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REVIEW

Intermittent energy restriction and weight loss: a systematic review

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BACKGROUND/OBJECTIVES: Intermittent energy restriction (IER) is an eating pattern of regular daily periods of restricted energy intake followed by periods of unrestricted energy intake. This is gaining prominence as an alternative weight-loss strategy to daily energy restriction (DER). The aim of this systematic review was to determine the effectiveness of IER on weight loss in overweight and obese adults and compare this with DER.
SUBJECTS/METHODS: A systematic literature search was conducted using the CINAHL, Embase, Medline, PsycINFO, Cochrane and Scopus databases. Eight studies that assigned overweight or obese adults to IER or to a DER 'control' were deemed eligible for inclusion.
RESULTS: All studies reported significant weight loss for IER groups. Average weight loss was approximately 0.2–0.8 kg per week. IER resulted in comparable weight loss to DER when overall energy restriction remained similar between diets. The majority of studies that reported body composition outcomes have shown equal efficacy for fat mass, fat-free mass and waist circumference.
CONCLUSIONS: Weight loss was achieved in overweight and obese adults following IER and this loss was comparable to a DER diet. IER may be an effective alternative strategy for health practitioners to promote weight loss for selected overweight and obese people.

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INTRODUCTION

Effective weight-loss strategies are required because of the increasing incidence of overweight and obesity worldwide[1] and its relationship with a number of disease states[2] such as type 2 diabetes, cardiovascular disease and cancer. For adults a daily energy restriction (DER) of 2500 kJ is considered the best practice dietary strategy for weight reduction, with a greater restriction often considered for individuals classified as obese or with additional comorbidities.[3] Despite being the current best practice weight-loss recommendation, compliance is often low and there is a high likelihood of regaining weight in the long term.[4] Given these shortcomings, alternative forms of effective weight loss are of interest.

An alternative form of dietary strategy known as 'intermittent fasting'[5–9] or intermittent energy restriction (IER)[10,11] is emerging in the scientific literature and has gained significant media attention.[12] IER involves a period of energy restriction alternated with a period of unrestricted or minimally restricted dietary intake.[5] Various terms are currently used for this style of diet, including 'alternate-day fasting'[5] and '5:2 diet'.[12] For the purposes of this review the dietary strategy is referred to as IER. The design of IER protocols vary, with some studies employing an alternate-day method[5] and others implementing an alternating set of days, such as 5 'feed' days followed by 2 'fast' days.[13] The core concept of IER is that energy restriction is alternated with minimal dietary intervention, making IER different from the usual ongoing DER.

Proponents of IER argue that the diet has the potential to increase compliance[14] and to provide benefits over and above traditional DER diets, such as better retention of lean body mass,[5] the reduction of triacylglycerol and low-density lipoprotein cholesterol concentrations,[14] increased longevity and the reduction of oxidative stress that is not seen in traditional weight-loss studies.[15] A 2014 literature review on IER studies suggests superior weight loss for DER diets compared with IER diets but a comparable reduction in fat mass.[8] In light of these claims and the increasing popularity of IER, it should be acknowledged that relatively few studies have addressed the effectiveness of IER on weight loss.[14] Furthermore, although there have been reviews on this topic,[6,8] as yet no systematic review of the literature on controlled studies that include both DER and IER in the study design has been undertaken.

The aim of this study is to provide a systematic review of the literature to determine the effect of IER on weight loss in overweight or obese adults and to compare weight-loss outcomes with that achieved on the traditional DER diet using clinical controlled trials.

MATERIALS AND METHODS

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed throughout the design, implementation and analysis of this study.[16] A systematic search was conducted for studies using IER for overweight and obese adult subjects (⩾18 years of age) to determine the effect of the diet on body weight. Both overweight and obese are defined as a waist circumference >80 cm for women and 94 cm for men or a body mass index (BMI) $\geqslant 25\ kg/m^2$.[17] IER was defined as a period of low energy intake (fast) alternated with a period of normal food intake (feed). Included studies defined low energy intake as consisting of 25–50% of a participant's calculated daily energy requirements or a predetermined energy intake such as 400–1400 kcal per day. The feed period was defined as either *ad libitum* feeding or a controlled intake no less than 1400 kcal per day. The reason for this cut-off is that many IER protocols, such as the popular 5:2 Diet, do not promote unrestricted energy consumption on feed days.[13] Other variations of the IER regimen accepted include alternating between fasting and feeding every 24 h, 2 or 4 days of fasting per week, and 5 weeks of feeding followed by 5 weeks of fasting. All papers up to January 2015 were included. Length of study was not specified, as long-term studies (>12 months) have not been conducted.[5]

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A database search was conducted of CINAHL, Embase, Medline, PsycINFO, Cochrane and Scopus in September 2013 and was updated in January 2015. A proximal search strategy was employed linking the terms or variations of 'intermittent', 'alternate', 'modified' and 'every other day' with the terms 'fasting', 'calorie', 'restriction' and 'energy'. The search was further refined by linking outcome measures 'fat', 'mass', 'weight', 'muscle', 'adiposity', 'abdominal', 'waist' and 'BMI'. Limits were applied to exclude non-English-language articles and animal studies. Two assessors independently performed each database search to ensure consistency. The search strategies employed for each database may be found in Supplementary Appendix 1.

