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SYSTEMATIC REVIEWS AND META-ANALYSES

Effectiveness of intermittent fasting for weight loss in individuals with obesity: A meta-analysis of randomized controlled trials☆

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Abstract *Aim:* To assess whether intermittent fasting (IF) diets are associated with improvement in weight loss, metabolic parameters, and subjective well-being, in people with obesity.
Data synthesis: We performed a Meta-analysis of Randomized Controlled Trials longer than 2 months, retrieved through an extensive search on MedLine, Cochrane CENTRAL Library, and Embase online databases, comparing weight loss with IF diets and control diets in people with Body Mass index (BMI) > 30 kg/m^2. We retrieved 9 trials, enrolling 540 patients. IF was not associated with a significantly greater reduction of body weight or BMI at any time point with respect to controls or in respect to continuous restricted diets, with low-to moderate quality of evidence; no significant difference in efficacy between alternate day fasting and time restricted eating was found. Differences in fasting plasma glucose, total or high-density lipoprotein cholesterol or blood pressure at any time point were not statistically significant, whereas a reduction of low-density lipoprotein cholesterol (MD −8.39 [−15.96, −0.81] mg/dl, P = 0.03; I^2 = 0%) was observed at 2–4 months, but not in the longer term. Data on psychological parameters and overall well-being were insufficient to perform a formal meta-analysis, whereas a qualitative synthesis did not show any difference between IF and controls.
Conclusions: IF is not associated with greater or lesser weight loss than non-intermittent fasting diets. Further data on psychological parameters and overall well-being are needed to properly assess the role of IF diets in the management of obesity.

1. Introduction

The increasing worldwide prevalence of obesity and its complications [1] and the limited long-term efficacy of some of the traditional therapeutic approaches [2] drive growing efforts on implementing new treatment strategies: among those, Intermittent fasting has been proposed [3]. Long fasting periods have been experimented for

Abbreviations: ADF, Alternate Day Fasting; TRE, Time Restricted Eating; BMI, Body Mass Index.

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centuries by human societies for practical reasons or religious purposes. Fasting longer than 8–12 h enhances ketogenesis and lipolysis, and it also activate intrinsic defenses against oxidative and metabolic stress [4]. Meal timing may also play a role in weight management, since circadian rhythms alter lipid and glucose metabolism and inflammatory pathways [4]; accordingly, individuals with a restricted feeding time window seem less likely to be affected by overweight, obesity and hypertension [5] and less prone to cognitive decline in the older age [6]. On the other hand, eating three meals each day, may lead to higher plasma triacyl glyceride concentrations, possibly enhancing fat accumulation [7].

Intermittent fasting is defined as a reduction of the daily duration of calorie intake [8], and it can assume different patterns. Fasting one or more days a week is defined Periodic Fasting (PF), whereas in Alternate Day Fasting (ADF) a day of fasting is alternated to a day of eating; Time Restricted Eating (TRE) is a diet in which the subject must fast 12–18 h a day. All those diets have been associated a significant weight loss in some clinical trials [9–12]. Available meta-analyses, recently summarized in an umbrella-review [13], provided conflicting results, as some suggest that intermittent fasting could induce a greater weight loss than controls, with a beneficial effect on insulin resistance and lipid profile [14–20], whereas others did not find any significant difference [21–24]. As regards to psychological well-being, patients undergoing intermittent fasting report a transient improvement in overall mood [25], and decreased anger [26]. Underlying mechanisms may include an increase in cerebral blood flow, brain serotonin, endogenous endorphins, and glucocorticoids release [27,28]. Conversely, the long-term effects of fasting on mental health are controversial [29], as mixed outcomes on mood, fatigue, concentration difficulties, and irritability during the fast days, have been reported [30]. Furthermore, a prolonged daily fasting time is associated to a higher risk of loss of control over eating in eating disordered patients [31]; no data are available on this topic, but it could be speculated that a reduction of the daily time feeding window could trigger the onset of a sub-threshold eating disorder in predisposed subjects.

