

ORIGINAL RESEARCH

Is two days of intermittent energy restriction per week a feasible weight loss approach in obese males? A randomised pilot study.

Running head: Intermittent fasting - a new weight loss approach?

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Abstract

Aim: The 5:2 diet (two non-consecutive days of 2460 KJ (600 calories) and five days of ad libitum eating per week) is becoming increasingly popular. This pilot study aimed to determine whether the 5:2 diet can achieve $\geq 5\%$ weight loss and greater improvements in weight and biochemical markers than a standard energy restricted diet (SERD) in obese male war veterans.

Methods: Twenty-four participants were randomised to consume either the 5:2 diet or a SERD (2050 KJ (500 calorie) reduction per day) for six months. Weight, waist circumference (WC), fasting blood glucose, blood lipids, blood pressure and dietary intake were measured at baseline, three and six months by a blinded investigator.

Results: After six months, participants in both groups significantly reduced body weight ($p < 0.001$), WC ($p < 0.001$) and systolic blood pressure ($p = 0.001$). Mean weight loss was 5.3 ± 3.0 kg ($5.5 \pm 3.2\%$) for the 5:2 group and 5.5 ± 4.3 kg ($5.4 \pm 4.2\%$) for the SERD group. Mean WC reduction for the 5:2 diet was 8.0 ± 4.5 cm and 6.4 ± 5.8 cm for the control group. There was no significant difference in the amount of weight loss or WC reduction between diet groups. There was no significant change in diastolic blood pressure, fasting blood glucose or blood lipids in either dietary group.

Conclusions: Results suggest that the 5:2 diet is a successful but not superior weight loss approach in male war veterans when compared to a SERD. Future research is

needed to determine the long-term effectiveness of the 5:2 diet and its effectiveness in other population groups.

Key words: 5:2 diet, intermittent energy restriction, obesity, war veterans, weight loss

Introduction

Obesity is one of the major health crises of our time. Despite a wealth of research in the area and numerous weight loss approaches, obesity rates continue to increase around the world. In 2011, 80% of Australian males aged 45-74 years were overweight or obese.¹ It is widely known that overweight and obese individuals are at an increased risk of a number of chronic health conditions including diabetes, hypertension, cancer, sleep apnoea and coronary artery disease.^{2,3} Management of obesity related co-morbidities represents an increasing health burden to both the individual and the health system.²

Modest weight loss of 5-10% of body weight can improve quality of life and reduce mortality and morbidity.² Energy restricted diets have been shown to help people achieve this degree of weight loss but long-term success is often limited. Many fail to lose weight or simply regain any lost weight quickly.² Bariatric surgery and weight loss medications have been shown to induce significant weight loss and help offset weight regain but both have side effects and require lifelong follow-up.² In light of the above, novel, cost effective and low risk dietary approaches to achieve and sustain weight loss goals are required. One possible approach that has appeared increasingly in the

scientific literature over the last 10-20 years (and the media more recently) is intermittent energy restriction (IER).⁴⁻¹¹

Intermittent energy restriction is a dietary strategy where individuals follow a heavily energy restricted intake on some days and a normal energy intake on others. Studies have shown that this form of energy restriction can lead to modest weight loss of 5.8-14.5kg over a three month period.⁸ Furthermore, IER has been shown to induce a number of other metabolic health benefits including a reduction in fasting blood sugar levels, blood pressure and blood lipids.⁸ It is also suggested that the distinct advantage of IER over other dietary approaches to weight loss is that individuals do not have to constantly “diet”.⁷

Although the majority of studies into IER have been conducted in animals, a number of single arm trials investigating alternate day fasting (ADF) have shown that IER induces weight loss^{4,5,9} and improves lipid profile.^{5,9} Additionally, a two day per week IER has been shown to be as effective at inducing weight loss and clinically significant biochemical changes as a continuous energy restriction¹⁰ and in fact, may be more effective at reducing body fat and insulin resistance when a carbohydrate restriction is included.¹¹ Our study is the first to report on the 5:2 method of IER (where individuals consume only 600kcal on two non-consecutive days per week but eat normally on the other five days) as popularised by Dr. Michael Moseley.⁷ It appears this approach has some merit, but it is unclear whether the diet is safe and effective for an older male population.