Literature screening

After search results were combined and duplicate studies removed, articles were collaboratively assessed for inclusion by two researchers. Studies were excluded on the basis of title and abstract. Excluded papers were coded as follows: duplicate article; not a study of interest; not a population of interest; and not an intervention of interest. Full-text articles were then obtained and assessed for eligibility collaboratively by two researchers. Conference proceedings, meeting papers, poster abstracts and dissertations were excluded because of a lack of method detailed in these studies and considering that the peer review for these studies may not be as rigorous. The remaining studies were assessed on the basis of their NHMRC level of evidence.[18] There were sufficient Level II studies to include only randomised controlled trials and clinical controlled trials in this review. Studies that only compared one version of IER with another version of IER were excluded as they offered no comparison with DER and it was decided that the studies introduced an inherent bias to the results through the assumption that IER is already a valid weight-loss regimen. One study that only included a non-DER (no diet) control group was also excluded given the number of studies found that used a DER control group.

Data extraction

A template for extracting relevant data from the final list of included studies was drafted. All researchers conducted an independent data extraction on a test paper to ensure consistent results. Data extractions were compared, the template finalised and consensus achieved on how key outcomes were to be recorded. Relevant data were extracted from included articles individually using the designed template. Data for extraction included the following: publication details; study design; and classification of hierarchy of evidence according to NHMRC guidelines.[18] Sample size and participant characteristics were recorded, including age, sex, baseline body weight and/or BMI, and any comorbidities related to obesity. Baseline values for age, weight and BMI for IER and DER groups in the study by De Groot *et al.*[19] were calculated using data provided in the paper for each study participant. Details of IER protocol and DER regimen were recorded, including whether or not food was provided and whether subjects were counselled on food choices. Compliance, follow-up, physical activity details, potential study bias and funding sources were also noted.

The quality of studies was assessed using the Effective Public Health Practice Project (EPHPP) Quality Assessment Tool for Quantitative Studies.[20] This tool is useful to assess quality of evidence and is shown to have excellent consensus for final grade.[21] The EPHPP tool provides a hierarchical quality rating based on selection bias, study design, confounders, blinding, data collection methods and withdrawals/drop-outs. Quality assessment of the included studies was conducted independently by two researchers, with any discrepancies resolved through discussion until consensus was reached.

Outcome measures were recorded for both IER and DER groups, including change in body weight, reported as either kilogram change or as percentage change. For each measure, either s.d. or s.e.m. was recorded, as well as corresponding *P*-values for both within and between intervention groups. Surrogate markers such as changes in fat mass, fat-free mass, lean body mass, waist circumference, total cholesterol, high-density lipoprotein, low-density lipoprotein, blood pressure, heart rate, blood glucose, insulin and C-reactive protein levels were also recorded, where reported, for both IER and DER groups. Compliance and follow-up were also recorded where reported. Subjective measures reported in studies included quality of life, hunger and satiety assessments, and the results of these were also recorded. All results regarding baseline measures, dietary protocol, change in body weight, fat mass, fat-free mass, lean body mass and waist circumference were then compiled and tabulated by one researcher in two final tables.

RESULTS

Search results

The literature search identified 2853 records (Figure 1). After titles and abstracts were reviewed to determine eligibility, 77 records met the criteria and full-text articles were retrieved for further analysis and quality assessment. The reasons for exclusion are provided in Figure 1. The majority of full-text articles ($n = 22$) were

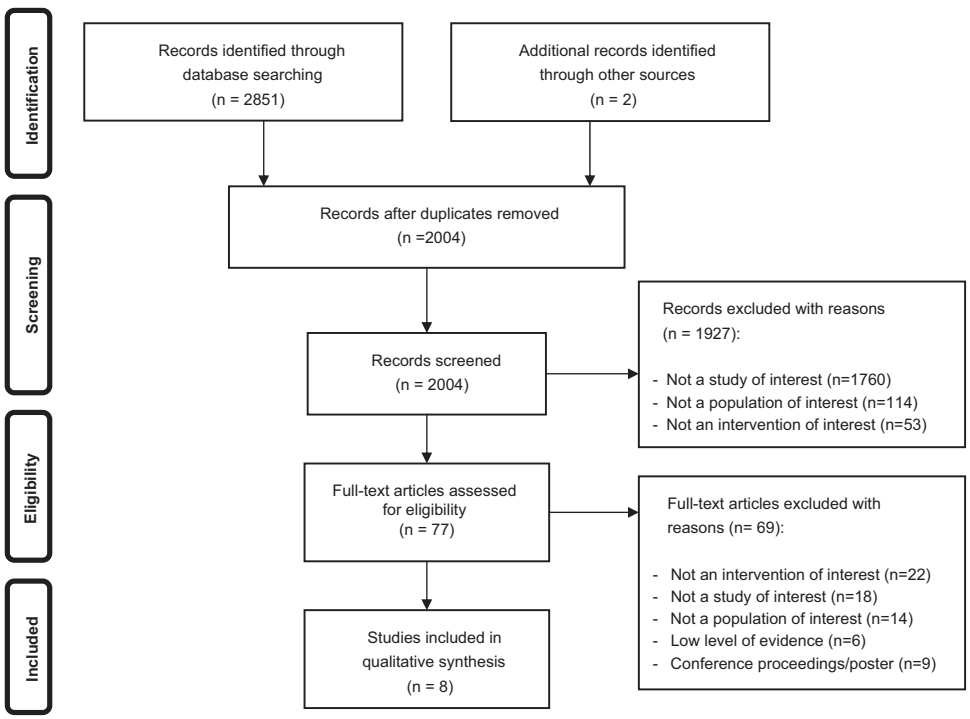

Figure 1. Flow diagram of the literature search and the exclusion process.

