

Review title

Intermittent fasting interventions for the treatment of overweight and obesity in adults aged 18 years and over: a systematic review protocol

Reviewers

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Review question/objective

Are intermittent fasting interventions an effective treatment for overweight and obesity in adults, when compared to usual care treatment (continuous daily energy restriction – reduced calorie diet) or no treatment (ad libitum diet)?

Background

Overweight and obesity (classified as Body Mass Index (BMI) of greater than or equal to 25 and 30 respectively), is a global public health concern, with more than 1.9 billion overweight adults in 2014 (over 600 million of whom are obese), resulting in more deaths worldwide than underweight. ¹ A raised BMI in adulthood is associated with an increased risk of developing a number of chronic diseases which include diabetes, cardiovascular disease, muscular skeletal disorders and some cancers.¹ In addition to this substantial impact on individual health and well being, there are also significant wider costs, for example in England the direct cost to the national health service for treating overweight, obesity and associated morbidity is estimated at over five billion pounds, with costs to the wider economy estimated at 27 billion.^{2,3} Therefore effective weight management is essential.

As overweight and obesity results from an accumulation of excess body fat, arising from an energy imbalance: consuming more energy (kcal) than are expended, the majority of weight management approaches centre around behaviours to address this imbalance i.e. reducing energy intake through caloric restriction and increasing energy expenditure through physical activity. However, the aetiology of overweight and obesity is highly complex, involving an interplay of biological, psychological, societal and environmental drivers.³ Consequently, effective weight management is challenging, and whilst there remains a plethora of available weight loss programmes, not all are comprehensively evaluated

and compared, and many weight loss attempts result in weight regain and poor long term results.⁴ It is therefore vitally important to review the effectiveness of all new approaches, to support an evidence based approach to weight management.

Intermittent fasting (IF), also known as alternate day fasting (ADF), periodic fasting or intermittent energy restriction (IER) is a relatively new dietary approach to weight management, that involves interspersing normal daily caloric intake with a short period of severe calorie restriction/fasting. In terms of the possible underlying biological benefits of intermittent fasting, there is some evidence, predominantly from animal studies, to demonstrate beneficial effects on weight loss and cardio-metabolic risk factors. Whilst the underpinning mechanistic evidence is limited,⁶ there is some evidence to suggest that the benefits may be explained mechanistically through fat utilisation and nutritional stress (which can at least in part result in cellular repairs and functional optimisation)⁷ that can result from fasting. However current NICE guidance on the treatment of adult obesity⁵ does not recommend the routine use of very low calorie diets (VLCD) (defined as a hypocaloric diet of 800 or less kcal/day) for the treatment of adult obesity. NICE state that this approach should only be recommended if there is a clinical rationale for rapid weight loss and must be nutritionally complete, part of a multi-component weight management strategy, including ongoing support, and should be undertaken for a maximum of 12 weeks (followed continuously or intermittently). Furthermore, the British Dietetic Association⁸ raise concern that rapid weight loss associated with fasting may largely be due to loss of water and glycogen rather than fat, and may result in fatigue, dizziness and low energy levels. Essentially IF involves the intermittent use of a VLCD, and there remain questions about the side effects of this approach, whether there is an optimal fasting pattern or calorie limit, and how sustainable it is for long term weight management.

Intermittent fasting has recently gained much popularity following significant media attention. In the UK this dietary approach reached mainstream after a BBC Horizon documentary aired in August 2012, featured an IF approach called the 5:2 diet, which involves 5 days of regular eating patterns interchanged with 2 days of fasting (max 500kcal for women and 600kcal for men). However other IF patterns are used such as alternate day fasting.⁶ Despite the recent popularity of intermittent fasting⁹ and associated weight loss claims,¹⁰ the supporting evidence base in humans remains small and there is only one published systematic review⁷ examining the health benefits of this approach, however the aim of this review was to examine the impact on wider health benefits, not specifically as a treatment approach for overweight and obesity, it also failed to provide a detailed methodology, and any meta analyses. . This review will address these gaps in the evidence base.

Inclusion criteria

Types of participants

This review will consider studies that include free-living (not hospitalised) male and female adults aged 18 years and over (adults of any age will be included, however age will be considered as a potential moderator) who are overweight or obese (i.e. have a BMI greater than or equal to 25 or 30) Participants will be excluded if they have secondary or syndromic forms of obesity; or are diabetic, undergoing bariatric surgery, pregnant or breast feeding, taking medication associated with weight loss

(e.g. orlistat, metformin) or weight gain (e.g. steroids, antipsychotics).

Types of intervention(s)/phenomena of interest

This review will consider studies that evaluate intermittent fasting interventions, defined as consumption of 800* kcal or less on at least one day, but no more than 6 days in a calendar week, that follow participants for at least 12 calendar weeks from the start of the intervention.

*as there is no accepted formal definition of 'fasting' - the NICE upper limit for a very low calorie diet will be used in this review ⁵.

Types of comparators

Interventions will be compared to control (no intervention) or usual care (which is likely to consist of advice to continuously follow a reduced calorie diet, which is usually around 25% of recommended energy intake).