Evidence for the safety and efficacy of weight loss in older people is lacking despite the increasing burden of obesity and chronic disease in this group.³ Current evidence indicates that the relationship between excess weight and all-cause mortality weakens with advancing age. However, quality of life and mobility become increasingly important outcomes.² Australian veterans are a subgroup of older adults who are in great need of health restoring strategies which support quality of life and psychological wellbeing. They are three times less likely than the general Australian population to rate their own health as good or excellent¹² and obesity rates are similar to that of the general population.¹³

This randomised pilot study aims to determine whether the 5:2 diet leads to 5% weight loss over a six month period and whether it leads to greater weight loss and greater improvements in blood sugar, cholesterol and blood pressure than a standard energy reduced diet. The study also aims to investigate whether there are differences in quality of life, adherence rates, side effects and dietary quality between the two diets.

Methods

Twenty-four male war veterans were recruited and consented to participate in this pilot trial. Volunteers were recruited via flyers placed in Austin Health Veteran gyms and Veteran day group programs. Veterans meeting the inclusion criteria were included in the study: male aged 55-75yrs, a body mass index (BMI) greater than or equal to 30kg/m², weight stable (i.e. <5% weight loss or gain) for three months prior to the beginning of the study. Any participant with a medical contraindication (active cancer,

diabetic on insulin, end stage renal failure, psychiatric hospital admission within previous 12 months), a high alcohol intake (> 28 standard drinks per week) or taking antipsychotic medication associated with weight gain (mirtazapine, olanzapine, clozapine) were excluded from the study. This study was approved by the Austin Health Human Research Ethics Committee. The trial was prospectively registered with the Australian New Zealand Clinical Trials Registry Trial ID#: ACTRN12614000396628. No financial compensation was provided to participants for their participation.

The study consisted of a single centre, parallel group randomised controlled trial. Participants were randomised to one of two groups - A standard energy restricted diet (SERD) or an intermittent energy restricted 5:2 diet group (5:2 DIET) by a blinded investigator who drew one of two dietary groups from a concealed envelope.

Dietary Intervention: Standard energy restricted diet (SERD): Participants were required to follow a continuous daily energy restricted diet (500-calorie daily reduction from average requirement) based on Australian guide to Healthy Eating (AGHE) dietary principles (low saturated fat, high fibre, moderate protein and carbohydrate).

Intermittent energy restricted 5:2 Diet (5:2 DIET): Participants were required to “fast” for two non-consecutive days per week (restrict their daily calorie intake to 600 calories for the entire “fast day”) and eat ad libitum on the remaining five days (i.e. no specific dietary recommendations were made). Participants were encouraged to consume calorie free beverages on fasting days.

Educational material and sample meal plans were provided to participants in each group and all participants received five individual counselling sessions specific to their

dietary intervention. These were conducted by Austin Health Accredited Practising Dietitians at baseline, weeks two, four and eight and at three months. At the conclusion of the three month review participants were asked to continue with their dietary regimen for a further three months. During this time no formal review or further dietetic support was provided. Contact details for the dietitian were provided to participants in both groups and they were encouraged to initiate contact via telephone if they needed assistance. To monitor and maximise dietary compliance, participants were asked to keep diet diaries. Adherence to each dietary intervention was assessed by the dietitian by using patients self recorded dietary diaries and self reported diet histories taken during their dietetic appointments at two, four and eight weeks and at three and six months. Participants were advised to maintain their current physical activity levels throughout the study and did not receive specific exercise counselling.

Measurements were taken at baseline and at three and six months. A blinded investigator took all measurements in the morning after a 12-hour fast. Height was measured to the nearest 0.5cm using a wall mounted stadiometer. Weight was measured to the nearest 0.1kg using digital scales (Wedderburn Tanita BWB-600) and waist and hip circumference were measured to the nearest 0.5cm using a standardised measuring tape. Systolic and diastolic blood pressure was measured twice with a 10-minute rest between measures and the mean value calculated (Omron m5-1 Omron Health Care Limited). Fasting blood glucose (CV 1.0% at 4.6 mM & 0.9% at 15.5 mM), total cholesterol (CV 1.9% at 2.8 mM & 1.6% at 6.5 mM), high density lipoprotein (HDL) (CV 2.2% at 0.55 mM & 3.7% at 1.0 mM) and low density lipoprotein (LDL) CV

calculated using the formula of *Friedewald equation* were measured at Austin Health Pathology by a trained Austin Health phlebotomist using standardised Austin Health pathology procedures.

