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Etiology and Pathophysiology/Obesity Management

Short-term intermittent energy restriction interventions for weight management: a systematic review and meta-analysis

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Summary

This systematic review synthesized the available evidence on the effect of short-term periods of intermittent energy restriction (weekly intermittent energy restriction; ≥7-d energy restriction) in comparison with usual care (daily continuous energy restriction), in the treatment of overweight and obesity in adults. Six electronic databases were searched from inception to October 2016. Only randomized controlled trials of interventions (≥12 weeks) in adults with overweight and obesity were included. Five studies were included in this review. Weekly intermittent energy restriction periods ranged from an energy intake between 1757 and 6276 kJ/d^{-1}. The mean duration of the interventions was 26 (range 14 to 48) weeks. Meta-analysis demonstrated no significant difference in weight loss between weekly intermittent energy restriction and continuous energy restriction post-intervention (weighted mean difference: −1.36 [−3.23, 0.51], p = 0.15) and at follow-up (weighted mean difference: −0.82 [−3.76, 2.11], p = 0.58). Both interventions achieved comparable weight loss of >5 kg and therefore were associated with clinical benefits to health. The findings support the use of weekly intermittent energy restriction as an alternative option for the treatment of obesity. Currently, there is insufficient evidence to support the long-term sustainable effects of weekly intermittent energy restriction on weight management.

Keywords: Continuous energy restriction, intermittent energy restriction, weight loss.

Abbreviations: BMI, Body mass index; CER, Continuous energy restriction; CI, Confidence interval; CINAHL, Cumulative Index of Nursing and Allied Health Literature; GRADE, Grading of Recommendations Assessment, Development and Evaluation; IER, Intermittent energy restriction; SD, Standard deviation; VLED, Very low energy diet; WMD, Weighted mean difference.

Introduction

Lifestyle interventions in the management of obesity aim to support weight loss primarily through modification of dietary intake and physical activity (1,2). International clinical guidelines for the management of obesity (3–6) have defined treatment success of interventions as achieving a clinically meaningful weight loss of 5–10%, as this is shown to have improvements in health and a reduction in the risk of obesity-related conditions including type II diabetes and cardiovascular disease (3,4). To achieve a clinically important weight loss, continuous energy restriction (CER) of approximately 2510 kJ (600 kcal) per day energy deficit is recommended as part of a multi-component weight management intervention (3,4). As the prevalence of overweight and obesity continues to increase and present a major public health concern (7), research on alternative treatment approaches to the management of obesity continues to evolve.

Intermittent energy restriction (IER) is one such dietary approach that has received recent attention (8,9), especially in the media, for its potential efficacy for the management of obesity. IER typically involves periods of restricting energy intake or 'fasting' (consuming a very low energy diet [VLED] approximately 2092–2510 kJ [500–600 kcal]), interchanged by periods of *ad libitum* energy intake on non-restriction periods. However, there is no clear definition provided of IER, which acts as an umbrella term that encompasses various dietary regimens. These include diverse interventions such as alternate day fasting (1 d of energy restriction followed by a day of *ad libitum* energy intake) (10–12), the 5:2 diet (2 d of energy restriction per week) (13,14) and longer cyclic IER periods (15,16).

The growing body of evidence from systematic reviews demonstrates that IER achieved comparable weight loss as CER (17–19). Current reviews have primarily focussed on dietary IER interventions that have involved IER from 1 up to 6 d per week (17–19). The most recent review by Harris *et al.* (19) investigated the effectiveness of randomized controlled trials of IER in comparison with treatment as usual (CER) or no treatment (*ad libitum* energy intake). Studies were defined as IER if they included energy restriction on at least 1 d per week but not greater than seven. This evidence synthesis included the most publicized 5:2 diet and alternate day fasting approaches, concluding that IER was as effective as CER for short-term weight management. During the investigation of this review, cycles of longer term periods of IER (i.e. 1 to 12 weeks of energy restriction periods interspersed with periods of no prescribed dietary restriction or a lesser degree of prescribed dietary restriction, henceforth termed weekly IER) were identified; however, these were not included in this review. To move beyond the 'one-size-fit-all' approach to managing obesity, it is important that all IER strategies are evaluated for their potential to support weight loss. Due to the chronic relapsing nature of obesity (1,2,20), weight management strategies have proposed that a 'break' in energy restriction could prolong weight loss by maximizing dietary compliance. This study, therefore, aimed to systematically review the available evidence and quantify the pooled effect of weekly IER in the treatment of overweight and obesity in adults, when compared with usual care treatment (CER) or no treatment (*ad libitum* diet).

Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement guided the reporting of this review (21).

Literature search

An extensive search strategy was developed to identify relevant papers from the following electronic databases: Medline (via OVID Host), Embase (via OVID Host), Cochrane Library, Cumulative Index of Nursing and Allied Health Literature ([CINAHL] via EBSCO Host) and PsychINFO (via EBSCOHost). The full search strategy is presented in the onlnine supporting information (Appendix A). Protocols and ongoing trials were also identified through the International Standard Randomized Controlled Trial Number trial registry. The search was conducted initially in September 2015 and updated in October 2016. Articles were searched from database inception. Hand searches of reference lists of key systematic reviews in the field and the reference lists of retrieved full-text articles were also conducted to ensure that papers that fulfilled the eligibility criteria were not omitted.