Mixed results on weight loss and psychological status may have many explanations: most current trials, and all available meta-analyses, included overweight individuals without obesity, along with patients with obesity. This is likely to introduce a bias, since the effect of any intervention on a metabolic parameter can be expected to be greater when that parameter has a wider deviation from normal. In other words, the inclusion of subjects with near-normal weight may have limited observed weight loss, thus inducing an underestimation of the efficacy of IF in the treatment of obesity. In addition, in some trials, intermittent fasting was compared with a dietary regimen with a higher overall calorie intake [19], producing an evident distortion. Furthermore, some reviews included Ramadan, which is a religious fasting, therefore involving spiritual and social dimensions which may alter its effects on metabolic parameters and wellbeing [29]. In fact, it is conceivable that the adherence to specific religious precepts in a determined social setting is associated with a number of behaviors which are different from those of patients in other contexts, possibly interfering with their weight.

The primary aim of our meta-analysis is to assess the specific effect of intermittent fasting in the treatment of obesity, excluding overweight subjects and non-medical precepts; thus, we explored differences between intermittent fasting diets and non-intermittent fasting diets concerning weight loss in individuals with obesity. Moreover, we included only trials with a minimum duration of 8 weeks, in order to exclude very short-term interventions which are unlikely to produce major weight changes in people with obesity. The secondary aim is the exploration of possible effects of intermittent fasting on blood pressure, lipid profile, and blood glucose, together with its effects on the perceived quality of life, psychological status, and adherence to the prescribed diet.

2. Methods

This meta-analysis is reported following the criteria of the PRISMA statement [32]. Review Protocol was submitted for registration to the PROSPERO website (#319029; https://www.crd.york.ac.uk/PROSPERO/).

2.1. Search strategy and selection criteria

A systematic search on PubMed, Cochrane CENTRAL, Clinical Trials.gov and Embase databases was performed, collecting all randomized clinical trials written in English and performed on humans up to September 10th, 2022. The full search string is reported in Appendix, Table 1S. Further studies were manually searched in references from retrieved papers.

Studies were included if they fulfilled the following criteria: randomized controlled trials-randomized controlled trials; - comparison of an intermitted fasting diet with a continuous restricted (CR) diet, or an unrestricted diet (ad libitum diet, see below for definitions);- apart from meal timing, no difference in treatment of obesity between the two arms (e.g., physical activity, drugs, etc.); - duration of the trial of at least 8 weeks; - end-of-study body weight, or BMI, reported for both treatment arms;- studies enrolling only individuals with BMI >30 kg/m^2 (27.5 kg/m^2 if enrolling Asian subjects), or separate analyses of subgroups of cases with BMI >30 kg/m^2 in trials with wider inclusion criteria.

2.2. Intervention

Intermittent fasting (IF) is a term used to describe a variety of eating patterns in which no or few calories (800 kcal or $<25\%$ of estimate energy needs) are consumed for time periods that can range from 12 h a days to several days a week, on a recurring basis. In our meta-analysis, we included the following diets:

Table 1 Baseline characteristics of the included studies.

Name	Country	D	Age	M	PA	Diets		N		BMI		Energy intake		Excl. Criteria		
						I	C	I	C	I	C	I	C	Dm	CVD	Smoke
Bhutani 2013 [43]	USA	3	45.5	3.8	1	MADF (450 kcal 3.5 d/w)	ALD	43	40	35	35	nr	nr	1	1	1
Catenacci 2016 [35]	USA	8	41	24	1	ADF (3.5 d/w)	CER	14	12	35.8	39.5	700	2064	1	1	1
Cienfuegos2020 [42,44]	USA	2	46	11	0	TRE (20 h/d)	ALD	16	14	37	36	nr	1533	1	1	1
Conley 2017 [36]	Australia	6	67.5	100	1	5:2 (600 kcal 2 d/w)	CER	11	12	33.4	36.2	nr	1762	0	0	1
Coutinho 2017 [37]	Norway	3	39.2	21.5	1	MPF (600 kcal 3 d/w)	CER	14	14	35.6	35.1	1467	1255	1	0	1
LIU 2022 [39]	China	12	31.9	51	1	TRE (16 h/d)	CER	69	70	31.8	31.3	1500	nr	1	1	0
Maruthur 2020 [40]	USA	3	59.4	7.3	0	TRE (18 h/d)	CER	21	20	nr	nr	nr	nr	0	nr	nr
Oliveira 2020 [41]	Brasil	12	31.5	0	0	TRE (12 h/d)	CER	31	27	34	33	−750*	−750*	1	1	1
Sundfør 2018 [38,45]	Norway	12	47.8	50.8	1	5:2 (500 kcal 2 d/w)	CER	54	58	35.1	35.3	−27%*	1642	0	1	1