Dietary analysis examining mean energy, protein, fat, carbohydrates and micronutrients was conducted using a validated electronic food frequency questionnaire (The Dietary Questionnaire for Epidemiological Studies Version 2 (DQES v2) Cancer Council Victoria). Quality of life was measured using a quality of life scale AQoL-8D.¹⁴ Any side effects (i.e. light-headedness, dizziness) were recorded in individual participant visit notes.

A convenience sample was selected. Differences in general characteristics at baseline between groups were analysed using Two-sample Wilcoxon Rank-sum (Mann-Whitney) tests. Wilcoxon Signed-rank tests, Two-sample Wilcoxon Rank-sum (Mann-Whitney) and linear regression with robust standard error adjustments were used to determine any significant changes and difference between groups from baseline to six months for measures of weight, WC, BMI, blood glucose, blood lipids, blood pressure, dietary intake and quality of life. Significance was accepted at an alpha level of $p < 0.05$ for all statistical measures and all analyses were performed using STATA data analysis and statistical software version 14 (StataCorp LP).

Results

A Consolidated Standards of Reporting Trials (CONSORT) flow chart of the participant randomisation is outlined in Figure 1. Eligible war veterans were recruited from May

2014 to April 2015. Twenty-four participants commenced the study and 23 participants completed the entire 6-month trial. One participant withdrew due to a long hospital admission. There was no deviation to the outlined protocol. Participants commenced the study within two weeks of consenting to participate.

Patient demographics and clinical characteristics are displayed in Table 1. There were no significant differences in baseline characteristics among the groups. Both diets had a positive effect on weight, waist circumference, BMI, and systolic blood pressure. After six months, mean weight loss for participants on the 5:2 diet was $5.3 \pm 3.0\text{kg}$ ($5.5 \pm 3.2\%$) and for participants following the SERD it was $5.5 \pm 4.3\text{kg}$ ($5.4 \pm 4.2\%$). Waist circumference reduced over time in both dietary groups $p = > 0.001$. The SERD group on average lost $6.4 \pm 10\text{cm}$ from their waistline and the 5:2 diet group lost on average $8 \pm 10\text{cm}$ from their waistline after six months. There were no significant between-group differences in any of these anthropometric measures.

Both groups experienced significant reduction in systolic blood pressure; 10.2mmHg and 14mmHg reduction in the SERD and 5:2 diet respectively $p = >0.001$, but no change in diastolic blood pressure. Again, there was no significant between group differences in blood pressure reduction.

Fasting blood glucose and blood lipids did not significantly alter over the course of the study in either group. All these markers were within normal limits at baseline and continued to be within normal limits for the duration of the study.

Quality of life AQoL8D scores are displayed in Figure 2. After six months participants in both groups improved their 'psycho-social' dimension score $p = 0.001$,

‘physical’ dimension score $p = 0.03$ and overall AQoL8D score $p = 0.003$ suggesting that neither diet had a detrimental effect on the quality of life. When compared to Australian males of similar age this population group on average scored lower in all domains across all time points.¹⁵

There were no major adverse side effects experienced in either dietary group. Participants in both groups experienced only minor physical symptoms (see Table 2). The main mild side effect experienced by the 5:2 diet group was hunger. Over half of participants on the 5:2 diet experienced hunger after following the diet for two weeks. This improved over time, with only 18.2% of participants on the 5:2 diet experiencing hunger at six months.

Compliance rates were similar in both dietary groups across the duration of the study. Diet histories conducted by the dietitian indicated that 83% of participants on the SERD and 82% of participants on the 5:2 diet were deemed to be following their respective diets at three months. This adherence declined slightly over the course of the study in both groups, but remained strong with 75% of participants on the SERD and 73% of participants on the 5:2 diet following their prescribed diets at six months.