excluded because they did not meet the criteria for IER or did not include appropriate DER control groups and were therefore not considered to be an intervention of interest. Six studies did not meet minimum NHMRC Level II[14,15,22–25] evidence and were consequently excluded.

Characteristics of the included studies

The details of the eight studies that were determined eligible for this review can be seen in Table 1. Four of the studies were randomised controlled trials[11,26–28] and four were clinical controlled trials.[10,19,29,30] Only one study included a non-diet control group.[30] The length of the treatments ranged from 5 weeks[19] to 12 months,[28] with 18 months being the maximum follow-up time.[11] The majority of studies ($n=7$) achieved a moderate rating as defined by the EPPHP quality assessment tool.[20] None of the studies reported blinding. Five studies did not report any funding sources that would present a conflict of interest, and one study reported funding sourced from a pharmaceutical company and food company.[11] Three studies did not strictly control for exercise but asked participants to maintain their current level of physical activity.[10,28,30] Of the five remaining studies, one study strictly controlled for exercise,[19] one study excluded individuals who participated in exercise from their results or determined whether physical activity levels were maintained at a sedentary level throughout the duration of the study and excluded an individual who participated in exercise from the results,[26] two studies asked participants to increase their exercise gradually,[27,29] and one study did not report on exercise.[11] The paper by Keogh *et al.*[28] received an overall weak rating using the EPPHP quality assessment tool because of two weak component ratings (selection bias and withdrawals and drop-outs).

Participants

The total number of subjects involved in the included studies was 390. The maximum number of participants in any one study was 107[10] and the minimum was 20,[19] with 6 out of the 8 studies using a participant pool of <40. There were a greater number of female participants ($n=324$, 83%) than male ($n=66$, 17%) across the studies. Mean ages ranged from 34.3 years[19] to 61.8 years.[26] In total, 194 subjects undertook IER, whereas 196 subjects were prescribed DER. Mean BMI (reported in 5 studies) ranged from 28.6 kg/m^2 to 37.3 kg/m^2.[19,29] Mean body weight ranged from 77.5 kg[26] to 104.8 kg.[29] Two studies included subjects diagnosed with type 2 diabetes,[11,29] one study focused on postmenopausal women[26] and one on premenopausal women.[10] No significant baseline differences were reported between the IER and DER groups in any of the studies. Four studies reported 100% completion rate during intervention,[11,19,26,28] with the remaining studies reporting drop-out rates ranging from 13 to 33% for DER groups and from 11 to 21% for IER groups.[10,29,30] Reasons for drop-out where reported were similar across groups, with the main reasons including stress,[10] pregnancy,[10] change in employment,[10,29] problems adhering to diet,[10,27] personal or family illness[10,27,29] or moving to another region.[29]

Dietary protocol

The structure of the IER protocol varied across the 8 studies. Two studies prescribed alternating fast days and feed days.[19,30] Three studies used patterns of two or four consecutive fast days per week followed by consecutive feed days.[10,11,27] One study involved three cycles of 5 weeks of fasting followed by 5 weeks of *ad libitum* eating.[26] One study involved 1 week of IER alternated with 1 week of normal feeding.[28] The study by Williams *et al.*[29] consisted of two IER regimens—Group A and Group B. Group A was prescribed 1 week of 5 fast days and 2 feed days followed by 1 fast day per week for the remainder of the study. Group B was prescribed four cycles of 5 fast days and 2 feed days alternating with a 4-week period of consecutive feed days.[29] Consumption on feed days within individual studies varied, with three studies allowing for unrestricted *ad libitum* consumption[11,28,30] and the remaining five studies specifying a degree of restriction as shown in Table 1. Energy restriction on IER fast days and for DER diets also varied between studies, as shown in Table 1.

The difference in total energy prescribed between the IER group and the DER group varied across studies. One study prescribed a lower energy intake for IER compared with DER[29] and one study prescribed a lower energy intake for the DER diet compared with the IER diet.[19] The remaining studies prescribed equal total energy consumption between the diets.

Prescribed macronutrient content varied slightly between studies, as shown in Table 1.