D = Duration (expressed as months); M = Males; N = Number; I = Intervention; C = Control; MADF = Modified Alternate Day Fasting; ADF = Alternate Day Fasting; eriodic Fasting; ALD; Ad Libitum Diet; CER; continuous Energy Restriction; TRE = Time Restricted Eating, MPF; Modified PF; PA = Physical Activity; CVD = Cardiovascular Disease; DM = Diabetes Mellitus; BMI = Body Mass Index; Nr = Not Reported. d/w = days a week; h/d; hours a day; kcal = kilocalories; Prescribed Energy intake is marked with * when reported as a difference between baseline energy intake and prescribed energy intake.

- Time-restricted eating (TRE): also termed time-restricted feeding (TRF), a diet in which food and energy intake is restricted within a specific time frame daily, which is less than 12 h each day [8].
- Periodic fasting (PF). A diet in which no calories (zero-calories PF) or severely limited energy intake, such as 800 kcal, or less than 25% of estimated energy needs (modified PF, MPF) are consumed on fasting days, which are 1–4 days a week, whereas unrestricted days are 3–6 a week. Such diet is defined "alternate day fasting (ADF)" if fasting (zero-calories ADF), or severely restricted (modified ADF, MADF) days are alternated with a day of unrestricted food intake or "feast days" [8]. This type of regimen also includes the popular "5:2 diet", which involves energy restriction (<25% of estimated energy needs) for 2 nonconsecutive days per week and unrestricted food intake for the remaining 5 days.

All the diets included were suitable to be prescribed in clinical routine as long-term therapies: we therefore excluded studies based on Ramadan religious fasting, as well as studies built upon periods of fasting lasting more than a week consecutively, followed by weeks or months of non-fasting diet.

2.3. Control

Control diet were diets in which the interval prescribed between meals were shorter than 12 h. Control diet may provide a reduced caloric intake (CR diet), as well as an unrestricted daily caloric amount (ad libitum diets).

2.4. Endpoints

The principal endpoints were:

- Difference in mean body weight (expressed as kg) and Body Mass Index (BMI, expressed as kg/m^2) between all Intermittent fasting diets and controls after 2–4, 6–8, and 12 months.

Secondary endpoints were:

- Difference in mean, Total, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) Cholesterol, triglycerides (all expressed as mg/dl), and Systolic and Diastolic Blood Pressure (SBP and DBP, respectively) between all Intermittent fasting diets and controls after 2–4, 6–8, and 10–14 months.
- Difference in quality of life and adherence to prescribed diet between all Intermittent fasting diets and controls after 2–4, 6–8, and 10–14 months.
- Differences in scores of psychometric tests exploring mood, eating disorder psychopathology, and other areas of mental health, if available, including, but not limited to, Beck anxiety inventory (BAI), Beck depression inventory (BDI), binge-eating scale (BES), belief score (BS), body uneasiness test (BUT), food craving index (FCI), impact of weight on quality of life-lite

questionnaire (IWQOL-lite); Short-Form Health Survey Questionnaire.

Other variables of interest were: year of publication; trial duration; number, age and sex of participants; type of diet and calories prescribed in both arms; trial exclusion criteria.

2.5. Data collection

Titles and abstracts were screened independently by two authors, and potentially relevant articles were retrieved in full text. For all published trials, results reported in published papers and supplements were used as the primary source of information; when the required information on protocol or outcomes was not available in the main publication secondary publications were used for retrieval of missing information; whenever needed an attempt at retrieval of missing information was performed consulting the clinicaltrials.gov registry. The identification of relevant abstracts, the selection of studies, and data extraction were performed independently by two of the authors (G.A.S and B.C.), and conflicts were resolved by a third investigator (E. M.). The risk of bias was assessed using the updated parameters proposed by the Cochrane Collaboration [33] by two of the authors (F.C. and F.S.), and conflicts were resolved through discussion with a third investigator (E.M.); reporting bias was assessed for each main outcome. The GRADE methodology [34] was used to assess the quality of the body of retrieved evidence, using the GRADE pro GDT software (GRADEpro Guideline Development Tool. McMaster University, 2015).