Eligibility criteria

Eligibility criteria aimed to match closely that of the previous review conducted by this research collaboration between the University of Glasgow and Teesside University (19,22). Therefore, articles were considered eligible if they met the following criteria: were an IER intervention (defined as consuming a reduction in energy intake, intermittently for a period of ≥7 d, interspersed with periods of no prescribed energy restriction or a lesser degree of prescribed energy restriction) that followed participants for at least 12-week duration (pre-intervention–post-intervention), were of a randomized control trial design including a comparator intervention consisting of no intervention (control) or usual care (which may consist of advice to continuously follow a reduced calorie diet, which is usually around 25% of recommended energy intake) and included adults (≥18 years) with overweight or obesity (body mass index [BMI] ≥25 kg m^{-2}). Participants were excluded if they had or were planning to undergo bariatric surgery, were pregnant or breastfeeding or taking medication associated with weight loss (e.g. orlistat, metformin) or weight gain (e.g. steroids, antipsychotics). Participants were also excluded if they had secondary or syndromic forms of obesity. However, due to the high prevalence of type II diabetes in participants with obesity (23,24), and with this condition shown to improve with weight loss achieved through lifestyle modifications (3,4,25), studies including participants with type II diabetes were not excluded from inclusion in this review.

Selection process

The articles identified by the search strategy were electronically imported into Covidence software for screening (www.covidence.org). The selection process was conducted by a group of independent researchers due to the extensive results of the search strategy. Four researchers formed two independent groups (group one: first and second authors; group 2: third and last author) and conducted the initial stage of screening of study titles and their abstract. Consensus on potentially relevant articles to be considered for full-text screening was then assessed by two independent reviewers (first and last author). Application of checklists for inclusion of full-text articles was also conducted by the first and last author, and any disagreements resolved by a consensus decision.

Data extraction

Two reviewers (first and last author) independently conducted the data extraction from a pre-specified data extraction template. The results were compared, and consensus was agreed. Data extraction consisted of the following characteristics:

- General study characteristics (e.g. the aim of the study)
- Elements of the intervention (e.g. dietary prescription regimens and duration of the intervention
- Outcome measure (change in body weight)
- Study-specific outcomes (e.g. adherence/compliance to the intervention, attrition rates and adverse events).

Risk of bias and overall quality of the evidence

Quality assessment was assessed using the Cochrane Collaboration's tool for assessing risk of bias (26). Five domains of potential risk of bias were assessed. These included selection bias (assessment of random sequence generation and allocation concealment), performance bias (blinding of participants and researchers), detection bias (blinding of outcome assessment), attrition bias (reporting of incomplete outcomes), reporting bias (selective reporting of outcomes) and other risk of bias (for example, confounding factors) (26). Each domain was rated as low, unclear or high risk of bias based on the criteria by the Cochrane Collaboration (26). Publication bias was also assessed by funnel plots of the study effect sizes, weighted mean difference (WMD) and the standard error of the WMD.

To assess the overall quality of evidence, the Grading of Recommendations Assessment, Development and Evaluation (GRADE) assessment (www.gradeworkinggroup.org/) was used (27). Assessment of the overall quality was based on the following domains: risk of bias, consistency of results across studies, directness and precision of results and likelihood of publication bias. GRADE assessments were conducted for the primary outcome included in the meta-analysis. Two independent researchers (first and last authors) performed the risk of bias and GRADE assessments, and consensus agreed.

Data synthesis

The pooled effect size (and 95% confidence interval [CI]) for each study was calculated as the WMD, the difference in the mean change in outcome between the weekly IER intervention and no treatment/CER intervention. Meta-analysis was pooled using a random-effect meta-analysis to provide a summary estimate. Standard deviation (SD) of the change in body weight was calculated from an imputed correlation coefficient in the study by Wadden *et al.* (28) based on the pre–post and change SD from the study by Arguin *et al.* (29). Studies that compared two treatment groups with a single (control group) were included by combining the treatments into a single independent effect size, to prevent multi-comparisons and a unit-of-analysis error (30). All analyses were conducted using Comprehensive Meta-Analysis (Version 3 for Windows: Biostat, Englewood, CO, USA). Heterogeneity was assessed using standard measure Cochrane's Q statistic (with $p < 0.05$ indicating evidence of statistical heterogeneity), the I^2 statistic and T^2 (31).

Results

A total of 30 253 studies were identified, and 5 met the inclusion criteria. The selection process of included studies is presented in Fig. 1.