Five studies reported utilising a dietitian to provide dietary information and counselling.[11,19,26,27,29] In addition to the dietary prescription, three studies utilised other strategies to facilitate weight loss, including a 20-week behavioural treatment programme[29] and cognitive-behavioural techniques.[10,27]

Food selection

Five of the eight studies did not provide any food to subjects during dietary intervention and allowed for self-selection with the advice of a dietitian or researcher on both feed days and fast days for the IER group and for the DER diet.[10,19,26–28] One study provided meals to the IER group on fast days and allowed for self-selection with the advice of a dietitian or researcher for IER feed days and for the DER group throughout the intervention.[29] Two studies provided meals for each fast day for the IER group and all meals for the DER group and allowed self-selection during the *ad libitum* period for the IER group.[11,30]

Weight-loss outcome

All eight studies reported significant weight loss due to IER over a 5-week to 12-month time frame. Average weight loss was approximately 0.2–0.8 kg/week, with the exception of the study by Keogh *et al.*,[28] which showed a weight loss of 0.04 kg/week at the end of the 12-month study period. However, weight loss recorded after 8 weeks in the same study[28] demonstrated a rate of weight loss of 0.2 kg/week. In general, the rate of weight loss was greater for shorter study durations. Weight loss on DER diets was also significant in all studies over the same time period. The study that included a non-diet control group[30] showed that weight remained stable in this group. Two studies reported a significant difference in weight loss between the IER group and the DER group over a 5-week to 5-month time period.[19,29] Of these, one study found that the DER group lost significantly more weight than the IER group[19] and one found that IER groups lost more weight comparatively.[29] Five studies found no significant difference in weight loss between diets.[10,11,26–28] Given the nonsignificant difference between groups reported by Ash *et al.*[11] the data were pooled in their reported results, making it impossible to report on weight loss for each group separately in this systematic review. One study did not report a *P*-value for between-group differences as weight loss was not the main outcome measured.[30] However, contact was made with the authors to confirm that there was no difference between groups.

Other body composition outcomes

Six of the included studies reported body composition outcomes other than weight loss,[10,11,19,26–28] as shown in Table 2. Measures reported include reduction in fat mass, percentage fat mass, fat-free mass, lean mass and waist circumference. A range of different measures were used to determine body composition. Arguin *et al.*[26] determined fat mass and lean body mass using dual-energy x-ray absorptiometry. Harvie *et al.*[10] determined fat

Table 1. Summary of eligible studies and weight-loss outcomes

Reference	*Length*	*Baseline characteristics*			*IER diet*			*DER diet*			*Group difference*
			IER	*DER*	*Protocol*	*BW lost (kg)*	*%*	*Protocol*	*BW lost (kg)*	*%*	
De Groot *et al.*[19]	5 weeks	n Age BW (kg) BMI (kg/m^2)	10 (F) 34.3 ± 6.9 s.d. 81.5 ± 12.2 s.d. 28.6 ± 4.5 s.d.	10 (F) 36.7 ± 8.7 s.d. 81.8 ± 13.5 s.d. 29.4 ± 4.2 s.d.	FAD = 14 days, 50% of ER FED = 14 days, 100% of ER PAT = 1 FAD; 1 FED MN = as per DER	3.9 ± 0.4 s.e.m.[a]	NR	50% of ER/day MN = 1st 2 weeks 46% CHO, 31% F, 23% P Remaining weeks MN = 46% CHO, 40% F, 14% P	5.8 ± 0.8 s.e.m.[a]	NR	Yes[a]
Ash *et al.*[11 b]	12 weeks 18-month follow-up	n Age BW (kg) BMI (kg/m^2)	14 (M) 54.3 ± 9.4 s.d. 96.7 ± 11.4 s.d. 31.2 ± 3.4 s.d.	17 (M) 54.9 ± 9.3 s.d. 101.4 ± 11.9 s.d. 32.7 ± 2.4 s.d.	FAD = 48 days, 1000 kcal/day (LMR) FED = 36 days, *ad libitum* MN as per DER PAT = 4 FAD; 3 FED Aimed for equal overall kcal to DER	6.4 ± 4.6 s.d.[c] [b]	6.5 ± 6.0 s.d.[c] [b]	1400–1700 kcal/day MN = 50% CHO, 30% F	6.4 ± 4.6 s.d.[c] [b]	6.5 ± 6.0 s.d.[c] [b]	No[d]
Varady *et al.*[30]	12 weeks	n Age BW (kg) BMI (kg/m^2)	13 (10 F, 3 M) 47 ± 2 s.e.m. NR 32 ± 2 s.e.m.	12 (10 F, 2 M) 47 ± 3 s.e.m. NR 32 ± 2 s.e.m.	FAD = 42 days, 25% of ER FED = 42 days, *ad libitum* PAT = 1 FAD; 1 FED Overall aim for 5% BW loss over 12 weeks	NR	5.2 ± 1.1 s.e.m.[c]	75% of ER/day Overall aim for 5% BW loss over 12 weeks MN = 55% CHO, 30% F, 15% P	NR	5.0 ± 1.4 s.e.m.[c]	No
Williams *et al.*[29] Group A	20 weeks	n Age BW (kg) BMI (kg/m^2)	18 (9 F, 9 M) 51.4 ± 7.9 s.e.m. 103.5 ± 16.8 s.e.m. 35.4 ± 5.4 s.e.m.	18 (11 F, 7 M) 54.1 ± 7.0 s.e.m. 98.9 ± 17.6 s.e.m. 35.0 ± 5.2 s.e.m.	FAD = 20 days, 400–600 kcal/day FED = 120 days, 1500–1800 kcal/day PAT = 1 week of 5 FAD+15 weeks of 1 FAD per week MN as per DER	9.6 ± 5.7 s.e.m.[e]	NR	1500–1800 kcal/day F < 20%	5.4 ± 5.9 s.e.m.[e]	NR	Yes[e]
Group B		n Age BW (kg) BMI (kg/m^2)	18 (11 F, 7 M) 50.3 ± 8.6 s.e.m. 104.8 ± 13.7 s.e.m. 37.3 ± 4.8 s.e.m.	18 (11 F, 7 M) 54.1 ± 7.0 s.e.m. 98.9 ± 17.6 s.e.m. 35.0 ± 5.2 s.e.m.	FAD = 20 days, 400–600 kcal/day FED = 120 days, 1500–1800 kcal/day PAT = 1 week of 5 FAD+4 weeks FED MN as per DER	10.4 ± 5.4 s.e.m.[e]	NR	1500–1800 kcal/day F < 20%	5.4 ± 5.9 s.e.m.[e]	NR	Yes[e]
Arguin *et al.*[26]	25 weeks IER 15 weeks DER 12-month follow-up	n Age BW (kg) BMI (kg/m^2)	12 (F) 60.8 ± 5.5 s.d. 81.3 ± 11.4 s.d. NR	10 (F) 61.8 ± 7.3 s.d. 77.5 ± 9.8 s.d. NR	FAD = 105 days, kcal = NR MN as per DER FED = 105 days, kcal = NR MN as per DER PAT = 5 weeks FAD; 5 weeks FED Overall aim 1% BW loss/week	10.7 ± 3.0 s.d.[c]	NR	NR—overall aim for 1% BW loss/week MN = 55% CHO, 30% F, 15% P	9.5 ± 2.1 s.d.[c]	NR	No[d]
Harvie *et al.*[10]	6 months	n Age BW (kg) BMI (kg/m^2)	53 (F) 40.1 ± 4.1 s.d. 81.5(77.5–85.4)[f] 30.7 ± 5.0 s.d.	54 (F) 40 ± 3.9 s.d. 84.4(79.7–89.1)[f] 30.5 ± 5.2 s.d.	FAD = 48 days, 645 kcal/day, P = 50 g FED = 120 days, kcal = NR MN as per DER PAT = 2 FAD; 5 FED Overall aim for 75% of ER	Pre 81.5 (77.5–85.4)[a,f] Post 75.8 (71.4–80.2)[a,f]	NR	NR—overall aim for 75% of ER MN = 45% CHO, 30% F, 25% P	Pre 84.4 (79.7–89.1)[a,f] Post 79.9 (74.6–85.2)[a,f]	NR	No[d]

