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Is isocaloric intermittent fasting superior to calorie restriction? A systematic review and meta-analysis of RCTs

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ABSTRACT

Background and aim: Intermittent fasting (IF) has been demonstrated to enhance human health through several mechanisms. However, it is still unclear whether those health benefits are independent of caloric restriction (CR)-induced weight loss. This systematic review and meta-analysis aimed to compare isocaloric IF and CR regarding anthropometric measurements, adherence, metabolic profile, inflammatory biomarkers, and adipokines in adults and elderlies.

Methods and results: Comprehensive research was conducted usin four major databases including Embase, PubMed, Scopus, and Google Scholar without date restriction. Mean differences of the change from baseline ± change SD were calculated as the differences between IF and CR groups. Subgroup analysis was performed according to intervention duration (short-, medium-, and long-term). To determine the reliability of our findings, GRADE assessment was performed. As a result, 20 RCTs were included in this systematic review and meta-analysis. IF groups had significant reductions in fat mass (kg) ($P = 0.006$) and Interleukin-6 ($P < 0.00001$) in the short term and fat mass (%) ($P = 0.0002$), waist circumference ($P = 0.005$), fasting blood insulin ($P < 0.00001$) and HOMA-IR ($P = 0.04$) in the long term. CR groups had significantly lower hunger ($P = 0.003$), fatigue ($P = 0.04$), and TG ($P = 0.03$).

Conclusions: IF may be an effective alternative to CR but is not superior to CR in enhancing human health. Due to the low number of long-term studies, future studies should focus on conducting longitudinal randomized trials comparing IF and CR in different populations, age groups, and IF patterns.

1. Introduction

Intermittent fasting (IF) has gained significant attention in recent years owing to its potential health benefits, while caloric restriction (CR) is a well-established dieting regime. IF involves alternating periods of eating and fasting, while CR focuses on reducing overall daily calorie intake. Both approaches have been extensively studied in relation to their effects on metabolic health, aging, and disease prevention [1–3]. In the context of IF, various methods exist, such as the 16/8 method, which involves fasting for 16 h and eating within an 8-h window, or the 5:2 method, which entails eating normally for five days a week and restricting calorie intake on the remaining two days. On the other hand, CR typically involves reducing daily calorie intake by a certain percentage, often around 20–40 % of the usual consumption [4,5].

Research on IF and CR has shown promising results in terms of improving metabolic markers, reducing inflammation, and promoting weight loss. Furthermore, both approaches have been associated with potential benefits in cardiovascular health, insulin sensitivity, and longevity. In this systematic review, we endeavored to elucidate whether IF is superior to CR in terms of weight loss and various health biomarkers [6].

Although both interventions are effective weight-loss strategies, it

Abbreviations: IF, Intermittent Fasting; CR, Calorie Restriction; ADF, Alternate Day Fasting; TRE, Time Restricted Eating; BMI, Body Mass Index; BW, Body Weight; T2D, Type 2 Diabetes; FM, Fat Mass; LBM, Lean Body Mass; WC, Waist Circumference; HC, Hip Circumference; FBG, Fasting Blood Glucose; FBI, Fasting Blood Insulin; HOMA-IR, Homeostatic Assessment of Insulin Resistance; TG, Triglycerides; TC, Total Cholesterol; HDL, High Density Lipoprotien; CRP, C-Reactive Protein.

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has become clear that no single dietary approach produces weight-loss in the general population [7]. The best weight-loss approach is that to which an individual can adhere the most [8,9]. Although adherence measurements in these studies are challenging, several factors can influence individual adherence to a dietary strategy, including adverse events and appetite. Assuming that both strategies provide similar weight-loss and health benefits when calories are equated, the strategy will be determined by these factors.

The efficacy of IF and CR in anthropometric measurements and metabolic profiles has been compared in several systematic reviews and meta-analyses. Some studies have concluded that IF is superior to CR in reducing body mass index (BMI), body weight (BW), fat mass (FM), fasting blood glucose (FBG), and Homeostasis Model Assessment for Insulin Resistance (HOMA-IR) [10,11]. Pascual et al. conducted a study that is similar to ours in the general concept, regardless of minor differences in the methodology. The study reported comparable results among groups, with a higher efficacy on weight-loss in the ADF group [12]. However, one of the most important flaws of these studies was that they did not consider total caloric intake between the IF and CR groups, which is the core of weight-loss and metabolic changes. Although other studies did not find any significant difference, they still did not consider calories as a powerful influencing factor [13].

Furthermore, a study in mice investigated the effects of CR with and without IF. Although there were no differences in most parameters, significant improvements in glucose and insulin homeostasis were observed [14]. Recently, a systematic review of overweight and obese subjects, which was exclusive to the inclusion criteria for IF + CR versus CR, found no difference between the two strategies [15]. However, due to a lack of statistical analysis, it is still unclear whether IF produces additional health benefits through CR-independent mechanisms. Moreover, the level of adherence among individuals in these groups when the CR is equal has not yet been assessed. Therefore, the objective of our study was to evaluate the effectiveness of the intervention that combines an IF with CR versus CR alone on anthropometric measurements, adherence factors, metabolic profile, and inflammatory markers over a period of 3–12 months, while ensuring that both groups consumed an equal number of calories per week. To facilitate more robust conclusions, we plan to employ quantitative analysis techniques, such as meta-analysis.

2. Methods

We performed a meta-analysis based on the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [16]. The study protocol was registered in PROSPERO with ID: CRD42024522279.

2.1. Search strategy

A search of online databases including PubMed, Embase, Scopus, and Google Scholar was conducted up to the cut-off date of 12-2-2024 by two independent authors (A.F and Y.R). The search was repeated on 2-5-2024 to include recently published relative articles. We systematically searched the literature to identify randomized clinical trials that assessed the effect of IF + CR versus CR. We used these key words in our search (Fasting OR intermittent fasting OR intermittent calorie restriction OR intermittent energy restriction OR alternate-day fasting OR time-restricted feeding OR time-restricted eating OR 5:2 diet OR 12:8 diet OR 4:3 diet OR calories restriction AND body mass index OR BMI OR weight OR blood glucose OR blood insulin OR HbA1c OR blood pressure OR cholesterol OR triglyceride OR LDL OR VLDL OR HDL OR inflammation OR inflammatory marker OR pro-inflammatory OR anti-inflammatory OR cytokine OR ghrelin OR glucagon-like peptide OR glp OR leptin OR hunger OR fullness OR appetite OR adhere* OR quality of life OR compliance AND chronic disease OR overweight OR obese OR obesity OR normal weight OR cardiovascular disease OR CVD OR diabetes OR diabetic OR cancer OR healthy OR insulin resistant OR insulin resistance AND Isocaloric OR equal calories OR calorie equivalent OR equal energy).

2.2. Inclusion criteria

The eligibility criteria of this study were precisely determined to answer the following question: does IF provide sustainable health benefits independent of CR-induced weight-loss in adults and elderlies? In order to answer this question, the included trials had to be similar in all dietary factors but differ in eating windows. Therefore, intervention and control had to have an equal energy restriction percentage or equal amount of consumed calories weekly (Isocaloric) as illustrated simply in (Fig. 1).