The proportion of participants who regained weight (defined as gaining $>1\text{kg}$ of body weight) between three to six months was similar with 2 participants in both groups regaining weight: 16.7% of participants in the 5:2 diet group and 18.7% of participants in the SERD group.

There were no significant differences in energy or macronutrient intakes between the groups at baseline (see Table 3). Diet composition was also similar at baseline in

both groups. Food frequency data indicated that on average at baseline, 22% and 21% of dietary energy was coming from protein, 36% and 38% from fat, 35% and 36% from CHO and 7% and 5% from alcohol in the SERD and 5:2 diet groups respectively.

Changes in dietary intake during the duration of the study are outlined in Table 3. Data from the food frequency questionnaires showed that all participants in both groups reduced their calorie intake after three months, and that this was generally maintained after six months.

Discussion

This pilot study aimed to determine whether the 5:2 diet can achieve $\geq 5\%$ weight loss and greater improvements in weight and biochemical markers than a standard calorie restricted diet (SERD). Results indicate that the 5:2 diet is as effective, but not superior to a SERD at inducing clinically significant weight loss (5%)² in a free living population. The two diets were well tolerated and weight loss was accompanied by a reduction in waist circumference and blood pressure in both groups. On average, participants in both groups went from being hypertensive to normotensive. No change was seen in blood sugar or blood lipid levels in either group but they were also not elevated at baseline. The 5:2 diet did not negatively impact wellbeing and provided sufficient nutrients with the exception of fibre. The study had an excellent retention rate in both groups indicating that the 5:2 diet is not any more difficult or taxing to follow than a SERD in a free-living situation.

Food frequency data shows there was no significant difference in total energy intake between the two diets at baseline or six months, which helps to explain why the rate and amount of weight lost in the two groups was the same. Essentially, the degree of energy restriction was the same, only the strategy to achieve that restriction differed. Previous research has already shown that participants following an IER diet do not overeat on the day following a “fast day” to compensate for the large energy restriction.¹⁶ Both groups lost the majority of weight in the first three months and only a small amount of additional weight in the three to six month period. This weight loss pattern is consistent with FFQ data which showed a significant reduction in energy intake between baseline and three months with little further change thereafter.

The nutritional quality of the 5:2 diet is an important determinant of its usefulness as a long term dietary strategy, particularly in an older adult population who are at risk of increasing frailty.² The SERD is based on the Australian Dietary Guidelines and met all Australian Nutrient Reference Values¹⁷ when analysed using Foodworks™ (Xyris Software Australia). It was not possible to perform the same analysis on the 5:2 diet as only a calorie limit was prescribed. However, FFQ data shows that when total energy intake significantly reduced between baseline and three months, energy intake from all major macronutrient groups also fell evenly, indicating that following the 5:2 diet does not encourage or require individuals to completely restrict or avoid a particular food group. A significant reduction in fat, sugar, and salt also suggests that participants were consuming fewer unhealthy food choices than at baseline. Both groups failed to meet recommended average intakes for fibre (30g/day for men aged 50-70yrs)¹⁷ and this may

have contributed to some complaints of constipation. According to the National Nutrition Survey 1998 the major source of fibre in the standard Australian diet is grain and cereal foods. This is a problem for weight management as the national average intake of these foods is well above the current recommended level.¹⁸ The average calcium intake for participants following the 5:2 diet was only borderline adequate for EAR (840mg/day) at six months. The 5:2 diet group met RDI (1000mg/day) at baseline and the SERD group met both EAR and RDI at all time points.¹⁷ Participants on the SERD received specific advice on how many servings of each food group are required whereas those following the 5:2 diet did not. Anecdotally, participants following the 5:2 diet reported that the two days of “fasting” facilitated having two alcohol free days per week, however this was not supported by FFQ data. The data showed that alcohol consumption did not reduce significantly over time. It is not clear if the number of participants that reported this is insufficient to induce a change in the data or if participants consumed additional alcohol on the other days to make up for the two-day abstinence.