Description of included studies

The aim of the randomized controlled trials included in this review was to examine the efficacy of weekly IER interventions (defined as consuming a reduction in energy intake, intermittently for a period of ≥7 d, interspersed with periods of no prescribed energy restriction or a lesser degree of prescribed energy restriction) on change in body weight in comparison with usual care (CER). An overview of study characteristics is presented in Table 1. Studies were conducted primarily in the USA (28,32,33), with one study also conducted in Canada (29) and one in Sweden (34). The mean duration of the active intervention period was 26 (range 14 to 48) weeks. Four studies conducted follow-up assessments of outcome measures at 6 months (33,34), 11 months (32) and 12 months post-intervention (29). Change in body weight was the primary outcome in all studies, with secondary anthropometric outcomes including changes in BMI (32), waist circumference (29) and percentage body fat (29). Change in cardiometabolic outcomes was also investigated and included glucose (29,32), insulin (32), lipid profiles (cholesterol and triglycerides) (29,32), blood pressure (32) and thyroid hormones (28). Mood was assessed through the Beck Depression Score (28,32), and lifestyle habits, i.e. diet and physical activity (29,33), were also reported. These were assessed using standard methodologies of prospective food diaries and physical activity

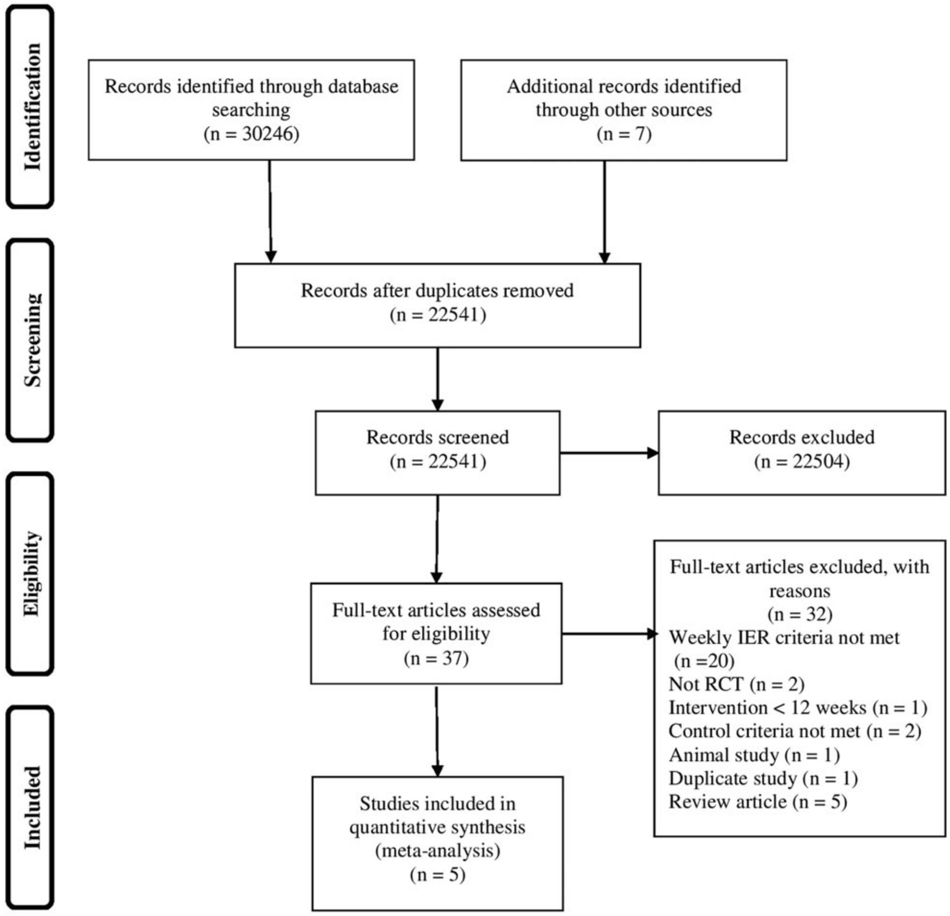

Figure 1 Overview of study search and selection process.

questionnaires. Meta-analysis was not conducted on secondary outcomes due to the limited number of studies reporting the same outcomes.

The main focus of studies was on weight loss. Although none of the studies offered an active weight maintenance phase, two studies advised participants to maintain body weight during no energy restriction periods (29,33). Energy intake was not prescribed during these periods, and therefore, participants could have had *ad libitum* energy intake. On completion of the intervention, these studies also provided advice on how to maintain weight loss (29,33).

The total number of participants enrolled across the studies was 376, with a mean sample size of 75 (range 15 to 142) participants. All participants had overweight or obesity with studies reporting a mean BMI range of 33.1 to 44.6 kg m^{-2} or a percentage over ideal body weight of 15 to 70%. One study included participants with type II diabetes (32). No other chronic conditions were reported, with the exception of obesity. The mean age range of participants was 42.6 to 61.0 years. The majority of participants were female (79%), with two studies recruiting solely female participants (28,29).

Description of dietary intervention

Intervention delivery

Interventions were, in general, delivered face to face through weekly group sessions that were delivered by multiple health professionals from various fields. These included dietitians (29,34), nutritionists, behaviour therapists, health educator and physicians (32), trained nurses and physiotherapists (34). It was not clearly reported who delivered the intervention in some studies (28,33).