The current meta-analysis followed the PICO (Population, Intervention, Outcomes) guidelines to ensure comprehensive and systemic inclusion and exclusion criteria (Supplementary Table 1). Briefly, the inclusion criteria involved selecting peer-reviewed, English-language, randomized clinical trials with a duration of 3–12 months, which included adult participants undergoing a weight loss strategy that combined IF and CR without emphasizing anthropometric measurements. All types of IF, such as alternative day fasting (ADF), time-restricted eating (TRE), and the 5:2 diet, combined with CR, were included in the study, provided that both the intervention and control groups follow an isocaloric diet during the study.

The exclusion criteria for this meta-analysis encompassed non-randomized clinical trials, as well as review articles, observational studies, and in vivo or in vitro studies. Non-peer-reviewed articles, articles published in foreign languages, and studies with a duration of less than 3 months were also excluded from the analysis. Additionally, studies involving participants who were not aiming for weight loss with IF, those younger than 18 years old, IF not combined with CR, and studies where there were considerable differences in the amount of CR between the intervention and control groups were excluded from this meta-analysis.

2.3. Data extraction

After the selection process of articles, with regard to the inclusion and exclusion criteria, the following information (first author's last name, publication year, study location, sample size, age, population BMI and health condition, intervention and amount of calorie restriction, control and amount of calorie restriction, intervention duration, and

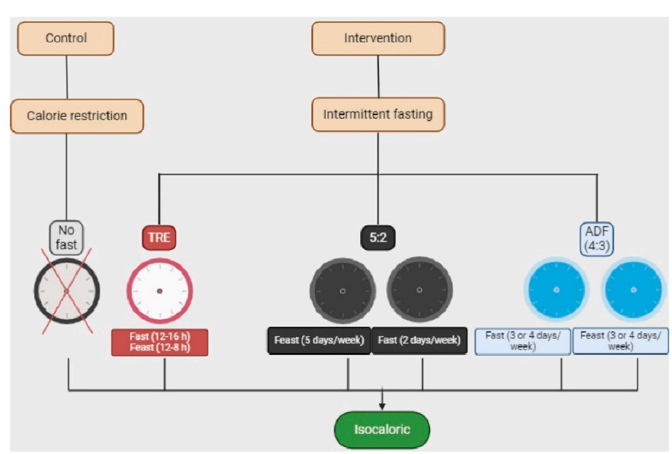

Fig. 1. This figure summarizes the different dietary patterns included in the study examining the evaluate the sustainable health benefits of intermittent fasting (IF) independent of calorie restriction (CR)-induced weight loss in adults and elderlies. The trials included had similar dietary factors but varied in eating windows.

method of energy intake measurement) were extracted by two independent authors (M.H and W.S) from the articles and listed in (Supplementary Table 2). Adherence-related information was collected and reported in (Supplementary Table 3).

2.4. Quality assessment

Quality assessment was performed by two independent authors (M.H and W.S), any disagreement between the authors was solved by third author (Y.R). The quality of the included studies was evaluated using the Cochrane Collaboration tool. This tool includes the following key parts: random sequence generation, allocation concealment, blinding, incomplete outcome data, and selective reporting. Each item was categorized as having low, unclear, or high risk of bias. Accordingly, studies with more than two items of low risk were categorized as studies with good quality, studies with two items of low risk were considered studies with fair quality, and those with fewer than two items were considered studies with low risk of bias [17].

2.5. Certainty of evidence

The strength of the overall body of evidence was assessed for primary outcomes including BW, BMI, FM (kg), LBM (kg), adherence, adverse events, and hunger, and secondary outcomes including FBG, FBI, HOMA-IR, TG, TC, HDL, and LDL using Grading of Recommendations Assessment, Development, and Evaluation (Grade) methodology [18].

2.6. Statistical analysis

The present meta-analysis was performed using the Cochrane Program Review Manager Version 5.4. Variables assessed in three or more studies were included. In this regard, net changes in the mean $\pm$ SD of BW, BMI, FM (kg), FM (%), lean body mass (kg) (LBM), waist circumstance (WC), hip circumstance (HC), hunger, dropouts, adverse events, (FBG), fasting blood insulin (FBI), hemoglobin A1c (Hba1c) (%), HOMA-IR, triglyceride (TG), total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), C-reactive protein (CRP), leptin, adiponectin, and insulin-like growth factor-1 (IGF-1) were assessed. Adherence outcome was not able to be included in the meta-analysis. Alternatively, relative information was reported narratively in (Supplementary Table 3). If adherence was measured in the original article, we reported the adherence results according to the study adherence successful criteria. Dropouts of the studies were reported as another adherence indirect indicator. Funnel plots were performed to assess publication bias in variables that were assessed in 10 studies at least [19].

Subgroup analysis was performed in all variables based on the duration of the intervention, which included baseline to 3 months, baseline to 4–6 months, and baseline to 10–12 months. Sensitivity analysis was performed by keeping one type of IF in each time (e.g. TRE, ADF, or 5:2).

In any case, reporting the standard error of the mean (SEM), standard deviation (SD) was calculated using the following formula: SD $=$ SEM $\times$ sqrt (n), where n refers to the number of participants. If change of SD was not given, SDs of mean differences were calculated by using SD $=$ square root [(SD pre-treatment)2 $+$(SD posttreatment)2 – (2R $\times$ SD pre-treatment $\times$ SD post-treatment)], where the correlation coefficient (R) was assumed to be 0.9 [20]. If the upper and lower limits were given with the mean, the SD was calculated using this formula: $SD = \sqrt{n} \times (\textit{upper limit} - \textit{lower limit})/3.92$. If the median with upper and lower limits was given, the estimation was based on the method described here [21]. In order to apply mean difference in forest plots, units were converted into one measurement by using appropriate equations, when applicable. The random-effects model was applied for pooling analysis to compensate for the heterogeneity of the studies [22,23]. Interstudy heterogeneity was explored quantitatively using Cochran's Q and I^2 statistics. $I^2 \leq 50$ % and $\geq$75 % indicated substantial and considerable heterogeneity, respectively [20]. P-values were considered statistically significant at $<$ 0.05.

3. Results

3.1. Literature selection

A total of 1532 citations were obtained from the initial search (Supplementary Fig. 1). All randomized controlled studies comparing isocaloric IF and CR were included in this research. 812 articles remained after excluding duplicates. 769 articles were excluded by the title or abstract. 43 articles were eligible for inclusion in the systematic review and meta-analysis. Of the 43 studies of interest, 23 were excluded for different reasons (Supplementary Fig. 1). The remaining 20 studies were included in the qualitative and quantitative analysis. Characteristics of the included studies are provided in (Supplementary Table 2).