There has been limited research into IER in humans and the majority available concerns ADF. Two studies have investigated, a two day IER in comparison with a continuous energy restriction in free-living individuals. Harvie *et al.* 2011 randomised 107 overweight or obese pre-menopausal women to either a IER diet (2 consecutive days VLCD (2710kJ), 5 days ad libitum) or continuous energy restriction (6276kJ/day) for six months. They observed similar results to our study, finding the two diets to be comparable in terms of weight reduction, waist circumference, body fat loss and

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numerous health biomarkers except fasting insulin and HOMA-IR, where IER produced greater reductions. They also found that side effects were minimal (e.g. hunger, constipation) but more likely to occur in the IER group.

A second study Harvie *et al.* 2013 compared two carbohydrate controlled IER diets (either 2500-2717kJ/day, <40g carbohydrate for 2 days per week or the same plus ad libitum protein and fat) with a daily energy restriction (6000kJ/day 7 days per week) among 115 overweight women (aged 20-69yrs). They found weight loss to be similar in all three groups but noted significantly greater improvements in insulin sensitivity and percentage body fat loss in the IER groups.

To the best of our knowledge, this is the first study to explore the effects of the 5:2 diet in the older male population and contributes to the relatively small body of research into the effects of weight loss in older adults. Consumption of adequate nutrients is particularly important in this population thus strategies to ensure adequate fibre and calcium need to be considered in order for this to be a feasible diet option for the older person. This could include tailored dietary advice and/or supplements.

A limitation of the present study was the relatively small single gendered sample size. As a result, we cannot conclude if women perform any differently to men. The short duration means we cannot conclude if weight loss would have continued or been maintained in the longer term. Due to budget constraints, we were unable to test body composition changes (DEXA scan is the only validated method in this population) which is an important consideration in an older adult population. Budget also limited the range of biochemical tests we could include, which is why fasting insulin was not

measured. We did not stipulate to the participants on the 5:2 diet when they should have their blood tests taken in relation to their “fasting day” thus we cannot rule out the fact that this may have affected the accuracy of the result in some participants. However, we did not find any significant differences between the groups in any of the biochemical tests which is consistent with other studies into a two day IER.^{10,11} As with any diet study, it is difficult to accurately determine compliance with the prescribed diet, particularly in free-living individuals.

Future studies are needed to determine the long-term effectiveness of the 5:2 diet, its efficacy in other population groups and if ongoing frequent follow-up improves weight loss over the longer term (>6 months). Body composition data is needed to determine the degree of fat loss compared with lean tissue loss, especially in an older population. It would also be interesting to see if the 5:2 method could be used as a framework to aid implementation of other dietary strategies such as the Mediterranean Diet.

In conclusion, this research shows that the 5:2 diet is a feasible weight loss strategy in this older male population and the study suggests that it is both well tolerated and efficacious. Participants were able to follow the diet sufficiently to induce magnitudes of weight loss similar to that of standard dietary modification practices and the diet does not appear to cause an unbalanced nutritional intake.

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Conflict of interest

The authors have no conflict of interest to declare.

Authorship

M.C and L.LF developed the study design, coordinated the data collection and analysis and drafted the manuscript. J.P and C.H acted as medical representation for the research trial and provided expert guidance with study design, data collect, results analysis and interpretation. All authors edited the paper. All authors were in agreement with the manuscript and declare that the content has not been published elsewhere. The Authors would like to thank Kate Desneves, Liza Alpers, Esti Adithama and Professor Leonid Churilov for their contribution to the study.

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Parameter	Baseline	3 months	6 months	P value*
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9	0.68
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Table 2. Symptoms experienced by participants

	Nausea <i>n</i> (%)	Headache <i>n</i> (%)	Dizziness / light- headedness <i>n</i> (%)	Hunger <i>n</i> (%)	Constipation <i>n</i> (%)
2 week					
SERD	0	0	0	0	3 (25)
5:2	0	1 (9.1)	1 (9.1)	6 (54.5)	3 (27.3)
3 Month					
SERD	0	0	0	2 (16.7)	0
5:2	0	1 (9.1)	1 (9.1)	4 (36.4)	2 (18.2)
6 Month					
SERD	0	0	0	0	0
5:2	0	2 (18.2)	0	2 (18.2)	0