Energy restriction regimens

The weekly IER regimens varied across studies in terms of the energy deficit and the number and duration of periods of energy restriction. Energy restriction periods ranged from an energy intake of between 1757 and 6276 kJ d^{-1} (420–1500 kcal d^{-1}). Weekly IER regimens consisted of two to three periods of reduced energy intake interspersed with either *ad libitum* energy intake on non-restriction periods or a prescribed energy intake of between 4184 and

Table 1 Overview of randomized controlled trials of intermittent energy restriction interventions in comparison with usual care

Reference	Study location	Study population					Intervention		Outcome measures	Attrition
			N	Age (years)	Gender (M/F)	BMI (kg m^{-1})	Dietary prescription	Duration (follow-up)		
Arguin *et al.* (29)	Canada	IER	12	60.8 (5.5)	All F	Obese	ER periods: 3 cycles of 5 weeks; EI equivalent to reduce body weight by 1%, ~6276 kJ d^{-1} (1500 kcal d^{-1}) Interspersed with weight-stable periods: 3 cycles of 5 weeks; EI equivalent to maintain body weight stable (±2 kg)	30 weeks (12 months after end of intervention)	Anthropometry: weight, waist circumference, %BF (FM and LM) Cardiometabolic: glucose, RMR, lipid profile (HDL, LDL, TAG) Physical activity scale for the elderly	0%
		CER	10	61.0 (7.3)	All F	Obese	15-week CER followed by 5-week weight-stable EI (as above for each period)			0%
Rossner (34)	Sweden	All IER	81	21–69	20/61	38.3 (4.2)	ER periods: 3 cycles of 2 weeks; EI 1757 kJ d^{-1} (420 kcal d^{-1}) or 2218 kJ d^{-1} (530 kcal d^{-1}) Interspersed with 2 cycles of 4-week LED; EI 6694 kJ d^{-1} (1600 kcal d^{-1})	14 weeks (26 weeks)	Anthropometry: weight	IER = 20.4%
		CER				39.2 (5.1)	6-week VLED; EI 1757 kJ d^{-1} (420 kcal d^{-1}) or 2218 kJ d^{-1} (530 kcal d^{-1}) Followed by 8-week LED 6694 kJ d^{-1} (1600 kcal d^{-1})			CER = 19.2%
Wadden *et al.* (28)	USA	IER	8	44.3 (9.0)	All F	40.7 (10.0)	2 cycles of 4 and 6-week LED; EI 5021 kJ d^{-1} (1200 kcal d^{-1}) ER periods: interspersed with 8 weeks of VLED 2092 kJ d^{-1} (500 kcal d^{-1})	18 weeks	Anthropometry: weight Cardiometabolic: thyroid hormones Mood: Beck Depression Score	None reported
		CER	7	44.9 (7.0)	All F	44.6 (9.0)	18-week LED; EI 4184–5021 kJ d^{-1} (1000–1200 kcal d^{-1})			None reported

(*Continues*)

Table 1 (Continued)

Reference	Study location	Study population					Intervention		Outcome measures	Attrition
			N	Age (years)	Gender (M/F)	BMI (kg m^{-1})	Dietary prescription	Duration (follow-up)		
Wing *et al.* (32)	USA	IER	38	52.3 (10.7)	15/30	37.4 (6.1)	ER periods: 2 cycles of 12-week VLED; EI 1674–2092 kJ d^{-1} (400–500 kcal d^{-1}) Interspersed with 2 cycles of 12-week LED; EI 4184–5021 kJ d^{-1} (1000–1200 kcal d^{-1}	48 weeks (12 months)	Anthropometry: weight, BMI Cardiometabolic: HbA1, glucose, insulin, lipid profile (total cholesterol, HDL, LDL, TAG), blood pressure Mood: Beck Depression Score	IER = 15.6%
		CER	41	51.3 (8.7)	18/30	38.3 (6.5)	48-week LED; EI 4184–5021 kJ d^{-1} (1000–1200 kcal d^{-1})			CER = 14.6%
Wing and Jeffery (33)	USA	All	142	42.6 (9.3)	22/120	33.1 (3.3)	IER 1: 2 cycles of 7-week VLED; EI 4184–6276 kJ d^{-1} (1000–1500 kcal d^{-1}) Interspersed with 5-week EI *ad libitum* IER 2: 4 cycles of 3-week (last cycle 5 weeks) VLED; EI 4184–6276 kJ d^{-1} (1000–1500 kcal d^{-1}) Interspersed with 4 cycles of 1-week (last cycle 2 weeks) EI *ad libitum*	19 weeks (6 months)	Anthropometry: weight, food frequency and physical activity log	Post-intervention IER1 = 23.4% IER2 = 6.4% Follow-up IER1 = 29.8% IER2 = 31.9%
		CER					14-week EI 4184–6276 kJ d^{-1} (1000–1500 kcal d^{-1}) Followed by 5-week EI *ad libitum*			Post-intervention CER = 20.8% Follow-up CER = 35.4%

IER, intermittent energy restriction; ER, energy restriction; CER, continuous energy restriction; EI, energy intake; kJ, kilo joule; kcal, kilo calorie; %BF, percentage body fat; FM, fat mass; LM, lean mass; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TAG, triglycerides; RMR, resting metabolic rate; VLED, very low energy diet; M, male; F, female.