3.2. Studies' characteristics

A total of 20 studies were included in this systematic review and meta-analysis [24–43]. These studies included a total of (1785) participants with an age range of 18–75. The type of fasting varied among the studies, the 5:2 diet was in 9 of them [27,29,30,33,37,39,42], ADF was in 4 of them [25,32,36,38], and TRE was in 7 of them [24,26,28,31,34,35,43]. The fasting period in TRE studies varied between 12 and 16 h. Studies were conducted in various locations, 6 studies in Australia [27,30,37,38,40,41], 2 studies in UK [39,42], 3 studies in Norway [25,29,36], 1 study in Germany [33], 3 studies in USA [31,32,43], 1 study in Brazil [35], 2 studies in China [24,34], 1 study in England [31], and 1 study in Turkey [26]. The duration of trials' interventions ranged from 3 months to 1 year without follow-up periods. Data of follow-ups aiming at weight loss, but not weight maintenance, was included in the study. Four studies included participants with BMI lower than 24.9 [37,39,41,42]. All the studies included participants who were overweight and obese. Two studies included patients with type 2 diabetes (T2D) [30,43], one study was on women with gestational diabetes [40], one study was on patients with non-alcoholic fatty liver disease [34], one study was on patients with metabolic syndrome [26], and two studies included patients at risk of T2D [38,43]. Four studies were exclusive to women [35,39,40,42]. BW was assessed in 16 studies [24–31,33–35,37,39,40,42,43], BMI was assessed in 9 studies [24,26,27,29,30,34,35,37,40], FM (kg) was assessed in 11 studies [24–28,30,31,34,37,39,42], FM (%) was assessed in 7 studies [24–26,34,35,37,42], LBM (kg) was assessed in 11 studies [24–28,30,31,34,37,39,42], WC was assessed in 9 studies [24,29,31,33–35,39,42,43], HC was assessed in 3 studies [29,39,42], FBG was assessed in 14 studies [24,26,27,29,31,33,34,36,38–43], FBI was assessed in 9 studies [26,31,33,38–43], Hba1c (%) was reported in 7 studies [26,29–31,34,38,40], HOMA-IR was assessed in 10 studies [24,26,31,34,36,39–43], TG, TC, and HDL were assessed in 13 studies [24,26,27,29,31,33,34,36,38,39,41–43], CRP was assessed in 5 studies [29,33,38,41,42], leptin was assessed in 4 studies [33,36,39,42], adiponectin was assessed in 3 studies [36,39,42], IGF-1 was assessed in 3 studies [33,39,42], adherence was reported in 6 studies [24,28,31,34,39,42], hunger was assessed in 4 studies [28,29,39,41], and adverse events were reported in 5 studies [24,29,34,38,39].

3.3. Risk of bias assessment

Risk of bias assessment was performed in all the included studies. The assessment revealed that none of the studies were at low risk of bias (high quality), 10 of the studies were at moderate risk of bias (moderate quality), and 11 of the studies were at high risk of bias (low quality). The detailed results of each item are presented in (Supplementary Fig. 2). Risk of bias summary is shown in (Supplementary Fig. 3).

3.4. Effect of IF + CR vs CR on anthropometric measurements

In the period of baseline to 3 months, no significant differences were observed in BW, BMI, LBM, FM (%), WC, and HC between the two groups, as shown in (Figs. 2–5). The intervention group experienced a significant reduction in FM (kg) (MD = −0.96 kg, 95 % CI: −1.65, −0.27, P = 0.006), as shown in (Fig. 4). However, the impact of IF + CR vs CR on anthropometric measurements in the period of baseline to 4–6 months revealed no significant differences in any variable between the intervention and control groups, as illustrated in the baseline to 4–6 months analysis. Lastly, in the period of baseline to 10–12 months, a significant reduction in FM (%) (MD = −1.51 %, 95 % CI: −2.29, −0.73, P = 0.0002) and WC (MD = −1.96 cm, 95 % CI: −3.34, −0.59, P = 0.005) was observed in the intervention group, while the results of BW, BMI, LBM WC and HC were not significant between the two groups.

3.5. Effect of IF + CR vs CR on adherence, hunger, adverse events, and dropouts

Seven studies were analyzed, with two following the 5:2 diet, three following the 16:8 TRE regimen, and two following the 14:10 TRE regimen. Adherence rates were higher in the 5:2 diet group at 3 and 6 months than in the control group. Meanwhile, participants following 16:8 TRE had higher adherence rates at 3, 6, and 12 months. In contrast, the 14:10 TRE group had lower adherence rates than did the control group (Supplementary Table 3). Regarding hunger levels, four studies used the visual analogue scale (VAS). The results indicated that hunger levels were significantly lower in the CR group (standardized mean difference [SMD] = −0.37, 95 % confidence interval [CI]: 0.12, 0.62, P = 0.003). Quality-of-life was assessed by recording the occurrence of side effects reported by the participants. There was a significant reduction in fatigue (odds ratio [OR] = 1.79, 95 % CI: 1.03, 3.09, P = 0.04) and total events of side effects in the control group compared to the intervention group (OR = 1.51, 95 % CI: 1.14, 2, P = 0.004) as shown in (Supplementary Fig. 4). Finally, there was no significant difference in the number of dropouts at any time point (Supplementary Fig. 5).

3.6. Effect of IF + CR vs CR on metabolic profile

Over the period of baseline to 3 months, no differences were observed in any variables, including FBG, FBI, HOMA-IR, Hba1c, TG, TC, LDL, and HDL, as depicted in (Supplementary Figs. 6–9). In the period of baseline to 4–6 months, the intervention group exhibited a significant reduction in FBI (mean difference [MD] = −0.83 μIU/mL, 95 % confidence interval [CI]: −1.59, −0.07, P = 0.03), as shown in (Supplementary Fig. 6), but no other differences were observed between the groups. Over the period of baseline to 10–12 months, both FBI and HOMA-IR demonstrated significant reductions in the intervention group (MD = −1.07 μIU/mL, 95 % CI: −1.48, −0.66, P < 0.00001) and (MD = −0.57, 95 % CI: −1.10, −0.03, P = 0.04) (Supplementary Figs. 6 and 7), respectively. In contrast, TG were significantly lower in the CR group