2.6. Statistical analyses

For each outcome, sample size mean values, standard deviation of both arms were retrieved at any time-point for which they were available; forest plot were then built collecting all data for each outcome at any given time-point. Between-group difference-in means (mean difference: MD) with 95%, CI were calculated, on an intention-to-treat basis, for each outcome at any given time-point, using the Wald type confidence interval methods calculator. Heterogeneity was assessed by means of I^2 statistics, through the Der Simonian and Laird variance estimator. We applied a random-effects model as the primary analysis, because it is more reliable than fixed-effect when the number and size of component studies is small. Results for primary outcomes were displayed as forest plots for each timepoint, whereas results for secondary outcomes were reported as summary effect estimate at each time point. A subgroup analysis was performed dividing trials performing PF and TRE diets; an additional analysis was also made, including only trials using a continuous restricted diet as a comparator. To evaluate the influence of each study on the overall effect size, sensitivity analysis was conducted using the one study remove (leave-one-out) approach. Funnel plots and Egger regression for body weight were examined to estimate possible publication/ disclosure bias. All analyses were performed using Review Manager 5.3.5; The Cochrane Collaboration, 2014, and IBM SPSS Statistics 28.

3. Results

3.1Trial characteristics

Fig. 1S of Supplementary materials reports the trial flow summary. Of the 7850 items, after removing duplicates, 886 were selected for retrieval of the full text. Of those, 9 trials, overall enrolling 273 participants on IF diets and 267 participants on continuous restricted diets, fulfilled the inclusion criteria. The main characteristics of included trials are reported in Table 1. Four studies were performed in the USA, 2 in Norway, one in Australia, China and Brazil, respectively. Mean age of participants was 44.7 years; proportion of male patients was 33%. Four studies compared PF with CR [35–38], three studies compared TRE with CR [39–41], whereas two studies study compared an ad libitum diet with TRE [42] and PF [43], respectively. The trial of Bhutani et al. [43] was composed of four arms, two of which associated PF and control diet with physical activity, whereas two performed dietary intervention alone; we therefore considered the two arms with physical activity and the two without as two separate trials. Four studies excluded smokers, five excluded those with previous CVD disease, six studies excluded individuals with diabetes mellitus, whereas one studies excluded only those on insulin. The risk of bias is reported in Figs. 2S and 3S of supplementary materials; briefly, all the trials were open label, with only one of the trials [36] reporting blinding of outcome assessment. Furthermore, seven trials were prone to allocation concealment; four trials reported only BMI without reporting body weight at endpoint. Overall, two trials were at low risk of bias [36,38], one at high risk of bias [35], whereas the remainder showed some concerns for bias.

3.2. Weight loss

Data on body weight were retrieved from 9, 5, and 3 trials at 2–4, 6–8, 10–14, 18–30 months, respectively (Fig. 1). IF diets were not associated with a significantly different body weight at 2–4 months (MD -2.05 [−5.85, 1.75], P = 0.29), at 6–8 months (MD -2.73 [−7.96, 2.49] kg, P = 0.30), and at 10–14 months (0.68 [−2.17, 3.52]kg, I^2 = 0 P = 0.64), in respect to control diets, with a moderate heterogeneity at 2–4 and 6–8 months (I^2 = 52 and I^2 = 65, respectively), and no heterogeneity (I^2 = 0) at 10–14 months. No publication bias was found (Egger's regression: bias 0.40 (−0.20; −0.99) p = 0.19; Fig. 4S of supplementary materials for funnel plot). A sensitivity analysis was performed to explore heterogeneity, excluding one trial at a time, which confirmed the results; notably, when excluding the study by Catenacci et al. [35], in which the mean baseline weight differed between the two treatment arms, heterogeneity was 0% (Table 3S of supplementary materials).

We performed a subgroup analysis exploring the differential effect of ADF diets and TRE diets on body weight at 2–4 months: patients on TRE did not show a