Table 1. (Continued)

Reference	Length	Baseline characteristics			IER diet			DER diet			Group difference
			IER	DER	Protocol	BW lost (kg)	%	Protocol	BW lost (kg)	%	
Harvie *et al.*[27]	3 months	n Age BW(kg) BMI (kg/m^2)	37 (F) 45.6 ± 8.3 s.d. NR 29.6 ± 4.1 s.d.	40 (F) 47.9 ± 7.7 s.d. NR 32.2 ± 5.6 s.d.	FAD = 24 days, 30% of ER, 40 g CHO FED = 60 days, kcal = NR MN as per DER PAT = 2 FAD; 5 FED Overall aim for 75% of ER	Pre 79.4 (74.6–84.1)[f] Post 74.4 (70.0–78.9)[f]	NR	NR—overall aim for 75% of ER MN = 45% CHO, 30% F, 25% P	Pre 86.0 (80.6–91.3)[f] Post 82.3 (77.1–87.5)[f]	NR	No[d]
Keogh *et al.*[28]	12 months	n Age BW (kg) BMI (kg/m^2)	19 (F) 59.5 ± 8.7 s.d. 86.9 ± 14.1 s.d. 33.1 ± 3.8 s.d.	17 (F) 60.8 ± 12.5 s.d. 90.2 ± 18.8 s.d. 33.0 ± 7.5 s.d.	FAD = 26 weeks, 1315 kcal/day MN as per DER FED = 26 weeks, *ad libitum* PAT = 7 FAD; 7 FED	2.1 ± 3.8 s.d.[a]	2.3 ± 4.1 s.d.[a]	1315 kcal/day MN = 46% CHO, 20% F, 34% P	4.2 ± 5.6 s.d.[a]	4.2 ± 4.9 s.d.[a]	No[d]

Abbreviations: BMI, body mass index; BW, body weight; CHO, carbohydrate; DER, daily energy restriction diet; ER = daily energy requirements; F, fat; F, Female; FAD, fast day; FED, feed day; IER, intermittent energy restriction diet; LMR, liquid meal replacement; M, male; MN, macronutrient breakdown; NR, not reported; P, protein; PAT, pattern of intermittent energy restriction. [a]Significance at $P < 0.05$. [b]Authors reported pooled results for all subjects as opposed to diet group comparison given that there was no significant difference between diet group. [c]Significance at $P < 0.001$. [d]Not significant ($P > 0.05$). [e]Significance at $P < 0.04$. [f]95% CI.

mass and fat-free mass by impedance (Tanita TBF-300A, Tanita Europe BV, Yiewsley, UK). Ash *et al.*[11] measured fat mass by dual-energy x-ray absorptiometry for the chest, abdomen and pelvic regions (Hologic QDR-4500A machine, Marlborough, MA, USA). De Groot *et al.*[19] reported fat-free mass—body volume was assessed by underwater weighing, with simultaneous correction for lung volume by helium dilution. The percentage fat was derived from body density using Siri's equation. Finally, Harvie *et al.*[27] determined fat-free mass by multi-frequency bioelectrical impedance (MC180MA; Tanita Europe BV).