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
1.1.1 Baseline to 3 months								
Coutinho et al., 2018	-13.9	5.94	14	-11.8	5.7	14	0.8%	-2.10 [-6.41, 2.21]
Gray et al., 2021	-4.2	2.26	32	-3.8	2.49	30	11.1%	-0.40 [-1.59, 0.79]
Harvie et al., 2010	-4.1	6	42	-3	7.9	47	1.9%	-1.10 [-4.00, 1.80]
Harvie et al., 2013	-5	6.29	37	-3.7	7.4	40	1.7%	-1.30 [-4.36, 1.76]
Jamshed et al., 2022	-6.3	3.66	45	-4	3.66	45	6.8%	-2.30 [-3.81, -0.79]
Keenan et al., 2022 (F)	-2.4	3.05	8	-2	3.12	9	1.8%	-0.40 [-3.34, 2.54]
Keenan et al., 2022 (M)	-4.7	2.53	9	-6.3	1.67	8	3.8%	1.60 [-0.42, 3.62]
Kunduracı & Özbek, 2020	-8.27	4.58	32	-5.8	3.73	33	3.8%	-2.47 [-4.50, -0.44]
Maruthur et al., 2024	-2.3	2.08	21	-2.6	1.7	20	11.6%	0.30 [-0.86, 1.46]
Schübel et al., 2018	-6.2	7	49	-5.2	6.84	49	2.1%	-1.00 [-3.74, 1.74]
Sundfør et al., 2018	-7.1	3.7	54	-7.4	3.8	58	8.1%	0.30 [-1.09, 1.69]
Thomas et al., 2022	-4.4	2.6	24	-3.6	3.3	23	5.4%	-0.80 [-2.50, 0.90]
Subtotal (95% CI)			**367**			**376**	**58.9%**	**-0.52 [-1.03, -0.00]**
Heterogeneity: Chi² = 17.54, df = 11 (P = 0.09); I² = 37%								
Test for overall effect: Z = 1.97 (P = 0.05)								
1.1.2 Baseline to 4 - 6 months								
Harvie et al., 2010	-5.7	6.14	42	-4.5	7.87	47	1.8%	-1.20 [-4.12, 1.72]
Liu et al., 2022	-9.4	5.61	69	-8.9	5.61	70	4.5%	-0.50 [-2.37, 1.37]
Sundfør et al., 2018	-9.1	5	54	-9.4	5.3	58	4.3%	0.30 [-1.61, 2.21]
Wei et al., 2023	-9.8	6.32	45	-9.7	6	43	2.4%	-0.10 [-2.67, 2.47]
Subtotal (95% CI)			**210**			**218**	**13.0%**	**-0.26 [-1.36, 0.84]**
Heterogeneity: Chi² = 0.81, df = 3 (P = 0.85); I² = 0%								
Test for overall effect: Z = 0.47 (P = 0.64)								
1.1.3 Baseline to 10 - 12 months								
Carter et al., 2018	-6.8	6.69	70	-5	6.54	67	3.2%	-1.80 [-4.02, 0.42]
De Oliveira Maranhão Pureza et al., 2021	-0.58	6.45	31	-0.52	4.59	27	1.9%	-0.06 [-2.92, 2.80]
Gray et al., 2021	-4.7	2.23	32	-6.3	2.47	30	11.3%	1.60 [0.43, 2.77]
Headland et al., 2018	-5	4.9	49	-6.6	6.1	53	3.4%	1.60 [-0.54, 3.74]
Liu et al., 2022	-8	6.19	69	-6.3	6	70	3.8%	-1.70 [-3.73, 0.33]
Thomas et al., 2022	-4.9	5.3	30	-4.3	5.3	30	2.2%	-0.60 [-3.28, 2.08]
Wei et al., 2023	-8.4	6.49	45	-7.8	6.17	43	2.2%	-0.60 [-3.25, 2.05]
Subtotal (95% CI)			**326**			**320**	**28.1%**	**0.31 [-0.44, 1.05]**
Heterogeneity: Chi² = 14.26, df = 6 (P = 0.03); I² = 58%								
Test for overall effect: Z = 0.81 (P = 0.42)								
Total (95% CI)			**903**			**914**	**100.0%**	**-0.25 [-0.65, 0.14]**
Heterogeneity: Chi² = 35.79, df = 22 (P = 0.03); I² = 39%								
Test for overall effect: Z = 1.25 (P = 0.21)								
Test for subgroup differences: Chi² = 3.19, df = 2 (P = 0.20), I² = 37.3%								

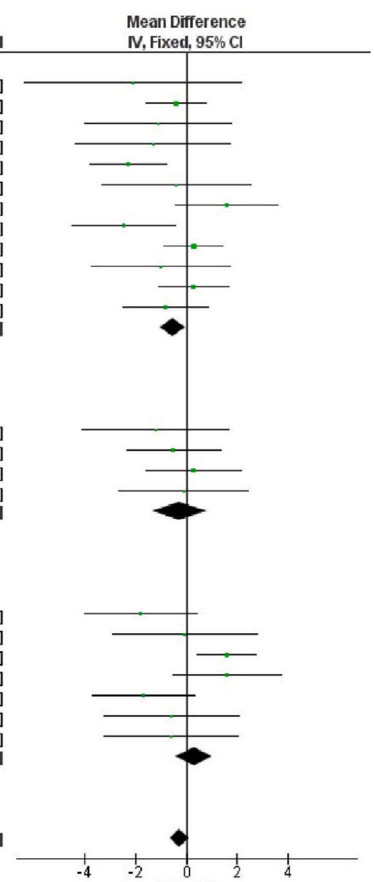

Fig. 2. Meta-analysis of change-from-baseline weight (kg). The forest plot shows effect estimates (green blocks) and 95 % confidence intervals (horizontal lines) for each RCT. Larger green blocks indicate a larger weight has been assigned to that RCT. Left of the 0 line shows a finding in favor of intermittent fasting (IF) interventions, whereas right of the 0 line shows a finding in favor of continuous energy restriction (CER) interventions. The diamond at the base of the plot demonstrates the pooled effect estimates and confidence intervals from RCTs included in the meta-analysis. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