6694 kJ d^{-1} (1000–1600 kcal d^{-1}). Energy intake on weekly IER periods was obtained from food sources without modified food supplements in three studies (29,32,33). Macronutrient composition of energy intake was, in general, advised to follow that of a healthy balanced diet (35) (55% carbohydrates, 30% protein and 15% fat) (29) or by restricting energy intake from energy-dense, high-fat and sugary foods (32). Two studies, which consisted of the lowest energy restriction periods (1674 to 2092 kJ d^{-1} [400–500 kcal d^{-1}]), provided participants with commercially prepared liquid formula meal supplements (e.g. Optifast) (32,34). Additional multi-vitamin and mineral supplements were also provided (28,32,34). Prescribed energy intake for the comparator intervention was a daily intake of between 4184 and 6276 kJ d^{-1} (1000–1500 kcal d^{-1}). The energy intake between the IER and CER interventions over the study duration was identical in three studies (29,33,34). However, in two studies, total energy intake on restriction periods was not controlled for between groups, with differences in energy prescription ranging from 2092 to 3347 kJ d^{-1} (500–800 kcal d^{-1}) (28,32).

Two studies included two weekly IER interventions in comparison with CER (33,34). Rossner (34) investigated the effect of two cycles of weekly IER in two groups of participants separated by a 1-year interval. Participants received either an energy intake of 1757 kJ d^{-1} (420 kcal d^{-1}) or 2218 kJ d^{-1} (530 kcal d^{-1}) on energy restriction periods. Wing and Jeffery (33) examined two different approaches of weekly IER, by providing interruptions or breaks to the dietary restriction period. One group received a 6-week continuous break in the middle of the intervention period, and another group was asked to take three smaller 2-week breaks intermittently (after the third, sixth and ninth week sessions). Both weekly IER regimens were equal in terms of energy restriction and non-restriction periods.

Lifestyle components

In addition to the energy restriction components, three studies included advice on increasing physical activity (32–34). Participants were encouraged to set physical activity goals and achieve a predetermined target of 150 min of physical activity per week (33) or to gradually increase physical activity to walking 10 mi per week (2 mi per day on 5 d per week) (32). Moreover, behavioural change strategies were also included as an intervention component. In addition to the aforementioned goal setting for physical activity, health education was provided, and coping strategies, such as stimulus control and relapse prevention, were advised. Participants were instructed to self-monitor their dietary intake and body weight. This was to maximize compliance with the dietary regimens and show progression (29,32,33).

Adherence

Self-monitoring of dietary intake and body weight, as described in the preceding texts, was included primarily as an intervention component. However, three studies also utilized this to estimate adherence to the intervention (28,29,33). Energy intake in the study by Arguin *et al.* (29) (assessed through a 3-d food diary) reported significant within-group differences in energy intake in both the weekly IER and CER interventions from baseline; however, this was not significantly different between the interventions. No significant between-group difference in change in self-reported energy intake was reported post-intervention in the study by Wadden and colleagues (28), probably due to participants in both weekly IER and CER being advised to consume eucaloric diets. However, during weekly IER periods when energy intake was restricted to 2092 kJ d^{-1} (500 kcal d^{-1}), significant differences were observed between groups. Adherence to the dietary intervention was assessed weekly and was, in general, also comparable between IER regimens and CER in the study by Wing and Jeffery (33).

Adverse events

Adverse effects resulting from the dietary regimens were reported in two studies (32,34). Both studies found that the diets were well tolerated. Wing *et al.* (32) reported adverse events solely for the weekly IER intervention that included hair loss, an increase in upper respiratory tract infections and constipation. Whereas Rossner (34) reported side effects for both weekly IER and CER interventions. Side effects were not significantly different between treatments and also included hair loss and muscle fatigue.

Risk of bias

Inadequate reporting of the methodology of studies prevented a clear risk of bias rating for 57% of assessments, with three domains (selection, detection and performance bias) all reported as unclear (Fig. 2). A low risk of bias was selected for 34% of assessments, with a high risk of bias representing 9% of assessments. The rate of attrition was comparable between weekly IER interventions and CER/control interventions. The mean attrition rate across studies was 13.5% (range: 0 to 32.4%) with two studies reporting no attrition (28,29). Attrition bias was only judged by reviewers as high in the study by Wing and Jeffery (33), with 32% of participants not completing the follow-up outcome assessment at 11 months. Other potential risks of bias that were judged as high were in relation to the study design, with one study measuring post-intervention outcomes at two different time points (20 and 30 weeks) (29) and one study recruiting participants who were already receiving a dietary intervention and participating in a controlled trial (28). Results from the

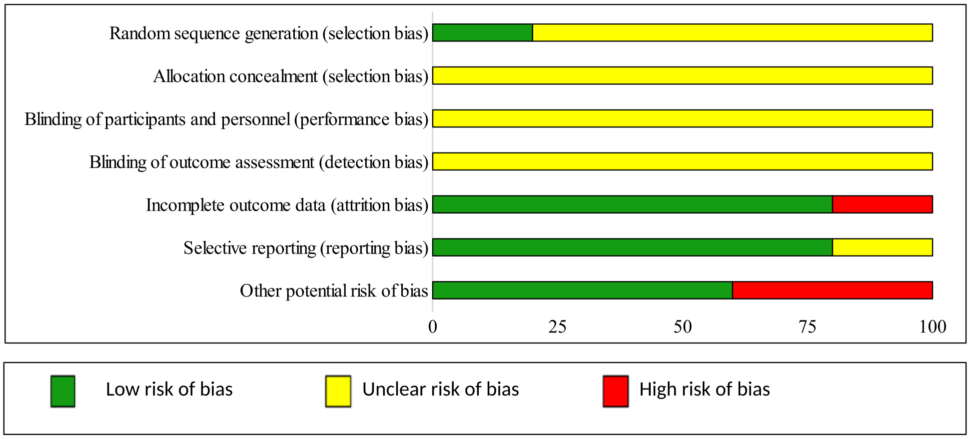

Figure 2 Risk of bias assessment. [Colour figure can be viewed at wileyonlinelibrary.com]

GRADE assessment can be found in the supporting information online (Appendix B). These indicate that overall, the evidence comparing IER to usual care as a treatment for overweight and obesity in adults was of low quality.