Both IER and DER diets saw a significant reduction across all measures. The study by Arguin *et al.*[26] reported a significant difference in body composition change between the diet groups, with the IER group losing significantly more lean body mass compared with the DER group. Interestingly, Harvie *et al.*[27] reported that those following the IER protocol lost significantly greater fat mass than those on DER.

Compliance

Four studies specifically reported on dietary compliance and this was measured through self-reported food intake[10,11,27] or a questionnaire asking about adherence to the diet.[28] Ash *et al.*[11] found a significant reduction in energy intake compared with baseline for both groups ($P < 0.001$) and that intake was similar for both groups ($P = 0.98$). Similarly, Harvie *et al.*[27] found that both groups reduced energy intake with no difference between groups ($P = 0.207$). Harvie *et al.*[10] found that both groups reported reductions in energy from baseline, but found that the IER group achieved a greater reduction in energy intake compared with the DER group ($P < 0.01$). Harvie *et al.*[10] also found that 58% of the IER group and 85% of the DER group stated that they planned to continue with their allocated diet after completion of the intervention; however, it is not clear whether all participants responded to this question. The same study also found a greater level of adverse effects experienced in the IER group, such as headache, lack of energy and problems fitting the diet into their daily routine. Keogh *et al.*[28] reported that 35 of the 36 volunteers responded to the questionnaire and that 67% of the respondents had not completely adhered to the diet (63% of the IER group; 71% of the DER group). The main reason for not continuing with the diet was the lack of support after the initial fortnightly follow-up period. Although not specifically testing for compliance, two other studies also reported on dietary intake, which was measured through self-reported food intake.[19,26] Arguin *et al.*[26]found significant decreases in daily energy intake from baseline in both groups ($P = 0.01$), with no significant difference between groups ($P = 0.69$). De Groot *et al.*[19] also found a significant decrease in energy intake from baseline in both groups ($P < 0.001$) and that intakes closely matched planned intake.

Follow-up

Two studies had follow-up periods.[11,26] Ash *et al.*[11] reported no significant difference in weight at 18 months compared with weight at baseline for both IER and DER groups ($P = 0.195$). Percent body fat was not significantly different from baseline at follow-up ($P = 0.83$), nor was waist circumference ($P = 0.480$).[11] There was no significant difference between groups for the 18-month follow-up measures of weight, percentage body fat and waist circumference ($P < 0.05$).[11] Loss to follow-up was 47% of the original participants, with the breakdown of numbers per group not provided.[11] Arguin *et al.*[26] reported maintenance of weight loss in both IER ($P < 0.01$) and DER groups ($P < 0.05$) at 12-month follow-up. Only the IER group maintained significant decreases in lean body mass ($P < 0.01$) and waist circumference ($P < 0.05$). Ninety-one percent of participants returned for follow-up (92% for the IER group and 90% for the DER group).[26]

Table 2. Body composition outcomes reported in eligible studies

Reference	*FM (kg)*	*FM (%)*	*FFM (kg)*	*LBM (kg)*	*WC (cm)*
Arguin et al.[26]					
IER	8.7 ± 2.6 s.d.[a]	5.6 ± 2.6 s.d.[a]		1.9 ± 1.4 s.d.[a]	10.6 ± 5.0 s.d.[a]
DER	8.7 ± 2.4 s.d.[b]	6.5 ± 2.7 s.d.[b]		0.8 ± 1.1 s.d.[c]	10.0 ± 3.6 s.d.[b]
Between groups	NS ($P = 0.79$)	NS ($P = 0.74$)		$P = 0.03$[c]	NS ($P = 0.78$)
Harvie et al.[10]					
IER (Pre)	33.6 (30.9–36.4)[d]	40.5 (39.0–42.0)[d]	47.6 (46.3–49.0)[d]		101.5 (97.8–105.2)[d]
IER (Post)	29.1 (26.0–32.3)[c,d]	37.3 (35.2–39.3)[c,d]	46.4 (44.9–47.9)[c,d]		95.4 (91.3–99.5)[c,d]
DER (Pre)	35.3 (31.9–38.7)[d]	40.5 (38.7–42.3)[d]	49.1 (47.7–50.5)[d]		102.5 (98.7–106.3)[d]
DER (Post)	31.7 (27.9–35.5)[c,d]	38.0 (35.8–40.3)[c,d]	48.3 (46.7–49.9)[c,d]		98.6 (94.2–102.9)[c,d]
Between groups	NS ($P = 0.34$)	NS ($P = 0.35$)	NS ($P = 0.21$)		
Ash et al.[11]					
IER		2 ± 1.1 s.d.[a]			8.1 ± 4.6 s.d.[a]
DER		0.9 ± 1.4 s.d.[a]			8.1 ± 4.6 s.d.[a]
Between groups		NS			Average all groups
De Groot et al.[19]					
IER			2.6 ± 0.9 s.e.m.[c]		
DER			1.6 ± 0.5 s.e.m.[c]		
Between groups			NS		
Harvie et al.[27]					
IER (Pre)	31.0 (27.9–34.2)[d]		48.5 (46.4–50.5)[d]		100.5 (96.6–104.5)[d]
IER (Post)	27.3 (24.6–30.0)[d]		46.7 (44.4–49.0)[d]		95.2 (91.4–99.1)[d]
DER (Pre)	35.7 (32.3–39.2)[d]		50.3 (48.2–52.3)[d]		106.0 (101.9–110.2)[d]
DER (Post)	33.7 (30.3–37.2)[d]		48.9 (47.1–50.8)[d]		102.7 (98.4–107.0)[d]
Between groups	$P = 0.007$[c]		NS ($P = 0.288$)		NS ($P = 0.088$)
Keogh et al.[28]					
IER					2.1 ± 4.0 s.d.[c]
DER					1.7 ± 5.6 s.d.[c]
Between groups					NS ($P > 0.05$)