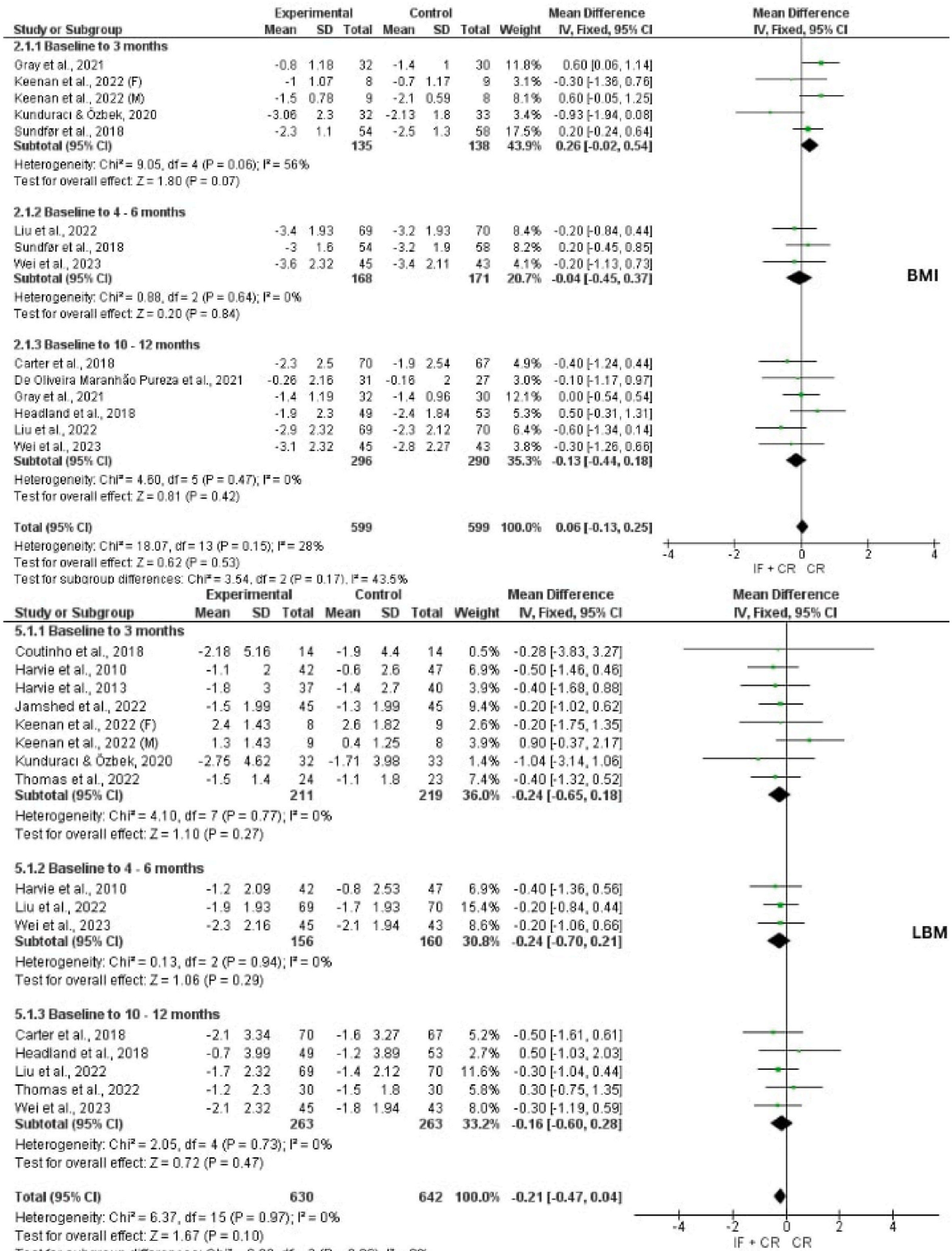

Fig. 3. Meta-analysis of change-from-baseline BMI and LBM (kg). The forest plot shows effect estimates (green blocks) and 95 % confidence intervals (horizontal lines) for each RCT. Larger green blocks indicate a larger weight has been assigned to that RCT. Left of the 0 line shows a finding in favor of intermittent fasting (IF) interventions, whereas right of the 0 line shows a finding in favor of continuous energy restriction (CER) interventions. The diamond at the base of the plot demonstrates the pooled effect estimates and confidence intervals from RCTs included in the meta-analysis. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

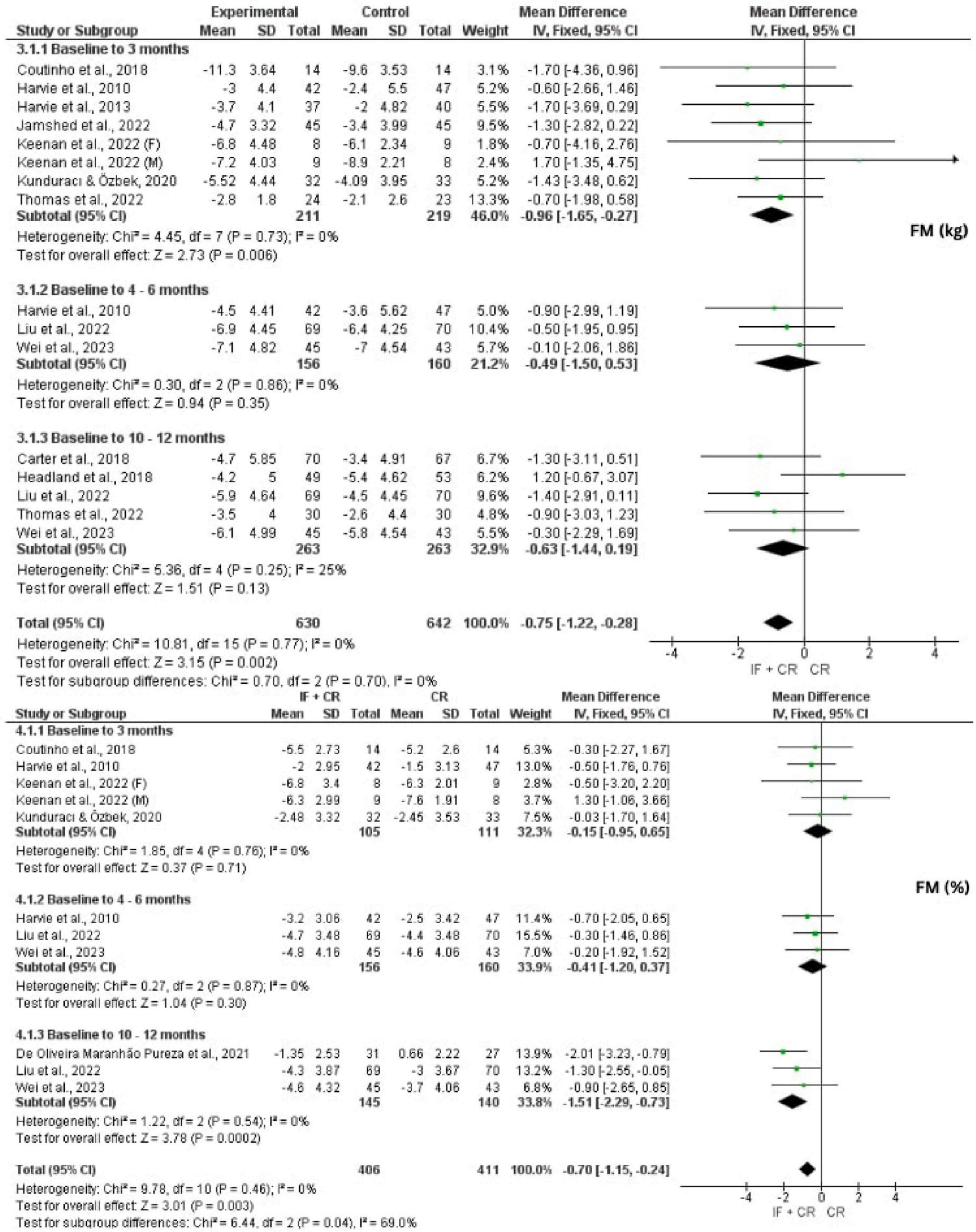

Fig. 4. Meta-analysis of change-from-baseline FM (kg) and FM (%). The forest plot shows effect estimates (green blocks) and 95 % confidence intervals (horizontal lines) for each RCT. Larger green blocks indicate a larger weight has been assigned to that RCT. Left of the 0 line shows a finding in favor of intermittent fasting (IF) interventions, whereas right of the 0 line shows a finding in favor of continuous energy restriction (CER) interventions. The diamond at the base of the plot demonstrates the pooled effect estimates and confidence intervals from RCTs included in the meta-analysis. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

than in the IF group (MD = 0.10 mmol/L, 95 % CI: 0.01, 0.19, P = 0.03) (Supplementary Fig. 8).

3.7. *Effect of IF and CR on inflammatory markers*

Over the period of baseline to 3 months, IF combined with CR demonstrated a statistically significant decrease in serum levels of interleukin-6 (IL-6) (MD) = −0.13 pg/ml, 95 % confidence interval (CI):

