabolic assessment to accurately study dietary intake data. However, similar trials to the present study where dietary intake assessment is dependent on self-reports or where free-living subjects are expected to estimate caloric intake and food portions tend to face under-reporting and under-estimating issues [138]. Based on our results, and even though participants did not report problems following the diet, we believe subjects undergoing the CR intervention might have experienced adherence problems and could have unintentionally underestimated total food intake.

IF vs CR Results

To date, no studies on CR vs IF showing identical results to the present trial have been found, although there has only been limited research directly comparing both dietary protocols. Wing et al. utilised an intermittent VLCD protocol that could be considered IF and compared it to a CR one in a 50-week weight loss trial for obese patients with type II diabetes, they found that subjects following the first protocol lost significantly more weight than did CR subjects during the trial [139]. The authors did not asses body composition changes and even though the first protocol produced better improvements similarly to what we have seen in our study, the CR diet also led to statistically significant weight loss.

Varady's studies have also examined weight and body composition outcomes as well as Coronary Artery Disease (CAD) risk indicators after different IF and continuous CR interventions in short-term trials of 10 and 12 weeks in obese

adults [4, 50,53,59,112]. Researchers have concluded that while IF is a safe and valid strategy to reduce total calorie intake, whether it is superior than continuous CR is still unclear. Seimon et al. published a large systematic review on CR vs IF for body composition changes, weight loss and several other biomarkers. They reviewed 40 human studies on different CR interventions, intermittent energy restriction and IF protocols, 12 of which were a direct comparison of CR vs IF interventions including overweight and obese participants [140], researchers concluded that both dietary protocols appear to induce equivalent weight loss and body composition outcomes, and concluded that neither of them seems to be superior to the other.

Two recent systematic reviews of randomised clinical trials have shown that IF appears to represent a valid option to continuous CR for weight loss, as the achieved weight loss in overweight and obese individuals undergoing IF interventions was comparable to that achieved by traditional CR interventions [140,141]. Davis et al. also concluded that IF represents an effective alternative strategy for health practitioners to promote weight loss in obese and overweight patients. Another recent systematic review and meta-analysis on IF weight and biological markers in long term intervention studies of >6 months duration have conluded that even though IF studies showed weight loss, there was no evidence that it provided specific benefits over continuous CR at least in the little long-term evidence available [126], although researchers concluded that future longer-term trials are required to fully evaluate any lasting benefits that IF might have over traditional CR.

Strengths of the Study

A large proportion of the available trials on both CR and IF does only assess subjects' body weight to evaluate the effectiveness of the interventions and also tend to measure different biomarkers such as blood glucose or total cholesterol [52, 53, 55,142], however, many of them do not account for body composition changes. The combination of both body composition and body weight has been seen in a limited number of previous CR and IF trials [59,61,111] and it represents an important advantage of the present study since it provides a more precise evaluation of the intervention's efficacy [56] since research shows that the part of the weight loss produced by prolonged isocaloric dieting is often caused not only by the reduction of adipose tissue but also by amino acid catabolism in muscle tissue [128].

Another advantage of the present study is the fact that we have studied both dietary protocols on physically active, non-obese (BMI < 29.9) [143] healthy subjects, which appears to be a novelty on IF vs CR research. According to Harvie and Howell's recent summary of evidence, to date, there are currently no data comparing IF with CR in normal-weight subjects [104].

One of the main findings is the difference in efficacy between the two protocols, as we believe it highlights the simplicity of the IF approach against the complexity of traditional CR [44], which seems to be one of the main difficulties with traditional CR [144,145]. Research shows that only 25-30% of individuals that undergo daily CR manage to adhere to it for more than 12 months [146]. In fact, data from independent reviewers and meta-analysis suggest that CR promotes short-term weight loss but the weight reduction has not been proved to be sustainable in the long-term [147].

Contrarily, recent data on IF is showing greater adherence rates for IF protocols: Harvie et al. compared a traditional CR Mediterranean diet against two WDF diets similar to our IF intervention. The IF protocols showed 76% and 74% adherence rates against 39% from the traditional CR diet [148]. In like manner, Wegman et al. studied the practicality and tolerability of IF and found strict adherence to the IF protocols, and all participants found the intervention as tolerable [149]. IF has indeed been described as a plausible weight loss aid [150] as it can improve compliance in human subjects [42,58]. In the US, it has been reported that 14% of adults have already used fasting as a means to control body weight [41], probably due to the fact that IF protocols provide a simple and relatively easy dieting option [151].