Meta-analysis

Change in body weight was reported across all studies and included as the primary outcome of interest in this review. The weekly IER interventions achieved a mean range of weight loss of −10.70 to −17.60 kg on completion of the active intervention period. Participants in the usual care interventions, within-group weight change, were similar with the mean weight change ranging from −8.20 to −13.97 kg. An estimate of the overall effect of weekly IER in comparison with CER on weight change was pooled in a meta-analysis. The pooled estimate demonstrated that weekly IER was as effective as CER for weight loss post-intervention (WMD −1.36 kg [−3.23 kg, 0.51 kg], p = 0.15; Fig. 3) and at follow-up (WMD −0.82 kg [−3.76 kg, 2.11 kg], p = 0.58; Fig. 4). Only three studies measured change in body weight at follow-up (6 to 12 months). Within-group mean weight change ranged from −5.70 to −17.36 kg and −7.20 to −13.41 kg following weekly IER and CER respectively.

Percentage weight change

Percentage weight loss was not, in general, reported as an outcome across studies, with the exception of one study (28). Participants in both the weekly IER and CER interventions achieved a clinically important weight loss (>5%), associated with improvements in health risk factors (3,4). Although there was no between-group differences, on completion of the weekly IER intervention, participants had lost −14.7% (SD 5.0%) in comparison with −9.6% (SD 6.0%) in the CER intervention. One

Reference	Intermittent energy restriction [IER]		Continuous energy restriction [CER]		Mean difference [95% CI]
	Mean [SD]	N	Mean [SD]	N	
Arguin *et al.* (29)	-10.70 [3.00]	12	-9.50 [2.10]	10	-1.20 [-3.41, 1.01]
Rossner, (34)	-17.60 [8.74]	42	-13.97 [7.02]	41	-3.63 [-7.05, -0.22]
Wadden *et al.* (28)	-15.40 [10.47]	8	-11.20 [19.12]	7	-4.20 [-19.51, 11.11]
Wing *et al.* (32)	-14.20 [10.30]	38	-10.50 [11.60]	41	-3.70 [-8.55, 1.15]
Wing & Jeffery, (33)	-7.54 [5.60]	80	-8.20 [3.70]	38	0.66 [-1.30, 2.62]
Pooled Estimate [Random Effect]		180		137	-1.36 [-3.23, 0.51]

Tests for heterogeneity: $T^2 = 1.58$; Q = 6.42, df = 4 [p = 0.17]; $I^2 = 37.67\%$
Tests for overall effect: Z = -1.43 [p = 0.15]

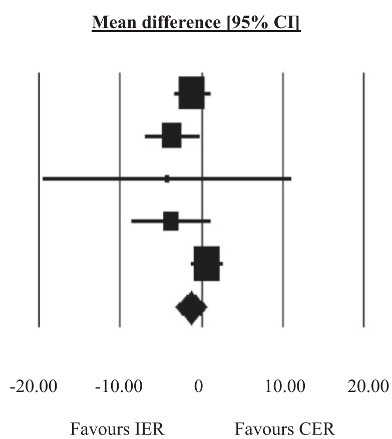

Figure 3 Meta-analysis of the effects of weekly intermittent energy restriction versus usual care comparison for weight loss [post-intervention].

Reference	Intermittent energy restriction [IER]		Continuous energy restriction [CER]		Mean difference [95% CI]
	Mean [SD]	N	Mean [SD]	N	
Rossner, (34)	-17.36 [9.17]	39	-13.41 [7.48]	42	-3.95 [-7.58, -0.32]
Wing *et al.* (32)	-5.70 [7.90]	37	-7.20 [8.00]	36	1.50 [-2.15, 5.15]
Wing & Jeffery, (33)	-7.46 [7.17]	65	-7.30 [5.10]	31	-0.16 [- 2.98, 2.66]
Pooled Estimate [Random Effect]		41		109	-0.82 [-3.76, 2.11]

Tests for heterogeneity: $T^2 = 3.81$; $Q = 4.61$, $df = 2$ [$p = 0.10$]; $I^2 = 56.62\%$
Tests for overall effect: $Z = -0.55$ [$p = 0.58$]

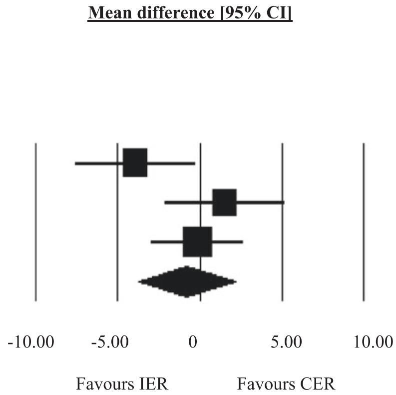

Figure 4 Meta-analysis of the effects of weekly intermittent energy restriction versus usual care comparison for weight loss [follow-up].

study reported the percentage of participants achieving a weight change of ≥15 and 20 kg (32). Forty-seven percent of participants in the weekly IER intervention lost 15 kg or more in comparison with the CER intervention (22%; $p < 0.05$). Furthermore, 32% of participants achieved a weight loss of 20 kg or more in comparison with 15% of participants in the CER intervention ($p < 0.05$) (32).