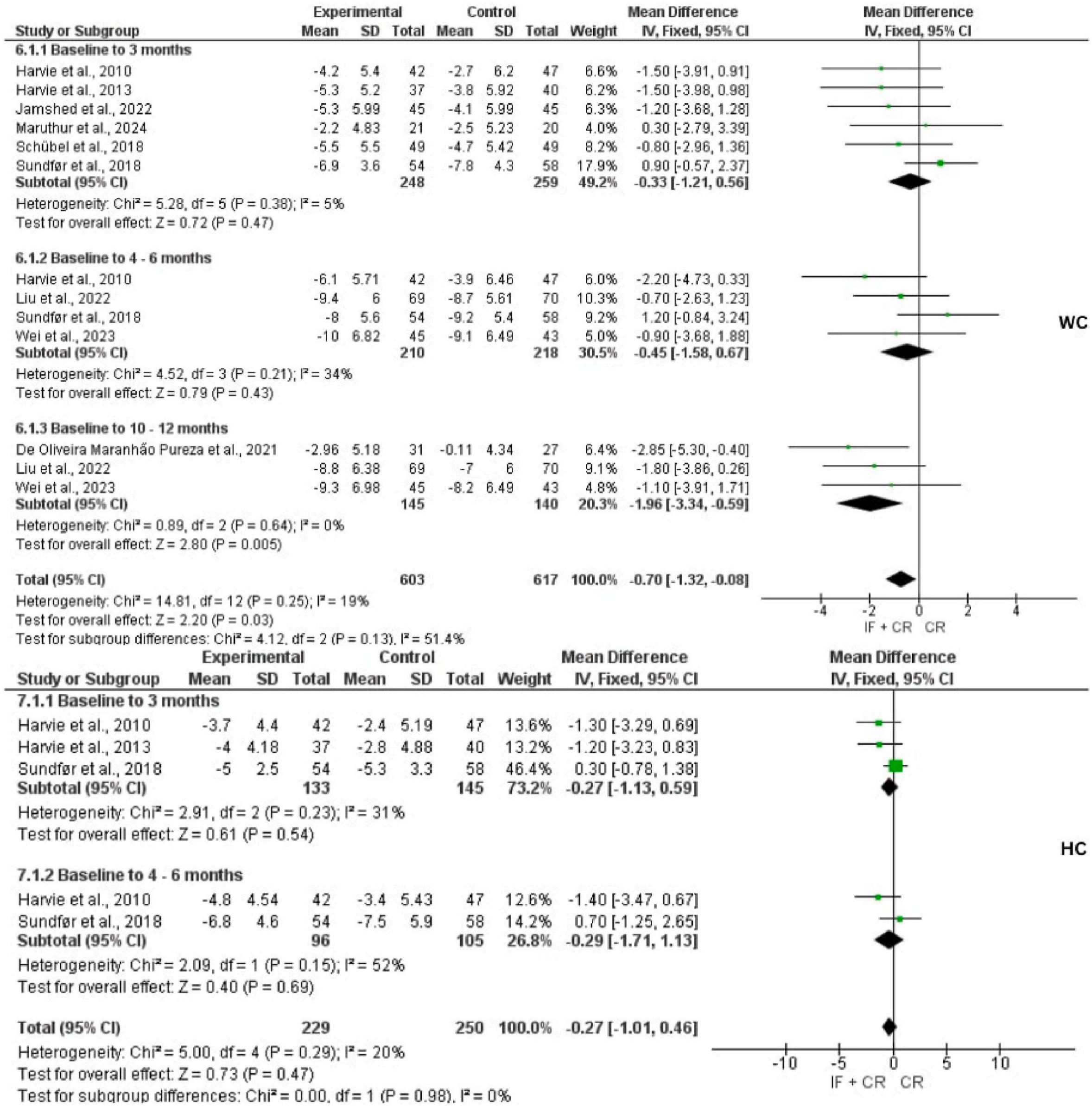

Fig. 5. Meta-analysis of change-from-baseline WC and HC. The forest plot shows effect estimates (green blocks) and 95 % confidence intervals (horizontal lines) for each RCT. Larger green blocks indicate a larger weight has been assigned to that RCT. Left of the 0 line shows a finding in favor of intermittent fasting (IF) interventions, whereas right of the 0 line shows a finding in favor of continuous energy restriction (CER) interventions. The diamond at the base of the plot demonstrates the pooled effect estimates and confidence intervals from RCTs included in the meta-analysis.

−0.19, −0.08, P < 0.00001) (Supplementary Fig. 10). However, in the period of baseline to 4–6 months, no significant difference was observed in IL-6 and CRP levels between the two groups. Regarding the effect of IF + CR versus CR on leptin, adiponectin, and IGF-1 levels, studies revealed no discernible difference between the groups (MD = −0.44 ng/ml, 95 % CI: −1.49, 0.61, P = 0.41), (MD = 0.33 μg/ml, 95 % CI: −0.31, 0.98, P = 0.31), and (MD = −5.29 μg/L, 95 % CI: −13.34, 2.75, P = 0.20) respectively (Supplementary Fig. 11).

3.8. Sensitivity analysis

Sensitivity analysis was conducted based on various patterns of IF. Across the ADF and 5:2 IF pattern, the direction of the effect was consistent. However, some variations were observed in TRE. In the period of baseline to 3 months intervention, four studies were included for BW, demonstrating an average decrease of −0.94 kg (95 % CI: −1.69, −0.18, P = 0.001). Additionally, three studies were included for FM (kg), showing an average decrease of −1.04 kg (95 % CI: −1.92, −0.16, P = 0.02). In the period of baseline to 4–6 months intervention, three studies were included for FBG, revealing an average decrease of −2.35 mg/dl (95 % CI: −4.31, −0.40, P = 0.02). Lastly, in the period of baseline to 10–12 months intervention, two studies were included for FM (%) and WC, demonstrating an average decrease of −1.66 % (95 % CI: −2.54, −0.79, P = 0.0002) and −2.23 cm (95 % CI: −3.81, −0.66, P = 0.005), respectively.

3.9. Certainty of the evidence

The GRADE approach was employed to assess the certainty of evidence for the primary outcomes, as presented in (Supplementary Table 4). The results demonstrated that the evidence for BW, BMI, FM (kg), and LBM (kg) was moderate, indicating that further research is likely to have a significant impact on our confidence in the estimate of effect and may alter the estimate. The certainty of the evidence for adherence was very low, indicating that any estimate of effect is highly uncertain. The certainty for adverse events was low, suggesting that further research is very likely to have a significant impact on our confidence in the estimate of effect and is likely to change the estimate. The certainty for hunger was moderate, indicating that further research is likely to have a significant impact on our confidence in the estimate of effect and may change the estimate. The certainty of the evidence for secondary outcomes, as presented in (Supplementary Table 5), was also evaluated. The results showed low certainty for FBG and FBI, very low certainty for Hba1c, and moderate certainty for TG, TC, HDL, and LDL.

3.10. Publication bias

We ran funnel plots, Begg's tests and Egger's tests. No publication bias was found in our research (Supplementary Figs. 12–19).

4. Discussion

To the best of our knowledge, this meta-analysis is the first to compare the effects of IF and CR in the isocaloric state. Our findings suggest that there is no evidence to support the superiority of IF over CR in enhancing human health, either in the short- or long-term. However, there are some exceptions, such as the reduction in FM (kg) in the period of baseline to 3 months and the reduction in FM (%) and WC in the period of baseline to 10–12 months. Our results do not align with systematic reviews and meta-analyses that have compared IF with a regular diet or no intervention [44–49], but they do align with some studies that have compared IF with CR [50–55]. Most previous meta-analyses that compared IF and CR did not divide the intervention into time periods, which could have influenced the results [44–53,55]. A study conducted by Silverii [54] on obese subjects at different time points found no significant effect of IF compared with CR on BW and BMI. Sensitivity analysis showed that TRE was more effective than CR in reducing BW and FM (kg). Our study aligns with a recent meta-analysis that concluded that subjects with TRE achieved higher reductions in anthropometric measurements, especially when participants were assigned *ad libitum* rather than prescribed energy intake [55]. In contrast, under an isocaloric state, in the 5:2 IF pattern, participants overcompensated on non-fasting days, leading to higher energy consumption [56]. Notably, none of the previous meta-analyses matched the CR intervention and control groups.