Study Limitations

The lack of weight loss and body composition changes found in the CR group could be explained by the nature of the dietary regimes, even though no participants withdrew from the study, the authors speculate that the IF protocol was probably easier to adhere to than the CR one. This in fact is considered one of the main strengths of the IF approach [53, 58, 150,152]. Both groups of participants received detailed information regarding the dietary intervention at baseline and were expected to follow them; however, while the IF protocol mostly requires that participants just avoid consuming any calories during a certain amount of time [14], the CR group had to estimate food portions and calculate calories on a daily basis, and even though they were given a simplified and detailed sample of daily meal plans, the well-established prevalence of underestimation of food intake [153] a free-living population might have resulted in the CR group dieting over their daily calorie target; which seems to be the main limitation of CR as supported by the literature [40,46].

Difficulties in the ability to perceive calories and intake autoregulation have been studied for decades [154] as problems with estimates of food quantity and calories are very commonly found in the literature. The causes of underestimation include inaccuracy in reporting food portions, psychological behaviours, social and cultural factors, memory disturbance and behavioural factors [155]. Avoiding food intake underestimation is in fact considered one of the main challenges that researchers encounter in trials with free-population, and even though food intake underestimation is considered especially extreme in overweight and obese individuals [156,157], it also appears to be prevalent among non- obese populations [158] such as our CR group sample.

Implications and Recommendations for Future Research

Based on the data obtained, the following topics for future research are recommended:

Additional research is needed on IF vs CR for weight loss and body composition changes in normal-weight individuals, since no other studies on normal weight subjects have compared both protocols [104] and obese and overweight studies have shown equal success rates for both.

Since IF has already been established as a valid alternative to continuous CR [44,103, 159], further research is needed to compare different IF versions and to establish the effectiveness of one IF method over the others. To date, no studies comparing different IF protocols against each other for weight loss and body composition changes have been found.

Additional research is also needed to further examine IF vs CR differences in adherence rates, as our study has shown higher compliance for IF in line with recent research [149] and several authors have speculated that IF regimes could improve adherence [58]. More research is need especially regarding long-term IF adherence in free-living populations, since CR has extensively shown poor long-term success [147] and IF might offer a reliable alternative. Further psycho-social data is also required to better examine behavioural factors that can modulate compliance to both diet protocols.

Future IF vs CR studies should always control food intake to avoid intake underestimation. As a preventive measure, we recommend that researchers always include regular food diaries during the trial, although this practise is common in CR studies of similar design [140,152,160,161]. Nevertheless, data is not conclusive on whether or not they can mitigate or reduce the prevalence of underestimation of food intake in free-living populations [138]. If possible, further trials should compare both protocols in settings where researchers are able to provide participants with all meals [40, 128,162], method that guarantees the absence of calorie underreporting and underestimation as researchers control total calorie intake [163]. Alternatively, researchers could utilise more rigorous methods to assess calorie intake to avoid underestimation; for example, in conjunction with food diaries, accuracy could be improved by contrasting reported energy intake with reliable measurement methods such as doubly labeled water measurements or even respiratory-chamber indirect calorimetry systems as they are well established and precise methods for metabolic assessment [164,165,166].

Conclusions

Our data suggest that IF is an effective strategy for weight loss and body composition improvement, as it provides a simplified method for reducing total energy intake that could possibly be easier to adhere than continuous CR. The complexity of daily CR seen in the literature might have influenced the presumed low adherence to the CR protocol in the present study. In a similar fashion, the positive adherence to the IF appears to be in line with recent IF research that shows improved adherence over traditional CR. Further research is required to better explain behavioural and physiological factors, that can enhance or reduce compliance to IF and CR interventions.

IF could potentially be a more practical method for achieving caloric deficit than continuous CR in individuals that tend to underestimate and underreport food intake. Thus, different IF protocols can be offered as an alternative to more traditional approaches of CR for reducing total body weight and optimising body composition.

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