Abbreviations: DER, daily energy restriction diet; FM, fat mass; FFM, fat-free mass; IER, intermittent energy restriction diet; LBM, lean body mass; NS, not significant; WC, waist circumference. [a]Significance at $P < 0.001$. [b]Significance at $P < 0.01$. [c]Significance at $P < 0.05$. [d]95% CI. [e]Not significant ($P > 0.05$).

DISCUSSION

Weight-loss and body composition outcomes

This systematic review of the literature shows that an IER diet regimen can result in weight loss in overweight and obese adults. The results of the eight studies reviewed show that the various forms of IER resulted in an average weight loss in the order of 0.2–0.8 kg/week, which, if maintained, for a 100 kg individual would result in a 5% reduction in weight over a 5-week to 6-month time period. For overweight or obese individuals, a 5% reduction in body weight is considered to be achievable and to reduce health risks by reducing blood pressure and the risk for type 2 diabetes.[3,31,32] Indeed, Arguin *et al.*[26] note that their participants showed between 50 and 100% improvement in total cholesterol, low-density lipoprotein cholesterol and triglyceride levels during the first 5% body weight loss. Given this weight-loss benefit, the results of this systematic review show that an IER diet has the potential to offer an effective weight-loss alternative for individuals.

The results are varied when weight loss for the IER and DER diets are compared. Harvie *et al.*,[10,27] Arguin *et al.*,[26] Ash *et al.*[11] and Varady *et al.*[30] aimed for a similar overall energy restriction for each group and reported no difference in weight loss between IER and DER. This finding suggests that IER is as effective as DER in achieving adherence to energy restriction and in achieving resulting weight loss. In terms of differences between groups, De Groot *et al.*[19] reported greater weight loss in the DER group compared with the IER group. However, this may be attributed to the fact that the subjects in the DER group were prescribed 50% of energy required for weight maintenance, less than the IER group, who were prescribed 50% of energy required for weight maintenance on one day alternated with 100% of energy required for weight maintenance on the following day.[19] Williams *et al.*[29] also reported a significant difference in weight loss between the groups, with IER achieving a significant greater weight-loss outcome compared with DER. Again, the energy intake between the two groups differed, with the IER group prescribed 18 000–28 000 kcal less than the DER group over the 20-week intervention.[29] It is unclear what factors assisted participants to adhere to the specified energy prescription in the groups that lost more weight. In comparing these two studies, it appears that both IER and DER are equally effective strategies for participants to adhere to the energy prescription specified by the researchers, given that in the study by De Groot *et al.*[19] DER participants were able to adhere to the increased restriction on this diet and lose more weight than the IER group, and conversely in the study by Williams *et al.*[29] participants in the IER group were also able to adhere to the increased restriction on this diet and lose more weight compared with the DER group. As such, IER and DER appear to be equally effective strategies for achieving dietary energy restriction and resulting weight loss. This is an important finding, as it suggests that IER may be offered as an alternative dietary strategy that has equal weight-loss benefits to the traditional DER diet.

Body composition changes are an important consideration for weight-loss dietary strategies with the aim to reduce fat mass and avoid loss of lean body mass/fat-free mass. This is based on evidence showing that greater fat-free mass is linked to a higher

basal metabolic rate, which is advantageous for weight loss.[33] Where measured, IER showed reductions in fat mass[10,11,26,27] as well as reductions in fat-free mass[10,19,27] or lean body mass.[26] Harvie *et al.*[27] reported greater reductions in fat mass in those following the IER protocol. Participants in the IER group also reported less carbohydrate intake (although overall energy intake between groups was not significantly different), which could suggest that reducing carbohydrate as part of an intermittent dietary protocol may produce better outcomes. The study by Arguin *et al.*[26] was the only one to show a significant difference between an IER and DER diet in relation to lean body mass, with all other studies showing that the diets were comparable in reducing both fat mass and retaining lean body mass or fat-free mass. Arguin *et al.*[26] showed that the reduction in lean body mass for postmenopausal women was two times greater (1.9 vs 0.8 g) in the IER group compared with the DER group. However, Arguin *et al.*[26] failed to find any association between loss of lean body mass and changes in resting metabolic rate, fasting plasma lipids, or fasting plasma glucose; thus, it is unclear whether the difference in lean body mass loss between groups is clinically meaningful. More studies are needed in postmenopausal women to confirm the findings of Arguin *et al.*[26] and to explore the reasons behind the finding and the clinical significance. In the meantime, it may be prudent for postmenopausal women to refrain from using IER as a weight-loss diet strategy.