Subgroups

The difference in weight loss by gender was reported in two studies (32,34). Wing *et al.* (32) reported that women in the weekly IER intervention lost significantly more weight at 1 year in comparison with women in the CER intervention (−14.1 and −8.6 kg; $p = 0.02$ respectively). Mean weight loss in men was comparable post-intervention (weekly IER = −15.4 kg; CER = −15.5 kg; $p > 005$). There was no gender-specific effect on weight loss between treatments in the study by Rossner (34), with male and female participants in both groups reporting comparable weight loss.

Discussion

This systematic review and meta-analysis developed the evidence base in the area of IER. The principal findings from the meta-analysis identified that short-term periods of IER (weekly IER; ≥7 d) are as effective for weight loss as CER over a 3 to 6-month period. Despite the promising short-term effectiveness of weekly IER in supporting weight loss, there is insufficient evidence to ascertain the effects on the sustainability of changes in body weight.

There is no clear definition on IER, which currently includes a diverse range of dietary interventions (17–19,36). This review defined IER as interruptions in dietary intake achieved through energy restriction periods of greater than 1 week. The energy intake prescribed in the primary studies of this review varied greatly, with studies including energy restriction periods as high as 6276 kJ d^{-1} (1500 kcal). This is in contrast to previous reviews that have attempted to define IER as an energy intake of ≤3347 kJ (800 kcal) (19,22). To provide an overview of the current literature on weekly IER, interventions included in this review were not restricted by a limit to energy prescription. The effect of the different energy intakes of weekly IER interventions was not assessed in this review due to the limited number of studies. Therefore, questions over the effect of varying energy intakes on weight loss and compliance with different dietary approaches remain unknown. Future research is required to provide a consensus definition of IER to elucidate the optimum approach to weight management of overweight and obesity.

The majority of weekly IER interventions, however, did adhere to intermittent periods of dietary intake defined as a VLED. Evidence from clinical obesity guidance states that this approach, while achieving greater weight loss at 3 to 4 months, does not differ from other dietary approaches in terms of weight loss at 12 months (3,4). Furthermore, clinical guidelines advocate that VLED regimes should be recommended only if there is a clinical rationale for rapid weight loss, and the VLED used must be nutritionally complete. For this reason, long-term use requires caution, and future research is necessary to elucidate the acceptability, safety and efficacy of long-term weekly IER based on VLED (37).

The typical trend in body weight following the completion of a weight loss intervention is for weight regain to occur (1,2,20). Therefore, weight loss maintenance is an integral component of the management of obesity; however, none of the studies included an active weight maintenance component. For weekly IER to be considered an effective treatment approach, longer term studies that examine the efficacy of IER as a weight maintenance intervention are required. Only two studies in this review examined the sustainability of changes in body weight at or after 12 months (29,32), which is recommended by clinical guidelines as the preferred time point to examine the efficacy of weight management interventions (3,4). The results could not be pooled in a meta-analysis as the study by Arguin *et al.* (29) reported weight change 5 weeks from post-intervention and not change from baseline. The results indicated contrasting findings, as participants in the study by Arguin *et al.* (29) maintained mean body weight (±3%) at 12 months from completion of both interventions, based on the definitions by Stevens *et al.* (38). Whereas, in the study by Wing and colleagues (32), participants in both interventions regained the weight they lost. The inability to maintain weight loss and sustain healthy lifestyle behaviours has been a known problem in the treatment of obesity. Therefore, future studies should aim to actively provide weight maintenance support to tackle the chronic relapsing nature of obesity (1,2,20).

It is well established that interventions informed by a theoretical framework are more likely to be successful in comparison with solely an empirical or pragmatic intervention approach (39). Best practice guidelines advocated by the Medical Research Council for developing and evaluating interventions recommend that interventions are developed using appropriate evidence-based theory (40,41). Evidence of the use of theoretical frameworks was not reported from the primary studies included in this review. However, the inclusion of behaviour change techniques was incorporated in some interventions to facilitate changes in lifestyle habits. The most frequent behaviour change technique incorporated across studies was self-monitoring of diet and body weight. This is consistent with the available literature on behaviour change techniques that demonstrates self-monitoring to be one of the key components to achieving healthy lifestyle behaviours (42), weight maintenance (43) and the prevention of weight gain (44).

In addition to the role of IER as a strategy to weight management, there is interest in the metabolic effects of IER on improvements in health outcomes (45,46). Findings from this review illustrate that the cardiometabolic effects of IER were of interest and investigated in the primary studies; however, as a limited number of outcomes were repeatedly reported across studies, there was insufficient collective evidence to advocate any additional beneficial effects on health outcomes of weekly IER. This is consistent with the accumulative evidence on popular daily IER interventions (9,19,47), and future research is necessary. Although direct evidence from improvements in health risk factors was not investigated in this review, the mean weight loss reported in both interventions were of considerable magnitude (>5 kg) and thought to be associated with clinical health improvements in reducing health risk factors (3,4).