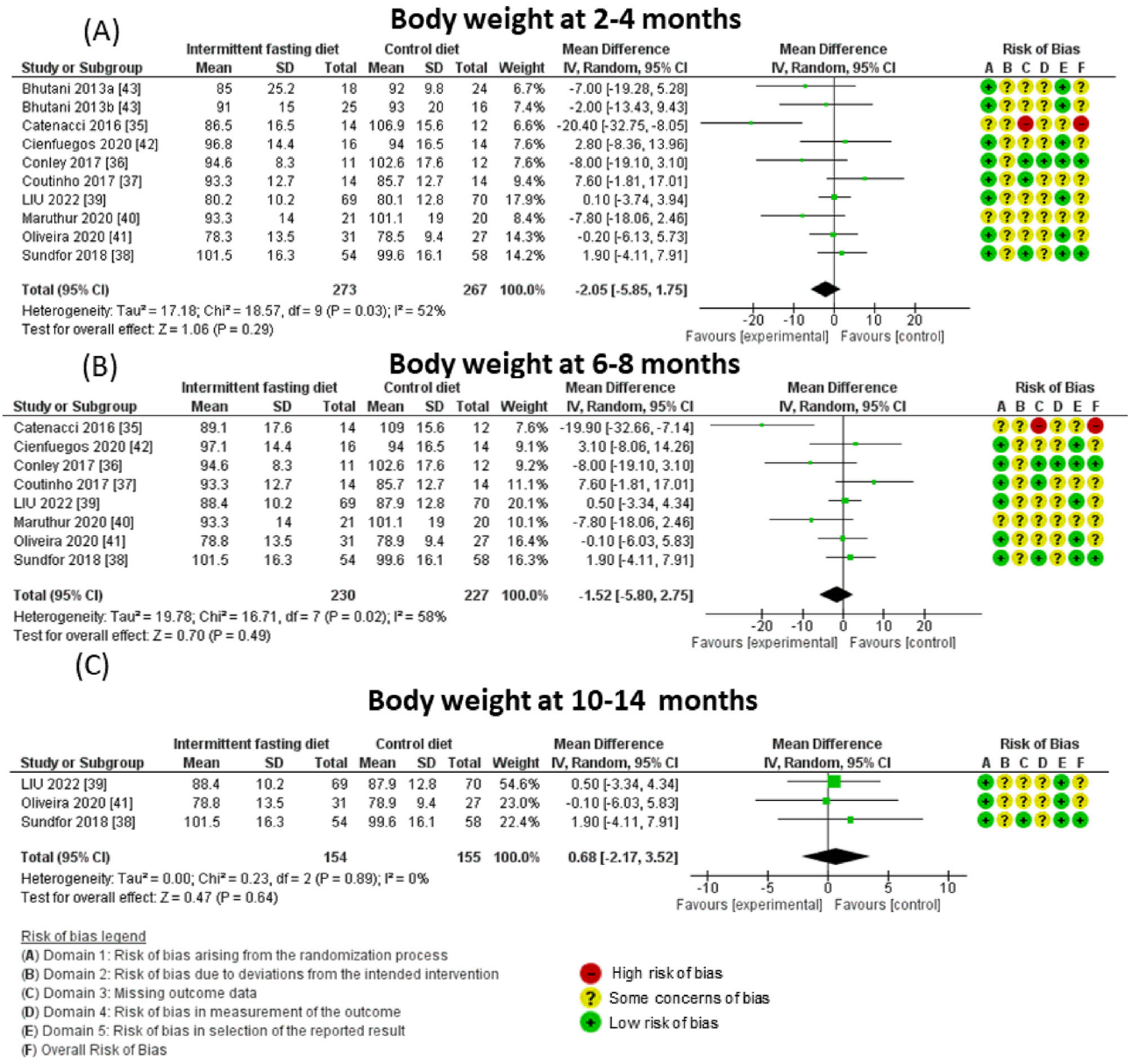

Figure 1 Difference in Body Weight (expressed as kg) at different timepoints between Intermittent Fasting Diets and controls N = number, SD = Standard Deviation, IV = Inverse Variance CI = Confidence Interval. Risk of Bias Legend: A = Random sequence generation (Selection bias); B = Allocation concealment (selection bias); C = Blinding of participants and personnel (performance bias); D = Blinding of outcome assessment (Detection bias); E = Incomplete outcome data (attrition bias); F = selective reporting for weight (reporting bias); G = selective reporting for renal function (reporting bias) H = other bias, "+" = low risk; "?" = unknown risk; "−" = high risk.

significantly different body weight (−0.42 [−3.39, 2.55] kg P = 0.49, I^2 = 0%), as well as patients on PF (MD -3.83 [−11.12, 3.45] kg, P = 0.30, I^2 = 69%), with no differences observed between subgroups (P = 0.40, Fig. 5S of supplementary materials). An additional analysis on weight at 2−4 months was performed, including only the seven trials comparing IF with CR diets, which showed no significant difference between the two diets (MD -2.43 [−6.52, 1.66] kg P = 0.25; I^2 = 61%, Fig. 6S of supplementary materials); such subgroup analysis could not be performed for longer durations, since all available trials compared IF with CR.