Types of outcomes

Primary outcome: any objective, validated measure of adiposity: measured (not self reported) body mass; body mass index; waist circumference; skin fold thickness; bio-impedance; hydrostatic or BodPod measures; dual X-ray absorptiometry (DXA) or magnetic resonance imaging (MRI) scans. Secondary outcomes: adverse events; quality of life; disease risk markers (e.g. blood glucose, cholesterol, blood pressure); diet; and physical activity.

Types of studies

This review will only consider randomised or pseudo randomised controlled trials.

Search strategy

The search strategy aims to find both published and unpublished studies. A three-step search strategy will be utilised in this review. An initial limited search of MEDLINE and CINAHL will be undertaken followed by analysis of the text words contained in the title and abstract, and of the index terms used to describe the relevant articles. A second search using all identified keywords and index terms will then be undertaken across all included databases. Thirdly, the reference list of all identified reports and articles will be searched for additional studies. Studies in English language, published since database inception will be considered for inclusion in this review.

The databases to be searched include:

Medline via OVID Host

Embase via OVID

Cinahl via EBSCO Host

Central

The search for unpublished studies will include:

Clinicaltrials.gov

ISRCTN registry

anzctr.org.au

Initial keywords to be used will be intermittent fasting or periodic fasting, alternate day fasting or intermittent calorie restriction, and overweight or obesity. A provisional full search strategy (to be confirmed following the initial search) is presented in appendix III.

Assessment of methodological quality

Papers selected for retrieval will be assessed by two independent reviewers for methodological validity prior to inclusion in the review using standardised critical appraisal instruments from the Joanna Briggs Institute Meta Analysis of Statistics Assessment and Review Instrument (JBI-MAStARI) (Appendix I). Any disagreements that arise between the reviewers will be resolved through discussion, or with a third reviewer.

Data collection

Data will be extracted from papers included in the review using the standardised data extraction tool from JBI-MAStARI (Appendix II). The data extracted will include specific details about the interventions, populations, study methods and outcomes of significance to the review question and specific objectives.

Data synthesis

Quantitative data will, where possible be pooled in statistical meta-analysis using JBI-MAStARI. All results will be subject to double data entry. Effect sizes expressed as odds ratio (for categorical data) and weighted mean differences (for continuous data) and their 95% confidence intervals will be calculated for analysis. Heterogeneity will be assessed statistically using the standard I-squared and tau-squared. Where possible, subgroup analyses will also be conducted based on baseline weight status of participants (i.e. overweight [BMI: 25-29], obese [BMI: 30-39] & morbidly obese [BMI 40+]); gender; age; length of study and IF approach.. Where statistical pooling is not possible the findings will be presented in narrative form including tables and figures to aid in data presentation where appropriate.

Conflicts of interest

The authors have no conflicts of interest to declare.

Acknowledgements

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References

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Appendix I: Appraisal instruments

MAStARI Appraisal instrument

JBI Critical Appraisal Checklist for Randomised Control / Pseudo-randomised Trial

Reviewer Date

Author Year Record Number

| | Yes | No | Unclear | Not Applicable |
|---|--------------------------|--------------------------|--------------------------|--------------------------|
| 1. Was the assignment to treatment groups truly random? | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 2. Were participants blinded to treatment allocation? | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 3. Was allocation to treatment groups concealed from the allocator? | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 4. Were the outcomes of people who withdrew described and included in the analysis? | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 5. Were those assessing outcomes blind to the treatment allocation? | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 6. Were the control and treatment groups comparable at entry? | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 7. Were groups treated identically other than for the named interventions | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 8. Were outcomes measured in the same way for all groups? | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 9. Were outcomes measured in a reliable way? | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 10. Was appropriate statistical analysis used? | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

Overall appraisal: Include Exclude Seek further info.

Comments (Including reason for exclusion)

Appendix II: Data extraction instruments

MAStARI data extraction instrument

JBI Data Extraction Form for Experimental / Observational Studies

Reviewer Date

Author Year

Journal Record Number

Study Method

RCT Quasi-RCT Longitudinal
Retrospective Observational Other

Participants

Setting _____

Population _____

Sample size

Group A _____ Group B _____

Interventions

Intervention A _____

Intervention B _____

Authors Conclusions:

Reviewers Conclusions:

Study results

Dichotomous data

| Outcome | Intervention () number / total number | Intervention () number / total number |
|----------------|---|---|
| | | |
| | | |
| | | |
| | | |

Continuous data

| Outcome | Intervention () number / total number | Intervention () number / total number |
|----------------|---|---|
| | | |
| | | |
| | | |
| | | |

Appendix III: initial list of search terms

intermittent fast* OR

alternate-day fast* OR

intermittent energy restriction OR

intermittent calorie restriction OR

fasting calorie restriction intervention OR

intermittent restrictive diet OR

very low calorie diet OR

periodic fasting OR

AND

body mass OR

body size OR

body weight OR

bodysize OR

body-size OR

fat OR

fatness OR

obes* OR

overnutrition OR

overweight OR

over-weight OR

weight OR

Weight gain OR

Weight maintenance OR

Weight management OR

AND

adiposity OR

adverse events OR

bio-impedance OR

blood glucose OR

blood pressure OR

bmi OR

bodpod OR

body mass index OR

cholesterol OR

diet OR

dxa (scan) OR

exercise OR

hydrostatic OR

MRI OR

physical activity OR

quality of life/QoL OR

skin-fold/skin fold thickness OR

waist circumference OR

weight loss