4.1. Primary outcomes

Our findings indicate that the combination of IF and CR was more effective in reducing visceral FM in the period of baseline to 3 months by 0.96 kg and in the period of baseline to 10–12 months by 1.51 % and WC by 1.96 cm. However, there were no significant differences in the other anthropometric measurements at any time point. Although IF showed a significant reduction in FM at 3 months, this effect diminished over time, suggesting that both interventions had similar long-term effects. The significant reduction in FM, but not in other anthropometric measurements, such as BW, BMI, and lean body mass (LBM), is primarily due to the small number of studies that assessed FM. Additionally, despite the absence of significant changes in BW and BMI, there was a trend towards BW reduction in the intervention group ($P = 0.05$) and BMI reduction in the control group ($P = 0.07$), which was also due to the difference in the number of studies. It is worth noting that the self-reported caloric intake in the included studies showed that participants in the IF group consumed slightly fewer calories than those in the CR group [24,29,31–33,38]. A possible explanation for this is expectation bias, as mentioned previously [53]. One of the challenges of these studies is the inability to blind the participants to the intervention. Despite the presence of a control group (CR), the population tends to anticipate more promising results from the intervention group (IF) than CR, potentially increasing adherence in completers (e.g., lower caloric intake) [57]. Furthermore, our study aimed to directly and indirectly compare the adherence levels in these studies in an isocaloric state. A direct comparison was done narratively due to intervention differences, and the successful adherence criteria of the studies were considered. No significant differences were found between studies. However, factors that affect adherence such as hunger rate, VAS revealed that individuals in the IF group felt hungrier compared to those in the CR group. Conversely, Elsworth et al., who assessed hunger among the interventions, found no significant differences between groups. The main difference in our results could be attributed to the higher number of studies included in the comparison [53]. Dropouts and adverse events were similar in both groups, except for fatigue, which was lower in the CR group. These data suggest that adherence to both dietary interventions is comparable.

4.2. Secondary outcomes

Furthermore, we did not detect any variation in FBG, Hba1c, and HOMA-IR at any point in time. FBI diminished during the 4–6 month and 10 - 12-month periods. The certainty of the evidence for these outcomes was moderate to low. This is mainly because the studies included diverse health conditions of participants, some of whom were diabetic [30,43], at risk of developing diabetes [26,38,40,43], and were athletic [37]. All of these factors can significantly affect glucose and insulin homeostasis [58]. Consequently, the indirectness domain is considered serious. Population health status and type of comparison are critical factors for blood glucose-related outcomes. For instance, a study revealed improvements in glucose metabolism in patients with metabolic syndrome when compared with pre-intervention [59]. Similarly, patients with non-alcoholic fatty liver disease showed better glucose metabolism than those without [45]. It is likely that these effects were caused by CR-induced weight loss rather than the IF itself. This notion is supported by a recent meta-analysis that found no effect of IF on glycemic control in patients with T2D when compared with CR [60]. Additionally, another recent network meta-analysis discovered that IF is as effective as CR, and both are superior to conventional diets in patients with T2D [61]. Therefore, IF could be an alternative approach to limit the total caloric intake of those who struggle to adhere to a regular CR diet. However, our results, which align with those of other studies, do not display superior results from IF compared to CR regarding glucose homeostasis. Furthermore, it was observed that TG levels were lower in the CR group at the 10-12-month mark, but no other differences were noted in the lipid profile, CRP, and adipokines such as leptin, adiponectin, resistin, or IGF-1. Additionally, IL-6 levels were significantly reduced. However, data from one study were significantly skewed, accounting for 96 % of the weight of the effect [36,39]. As a result, future studies are critical in determining the efficacy of IF on inflammation. In contrast, a study by Wang found that IF was effective in reducing CRP, but not IL-6 or tumor necrosis factor-alpha, in overweight and obese subjects [62]. A recent review of human trials also demonstrated that IF has minimal or no effect on inflammatory markers. CRP levels were reduced when 6 % weight loss was achieved in overweight and obese patients [63].

4.3. Strengths, limitations, and future implications

This systematic review and meta-analysis is notable for its strict eligibility criteria, which ensured that isocaloric intervention and control groups were included. Additionally, it provides a comprehensive analysis of different intervention durations, ranging from 3 to 12 months, including a substantial number of studies ($n = 20$). The research was conducted across four databases (PubMed, Scopus, Embase, and Google Scholar) as well as additional resources obtained through a review of previously published systematic reviews. The precision of the results was enhanced by calculating the change in the mean and SD (baseline value – certain time-point value) for all collected data. Furthermore, a grade assessment was performed on primary and secondary outcomes to evaluate the certainty of evidence. Despite these strengths, this study had significant limitations that undermined the reliability of the evidence. For instance, the variability in the assessment of anthropometric outcomes in the included studies was inconsistent. BMI, LBM, FM, WC, HC, and BW, all of which were classified under the same category, were not adequately measured.

Of the 20 studies examined, 11 measured BW in the period of baseline to 3 months analysis, while only four measured BMI. This inconsistency in reporting has led to disparate results. For instance, scientific evidence suggests that BW reduction should be accompanied by a reduction in BMI, but this was not observed in this study because of the limited number of studies reporting BMI. However, we did not find any evidence of publication bias for any of the variables assessed in this study. In addition, the age range of participants was between 18 and 75 and health conditions varied among them. Despite this, future research should focus on conducting longitudinal randomized trials examining the impact of IF on adherence, hunger, inflammation, and anthropometric measurements in different populations, age groups, and IF patterns due to the lack of knowledge about the long-term effects of IF on these variables. Additionally, the domain of risk of bias in GRADE was assessed as serious, which lowered the certainty of the results by one degree. In conclusion, IF combined with CR is an effective approach for achieving health benefits such as weight loss but does not provide additional health benefits beyond those achieved by CR. Stricter RCTs are necessary to draw stronger conclusions.

Authors' contributions

M.H. carried out the concept, design, and drafting of this study. Y.R. and A.F. searched databases, and screened articles. M.H. and W.S. performed the acquisition, data extraction, analysis, and interpretation of data. Y.R. and A.F. critically revised the manuscript. All authors approved the final version of the manuscript.

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Declaration of competing interest

The author(s) have declared the absence of any potential conflicts of interest concerning the research, authorship, and/or publication of this article.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.numecd.2024.103805.

References

[1] Hofer SJ, Carmona-Gutierrez D, Mueller MI, Madeo F. The ups and downs of caloric restriction and fasting: from molecular effects to clinical application. EMBO Mol Med 2021 Nov 15;14(1). https://doi.org/10.15252/emmm.202114418.

[2] Brandhorst S, Longo VD. Fasting and caloric restriction in cancer prevention and treatment. Recent Results Cancer Res 2016:241–66. https://doi.org/10.1007/978-3-319-42118-6_12.

[3] Anton S, Leeuwenburgh C. Fasting or caloric restriction for healthy aging. Exp Gerontol 2013 Oct;48(10):1003–5. https://doi.org/10.1016/j.exger.2013.04.011.

[4] Tang D, Tang Q, Huang W, Zhang Y, Tian Y, Fu X. Fasting: from physiology to pathology. Adv Sci 2023 Feb 3;10(9). https://doi.org/10.1002/advs.202204487.