Data on BMI were available for 5, 4, and 3 trials, at 3−4, 6−8 and 12 moths, respectively. IF diets were not associated with significant reduction of B MI at any time point (MD -1.33 [−2.79, 0.13] kg/m^2 at 3 months, −0.68 [−2.13, 0.78] kg/m^2 at 6 months, −0.00 [−0.73, 0.73] kg/m^2 at 12 months) (Fig. 2).

3.3. Glycemic control

Differences in fasting plasma glucose between IF diets and control arms were not statistically significant at any time point (Table 2S of Supplementary Materials).

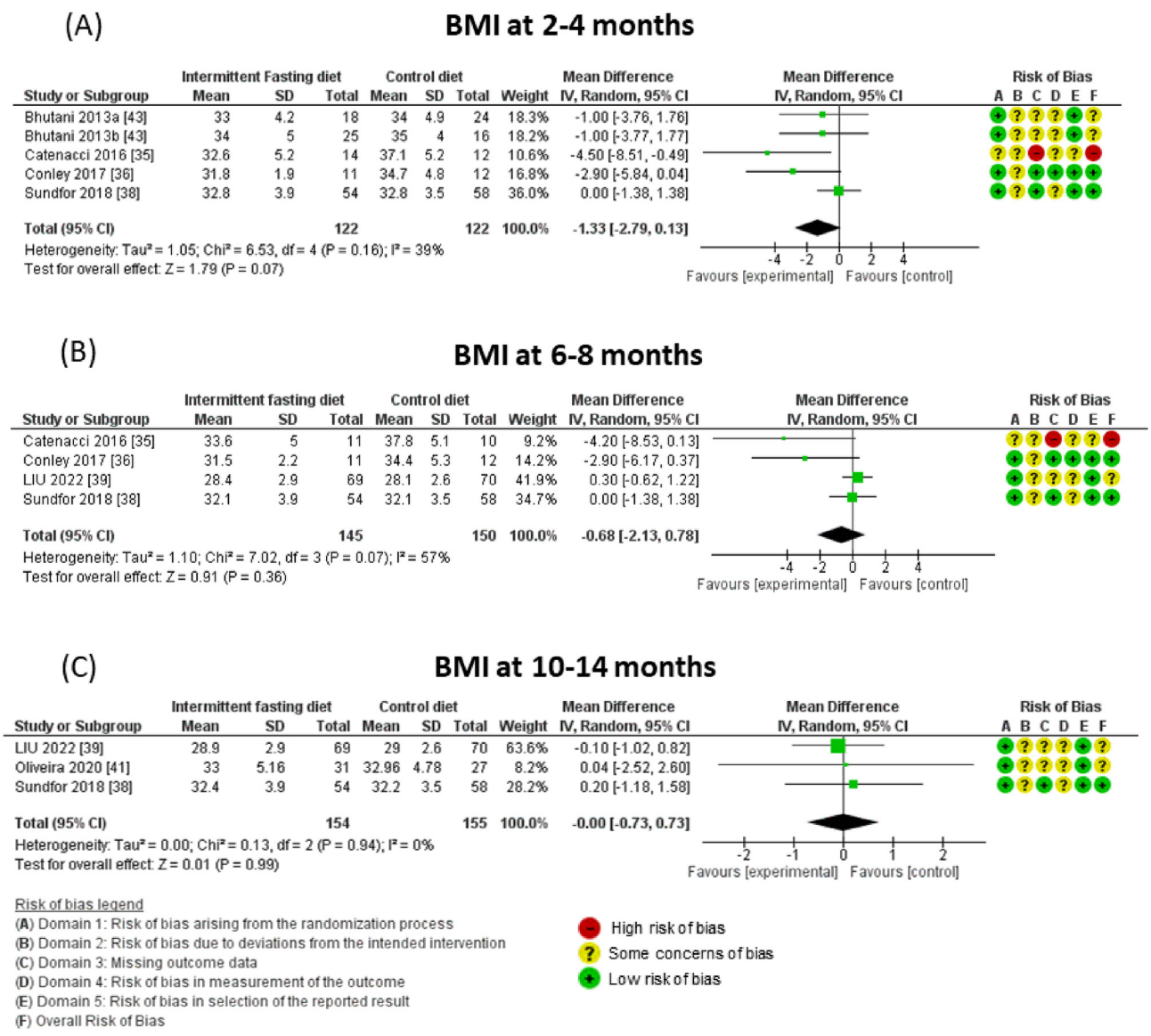

Figure 2 Difference in Body Mass Index (expressed as kg/m^2) at different timepoints between Intermittent Fasting Diets and controls. SD = Standard Deviation, IV = Inverse Variance CI = Confidence Interval. Risk of Bias Legend: A = Random sequence generation (Selection bias); B = Allocation concealment (selection bias); C = Blinding of participants and personnel (performance bias); D = Blinding of outcome assessment (Detection bias); E = Incomplete outcome data (attrition bias); F = selective reporting for weight (reporting bias); G = selective reporting for renal function (reporting bias); H = other bias."+" = low risk; "?" = unknown risk; "−" = high risk.

3.4. Cardiovascular risk factors

IF diets were not associated with a significant difference in Total cholesterol, HDL cholesterol or triglycerides at any time point with respect to controls. A transient reduction in LDL-Cholesterol at 2–4 months (MD −8.39 [−15.96, −0.81] mg/dl, P = 0.03; I^2 = 0%) was observed, which was not maintained in the longer term (MD −3.19 [−15.89, 9.51] mg/dl, P = 0.62, I^2 = 61%, at 6–8 months, and MD −0.88 [−21.65, 19.90] mg/dl, P = 0.93; I^2 = 86%, at 10–14 months).

No difference was found in systolic or diastolic blood pressure at any time point (Table 2S of Supplementary Materials).

3.5. Psychological parameters

Six trials provided information on quality of life and/or psychological parameters. Different psychometric tests were administered in available trials, preventing a formal meta-analysis. In one study, Short-Form Health Survey Questionnaire scores were similar in the TRE and CR groups at endpoint [39]. In another trial, after 6 months, participants in both IF and CR groups an improvement of Assessment of Quality of Life (AQoL8D) scores was observed after 6 months in both IF and CR treatment arms, suggesting that neither diet had a detrimental effect on quality of life, but no comparison between the two diets was made [36]. Cienfuegos et al. [42], assessed for sleep