Methodological quality of studies

The risk of bias of studies was critically appraised using criteria from the Cochrane Collaboration. However, inadequate reporting of the included studies prevented clear assessment of the methodological quality, in particular of reporting the sequence generation and allocation concealment methods. This is of concern as if these processes of randomization were not adequately conducted; the studies are at risk of selection bias and systematic differences between baseline characteristics of the treatment groups (26). Blinding of outcomes and investigators to treatment allocation was also infrequently reported. This can result in risk of systematic differences and contamination between the treatments provided and an exaggeration of the effects of the intervention (48). Insufficient reporting also extended to the reporting of adverse events, with only two studies reporting adverse effects from the intervention. This probably reflects the time when these studies were published, prior to the rigour required to fulfil current standards such as the Consolidated Standards of Reporting Trials recommendations (49). This is consistent with limited reporting of adverse events from the evidence on weight management achieved through bariatric surgery (50) which is concerning as adverse events may be more serious. Both weekly IER and CER dietary regimens were reported to be acceptable and well tolerated by participants, demonstrated by low attrition rates (in comparison with previous weight management reviews that report high attrition rates, equivalent to 30–60%) (1,51). Although adverse effects reported, e.g. repeated chest infections and hair loss may affect long-term adherence to the interventions, which is currently unknown. Future studies should aim to accurately report methodological processes in accordance with the Consolidated Standards of Reporting Trials recommendations (49). This will ensure the interpretation of the internal validity of the results and provide replicable methods in which the development of future trials can be founded upon.

The overall quality of evidence from randomized controlled trials was assessed as low. To influence decision making on recommendations for clinical practice (4,5), more evidence is required on the generalizability of findings to a wider population, including men and younger adults. Contributions from this review will, therefore, add to the rapidly increasing body of evidence in support of IER and potentially assist in changing current recommendation of a one-size-fit-all approach for the management of obesity.

Strengths and limitations

This review was conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines and adhered to the rigorous methodologies of independent screening of articles, data extraction and quality assessment to ensure the reliability of results. However, the small number of studies included in this review limited any exploratory subgroup or sensitivity analysis. Insight into the optimum approach to weekly IER could not be ascertained regarding the prescription of the optimum duration of restriction periods or intensity of the energy deficit. Furthermore, due to the small number of studies included in this review, publication bias could not be reliably assessed (30).

Comparison with previous literature reviews

The current available literature on IER regimens has increased over recent years; however, the majority of systematic reviews have focussed on IER regimens that consist of IER periods on 1 or 2 d per week (17–19). Comparison of the effects of weekly IER with the most recent daily IER revealed that similar findings with daily IER interventions were shown to be as effective as CER (19,22). This review, therefore, suggests that longer periods of IER such as weekly IER are as acceptable as daily IER to adults with overweight and obesity and that longer periods of weekly IER can achieve comparable clinically meaningful weight losses (19). However, the overall quality of both reviews is limited, and future research is warranted to define the optimum IER regimen. Two reviews have investigated the impact of longer term periods of weekly IER (36,52). The overall conclusions of both of these reviews are consistent with the findings of this review. However, this current review adds further to the available evidence by providing a more accurate estimate of the effect size by including evidence from randomized controlled trials only and also by differentiating the effect of weekly IER over daily IER.

Implications for future research

As the growing interest and body of evidence accumulate over IER practices, it is important that future studies build on the findings of this review and conduct rigorous randomized controlled trials adhering to clinical guidelines on the management of obesity. Recommendations on the methodological quality and reporting standards should also be satisfied to allow replication of study designs. Furthermore, in order to translate the research evidence into practice, it is essential that the key elements of IER are well defined in relation to the optimum duration and prescription of energy restriction periods associated with effectiveness. The next aim for this body of research conducted by this research collaboration is, therefore, to conduct an overarching systematic review of reviews, to provide an overview of the effect of different types of IER in the treatment of overweight and obesity in adults.

Conclusion

This systematic review and meta-analysis illustrated that short-term periods of weekly IER (≥7-d energy restriction, interspersed with periods of no prescribed energy restriction or a lesser degree of prescribed energy restriction) is acceptable and as effective for short-term weight loss. Weekly IER as an approach to adult weight management achieved comparable weight losses to current practice (daily CER). The weight loss achieved was clinically meaningful associated with improvements in health. The effects of weekly IER on maintenance of body weight were not investigated; therefore, future studies are required to support the sustainability of the effects of weekly IER on body weight and to investigate the optimum IER regiment in the treatment of overweight and obesity.

Conflict of interest statement

No conflict of interest was declared.

Supporting information

Additional Supporting Information may be found online in the supporting information tab for this article. https://doi.org/10.1111/obr.12593

Appendix A. Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE(R) and Ovid OLDMEDLINE(R) <1946 to present>.

Appendix B. Question: Weekly intermittent energy restriction compared with usual care for the treatment of overweight and obesity in adults.

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