Long-term outcomes

Long-term maintenance of weight loss is an important consideration of a weight reduction diet. However, data to support long-term weight maintenance by IER are limited in the studies reviewed. Ash *et al.*[11] reported follow-up after 18 months and found that the majority of participants in both the IER and DER groups regained weight and there was no difference from baseline measures. However, follow-up was not part of their original study protocol and hence participants were not informed of follow-up at commencement of the study and only approximately half of the participants were involved in follow-up measures. Therefore, it is unclear whether the participants not followed up maintained their weight loss.[11] In comparison, Arguin *et al.*[26] provided a 12-month follow-up of 20 of the 22 participants studied and found that decreases in body weight were maintained in both groups. The authors suggest that the success of these long-term outcomes may be attributed to several factors such as the diet, health education received during the study or the dietary guide that participants were taught to use.[26] Given the limited measures for long-term outcomes in the studies reviewed and differing results, it is unclear whether IER can benefit individuals in the long term and whether there is an attributable difference between DER and IER diet protocols. Further studies on IER with long-term follow-up are required.

Compliance

Individual participant compliance to their allocated dietary regimen was not measured or reported in the majority of studies. Ash *et al.*[11] provided details of compliance via administration of a 24-h dietary recall and a self-administered food frequency questionnaire used to validate the dietary recall. The authors found that mean energy intake was similar between the IER and DER groups, suggesting that compliance to the dietary protocols was similar.[11] Harvie *et al.*[10] aimed for a 25% overall energy restriction for both diet groups and measured compliance via 7-day food records and found a greater reduction in energy intake in the IER group compared with the DER group. However, the authors also found that fewer IER participants planned to continue with the diet beyond the 6 months of the study compared with the DER group.[10] This suggests effective short-term compliance but difficulty with long-term compliance. This may be attributed to the effect of the diet on quality of life, with a greater level of adverse effects experienced in the IER group, such as headache, lack of energy and problems fitting the diet into their daily routine (the diet suggested in this study was based on milk plus one piece of fruit and some vegetables, which may have been tedious),[10] which may be difficult to deal with in the long term. No clear conclusion can be made as to whether food provision and the type of food provided enhanced compliance to IER and weight-loss outcomes. This is because of the limited measurement of compliance in the studies and the heterogeneity of study designs, which made it difficult to compare weight-loss outcomes based on food provision across the studies.

Future directions

A number of important questions are raised after reviewing the studies comparing IER with DER. It is worth exploring whether certain population groups will benefit more from an IER dietary strategy compared with DER. Also, it is worth investigating whether certain IER protocols (that is, alternate day compared with a 5:2 diet) are more effective and whether there are factors that modulate the rate of weight loss for an IER diet (that is, exercise). This will allow a more tailored approach for practitioners recommending dietary strategies for weight loss. More research is also needed to explore long-term weight-loss outcomes of IER and whether there are any differences in these outcomes and in the rates of adverse events compared with DER. A greater number of studies are also required with greater participant numbers. The inclusion of a non-diet control group is recommended, as also suggested in a previous review of IER trials incorporating a non-diet group.[6] With the accrual of further evidence, the significant heterogeneity observed between trials in terms of both the nature and duration of the intervention and the range of participants recruited can be explored further, its impact on outcomes examined and a meta-analysis of study results undertaken.

CONCLUSION

This systematic review finds that IER may be an effective dietary alternative for promoting weight loss in overweight/obese adults in the short term (that is, over a 12-month period) for the treatment of overweight and obesity. Because of the small number of studies meeting the inclusion criteria and the heterogeneity of study designs it was not possible to undertake a meta-analysis of study results for weight loss and other body composition outcomes or to compare the IER protocols on these measures. The results show that IER can result in weight loss in overweight and obese adults that is comparable to the traditional DER. In addition, body composition outcomes in the IER diet, including loss in fat mass and retention in lean body mass/fat-free mass, are comparable to those of the traditional DER for the majority of studies. One exception is for postmenopausal women who may lose more lean body mass when on the IER diet compared with the DER diet. Further research is required to confirm the findings for this population group and to investigate the significance and mechanisms involved behind this difference. Future IER research must also focus on compliance and long-term outcomes and investigate whether compliance to IER is more suited to certain population groups.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Study conception and design: LR. Collection of data: CSD, REC, SNC, KNR, REW and CER. Analysis and interpretation of data: LR, CSD, REC, SNC, KNR, REW and

CER. Paper preparation CSD, LR and CEH. Revision of manuscript CSD and LR. All authors have actively contributed, read and approved the final manuscript.

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