quality through the Pittsburgh sleep quality index, showing no significant effect of treatment [44]. Coutinho et al. investigated fasting and postprandial feelings of hunger, fullness, desire to eat, and prospective food consumption, failing to detect any effect of treatment [37]. In the trial authored by Sundfør et al., despite a greater increase of cognitive restraint over eating with CR than with IER, and an increased hunger in the IF than CR [38], the effects of the two diets on uncontrolled and emotional eating were similar [45]; this was the only included trial in which eating disorder psychopathology was investigated. Finally, Catenacci et al. measured depressive symptoms at baseline and after 8 weeks of intervention using the Center for Epidemiologic Studies Depression Scale but they did not report their results [35].

3.6. GRADE scoring of available evidence

GRADE scoring for the principal endpoints is reported in Table 4S of supplementary materials. The overall quality of evidence was assessed as low for body weight at 2-46-8, and 10−14 months, and BMI at 3−4, 6−8, and 10−14 months.

4. Discussion

IF diets seem to be no more effective, nor less effective, than non-intermittent fasting diets, in inducing weight loss in patients with obesity. Some previous meta-analyses [14−20,46], performed on a mixed population of overweight subjects with or without obesity showed a greater efficacy on weight loss of intermittent fasting in comparison with control diets. On the other hand, a Cochrane review, also including both individuals with and without obesity, reported only a short-term reduction of body weight with IF when compared to ad libitum diet, with low-certainty evidence; when IF was compared to CER, the weight-reducing effect was uncertain in the short term, and unlikely in the medium term; a subgroup analysis was performed including subjects with overweight, but not for those with obesity [24]. In another more recent meta-analysis, MADF and the 5:2 diet were the only IF types associated with a statistically significant weight loss in adults with overweight or obesity [17]. Notably, all those meta-analyses included trials performed on, or including also, individuals not affected by obesity, who could have a different response to different dietary approaches than patients with obesity. In addition, some recent trials [39,40] were not available at the time in which those meta-analyses were performed.