Nutrient	Baseline	3 months	6 months	<i>P</i> value*
				0.091 > 0.001

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

Figure 2: Quality of life scores of participants over time

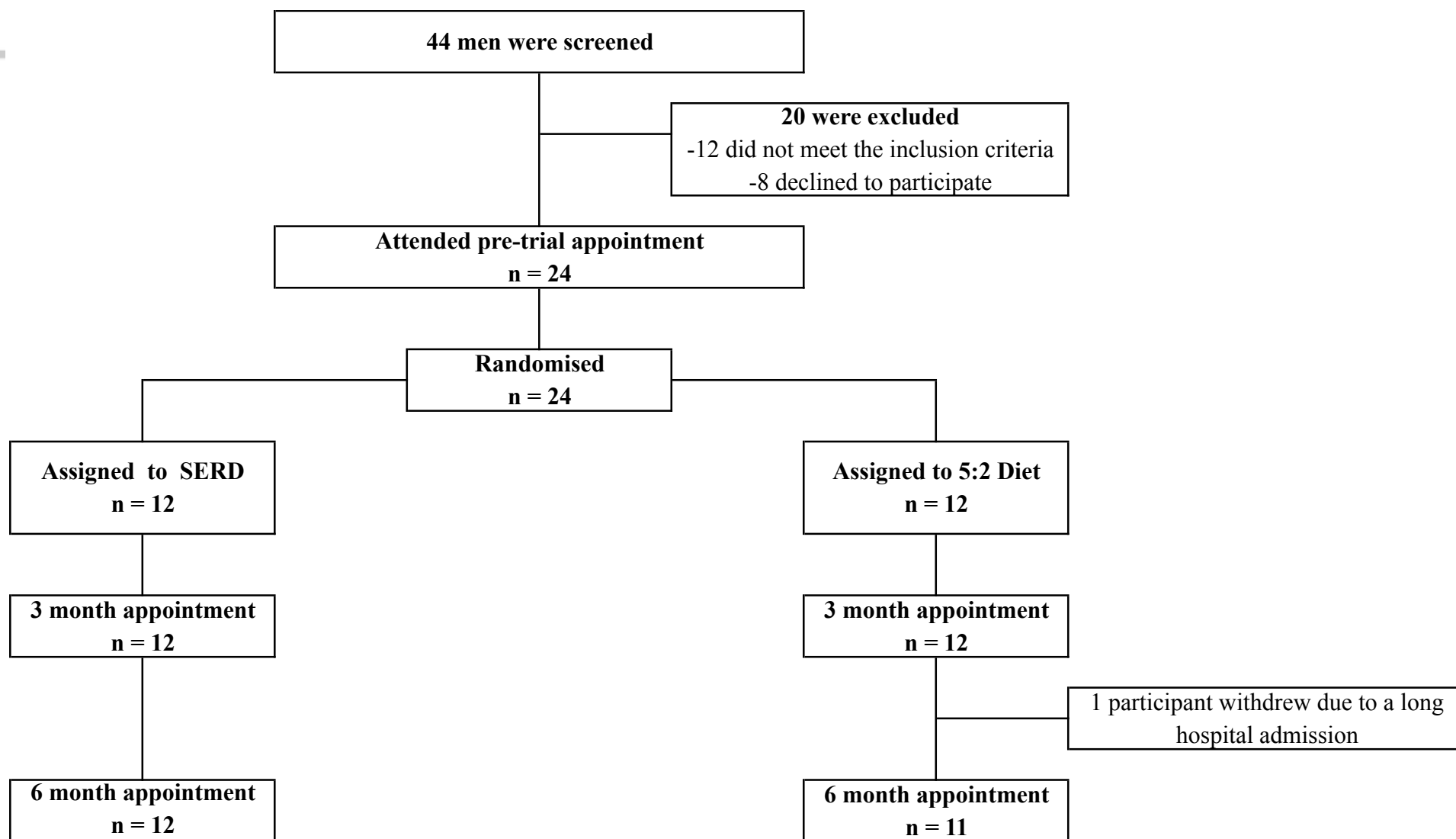


Figure 1. Study uptake and recruitment to trial.