The present meta-analysis does not show any relevant effect of IF, when compared to CR, on obesity-associated cardiovascular risk factors, with the exception of a short-term reduction in LDL, which had already been observed in a previous meta-analysis [47]; furthermore, an increase in LDL particle size and decrease in the proportion of small, dense LDL particles in adults with obesity has also been reported in clinical trials [48]. No difference in blood glucose between the two diets was found, in contrast to previous findings [20]. Notably, intermittent fasting did not seem to provide any advantage with regard to longer-term weight loss.

Many studies have highlighted the potential beneficial effect of IF on improving the hypothalamic responses to fasting in obesity [49], and studies on mice found a beneficial effect on gut microbiota, browning of adipose tissue [50], and insulin sensitivity [51]. All the aforementioned observation could provide a rationale for a greater efficacy of IF for weight loss and improvement of obesity-related cardiovascular risk factors; however, no relevant effect could be detected when combining all available relevant randomized trials performed in obese subjects. Notably, IF has been reported to increase resting metabolic rate and modulate incretin levels in normal-weight and overweight non-obese subjects [49], whereas such effects were not detected in obese patients [37]. This supports the hypothesis of differential effects of IF depending on the amount of excess weight. Finally, a reduced adherence may be hypothesized: adherence to prescribed regimens is a major limiting factor of the efficacy of dietary interventions in obesity [52], and including such diets, especially TRE, in daily routine, may be challenging for some categories of patients, given the social implications of eating timing [53]. On the other hand, IF may be considered as an alternative to CR, as it appears overall safe; even if no data on all-cause mortality, cardiovascular mortality, stroke, myocardial infarction and heart failure are available for IF diets [24], data on cardiovascular risk factors appear to be reassuring. In addition, no beneficial or detrimental effect on psychological parameters was observed, in contrast with previous observations [26,28]. Only one of the included trials administrated psychometric tests aimed at evaluating the possible onset of eating disorder psychopathology at follow-up. The onset of sub-threshold Eating Disorder with the presence of loss of control over eating during a prolonged fasting period, may theoretically represent a possible explanation for the failure of IF diets; however, insufficient data on this point are available to date in literature.

Some limitations should be considered in the interpretation of the results of this meta-analysis. Most trials are relatively small, limiting the precision of estimates of treatment effect. In addition, most studies have a short follow-up, reducing the possibility of extending results to longer-term treatment. Furthermore, some trials are affected by a relevant risk of bias (particularly allocation and detection bias), possibly distorting the estimates of efficacy of IF diets. In addition, the use of medication for obesity or other conditions (such as diabetes, hypertension, and hyperlipidemia) was not considered among outcomes; differences in medication use could therefore have interfered with results; however, most trials [35−39,42,43,49] excluded patients on medications known to affect appetite or induce weight loss, whereas some excluded patients on lipid-lowering [35,37,42,43,49], hypotensive [35,37,42,49], and glucose-lowering [35,37,42,43,49] drugs. In addition, no study reported any change in medication during the trial. Nevertheless, since

change in medications was not listed among outcomes in many trials, it cannot be excluded that the therapeutic intervention was associated with modifications in pharmacological therapy. On the other hand, this meta-analysis has some strengths: the clear definition of the target population for the dietary intervention (i.e., patients with obesity only) increases the reliability of results; the exclusion of observational studies, with the inclusion of randomized trials only, rules out the effect of unaccounted confounders.

This meta-analysis shows that IF produces a similar weight loss, and is similarly tolerated, as control diets with continuous caloric restriction. In particular, IF does not appear to provide any additional weight loss in the longer term. Therefore, currently available evidence does not allow to formulate a preference for one or the other alternative. Further, longer-term trials, providing a more thorough reporting of potential detrimental effects, a wider assessment of psychological wellbeing and quality of life, and the exploration of further outcomes, such as major cardiovascular events, or the incidence of diabetes, would provide a more robust assessment of the clinical effects of IF in the treatment of obesity.

Funding and data transparency

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Potential conflicts of interest

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Compliance with ethical standards

This article does not contain any studies with human participants or animals performed by any of the authors.

Authors' contributions

GAS was involved in design, data collection, analysis and writing manuscript.

FR and **BC** were involved in design, data collection, and manuscript revision.

EM was involved in the design, analysis, writing manuscript.

FS and FB were involved in data collection, and manuscript revision.

The manuscript was drafted, revised, and approved by all the authors in accordance with ICJME standards for authorship. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Data availability statement

The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.numecd.2023.05.005.

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