[5] Janaswamy R, Yelne P. A narrative review on intermittent fasting as an approachable measure for weight reduction and obesity management. Cureus 2022 Oct 17. https://doi.org/10.7759/cureus.30372.

[6] Song D-K, Kim Y-W. Beneficial effects of intermittent fasting: a narrative review. Journal of Yeungnam Medical Science 2023 Jan 31;40(1):4–11. https://doi.org/10.12701/jyms.2022.00010.

[7] MacLean PS, Wing RR, Davidson T, Epstein L, Goodpaster B, Hall KD, et al. NIH Working Group Report: innovative research to improve maintenance of weight loss. Obesity 2014 Dec 2;23(1):7–15. https://doi.org/10.1002/oby.20967.

[8] Johnston BC, Kanters S, Bandayrel K, Wu P, Naji F, Siemieniuk RA, et al. Comparison of weight loss among named diet programs in overweight and obese adults. JAMA 2014 Sept 3;312(9):923. https://doi.org/10.1001/jama.2014.10397.

[9] Dansinger ML, Gleason JA, Griffith JL, Selker HP, Schaefer EJ. Comparison of the atkins, ornish, Weight Watchers, and zone diets for weight loss and heart disease risk reduction: a randomized trial. ACC Curr J Rev 2005 Apr;14(4):19. https://doi.org/10.1016/j.accreview.2005.02.079.

[10] Zhang Q, Zhang C, Wang H, Ma Z, Liu D, Guan X, et al. Intermittent fasting versus continuous calorie restriction: which is better for weight loss? Nutrients 2022 Apr 24;14(9):1781. https://doi.org/10.3390/nu14091781.

[11] Cho Y, Hong N, Kim K, Cho S, Lee M, Lee Y, et al. The effectiveness of intermittent fasting to reduce body mass index and glucose metabolism: a systematic review and meta-analysis. J Clin Med 2019 Oct 9;8(10):1645. https://doi.org/10.3390/jcm8101645.

[12] Elortegui Pascual P, Rolands MR, Eldridge AL, Kassis A, Mainardi F, Lê K, et al. A meta-analysis comparing the effectiveness of alternate day fasting, the 5:2 diet, and time-restricted eating for weight loss. Obesity 2022 Nov 8;31(S1):9–21. https://doi.org/10.1002/oby.23568.

[13] Gu L, Fu R, Hong J, Ni H, Yu K, Lou H. Effects of intermittent fasting in human compared to a non-intervention diet and caloric Restriction: a Meta-Analysis of Randomized Controlled Trials. Front Nutr 2022;9. These 3389/fnut.2022.871682.

[14] Kim YH, Lee JH, Yeung JL-H, Das E, Kim RY, Jiang Y, et al. Thermogenesis-independent metabolic benefits conferred by isocaloric intermittent fasting in OB/Ob Mice. Sci Rep 2019 Feb 21;9(1). https://doi.org/10.1038/s41598-019-39380-2.

[15] Ezzati A, Rosenkranz SK, Phelan J, Logan C. The effects of isocaloric intermittent fasting vs daily caloric restriction on weight loss and metabolic risk factors for noncommunicable chronic diseases: a systematic review of randomized controlled or comparative trials. J Acad Nutr Diet 2023 Feb;123(2). https://doi.org/10.1016/j.jand.2022.09.013.

[16] Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the Prisma statement. PLoS Med 2009 Jul 21;6(7). https://doi.org/10.1371/journal.pmed.1000097.

[17] Higgins JP, Altman DG, Gotzsche PC, Juni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomized trials. BMJ 2011 Oct 18;343(oct18 2):d5928. https://doi.org/10.1136/bmj.d5928. d5928.

[18] Guyatt G, Oxman AD, Akl EA, Kunz R, Vist G, Brozek J, et al. Grade guidelines: 1. introduction—grade evidence profiles and summary of findings tables. J Clin Epidemiol 2011 Apr;64(4):383. https://doi.org/10.1016/j.jclinepi.2010.04.026. 94.

[19] Van Aert RC, Wicherts JM, van Assen MA. Publication bias examined in meta-analyses from psychology and medicine: a Meta-meta-analysis. PLoS One 2019 Apr 12;14(4). https://doi.org/10.1371/journal.pone.0215052.

[20] Higgins JPT, Green S, editors. Cochrane handbook for systematic reviews of interventions. The Cochrane Collaboration; 2011 [updated March 2011], Version 5.1.0. www.handbook.cochrane.org.

[21] Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. BMC Med Res Methodol 2005 Apr 20;5(1). https://doi.org/10.1186/1471-2288-5-13.

[22] DerSimonian R, Laird N. Meta-analysis in clinical trials. Contr Clin Trials 1986 Sept;7(3):177–88. https://doi.org/10.1016/0197-2456(86)90046-2.

[23] Higgins JP, Altman DG, Gotzsche PC, Juni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011 Oct 18;343(oct18 2):d5928. https://doi.org/10.1136/bmj.d5928. d5928.

[24] Liu D, Huang Y, Huang C, Yang S, Wei X, Zhang P, et al. Calorie restriction with or without time-restricted eating in weight loss. N Engl J Med 2022 Apr 21;386(16): 1495–504. https://doi.org/10.1056/nejmoa2114833.

[25] Coutinho SR, Halset EH, Gåsbakk S, Rehfeld JF, Kulseng B, Truby H, et al. Compensatory mechanisms activated with intermittent energy restriction: a randomized control trial. Clin Nutr 2018 Jun;37(3):815–23. https://doi.org/10.1016/j.clnu.2017.04.002.

[26] Kunduraci YE, Ozbek H. Does the energy restriction intermittent fasting diet alleviate metabolic syndrome biomarkers? A randomized controlled trial. Nutrients 2020 Oct 21;12(10):3213. https://doi.org/10.3390/nu12103213.

[27] Headland ML, Clifton PM, Keogh JB. Effect of intermittent compared to continuous energy restriction on weight loss and weight maintenance after 12 months in healthy overweight or obese adults. Int J Obes 2018 Nov 23;43(10):2028–36. https://doi.org/10.1038/s41366-018-0247-2.

[28] Thomas EA, Zaman A, Sloggett KJ, Steinke S, Grau L, Catenacci VA, et al. Early time-restricted eating compared with daily caloric restriction: a randomized trial in

adults with obesity. Obesity 2022 Apr 26;30(5):1027–38. https://doi.org/10.1002/oby.23420.

[29] Sundfør TM, Svendsen M, Tonstad S. Effect of intermittent versus continuous energy restriction on weight loss, maintenance and cardiometabolic risk: a randomized 1-year trial. Nutr Metabol Cardiovasc Dis 2018 Jul;28(7):698–706. https://doi.org/10.1016/j.numecd.2018.03.009.

[30] Carter S, Clifton PM, Keogh JB. Effect of intermittent compared with continuous energy restricted diet on glycemic control in patients with type 2 diabetes. JAMA Netw Open 2018 Jul 20;1(3). https://doi.org/10.1001/jamanetworkopen.2018.0756.

[31] Jamshed H, Steger FL, Bryan DR, Richman JS, Warriner AH, Hanick CJ, et al. Effectiveness of early time-restricted eating for weight loss, fat loss, and Cardiometabolic Health in adults with obesity. JAMA Intern Med 2022 Sept 1;182 (9):953. https://doi.org/10.1001/jamainternmed.2022.3050.

[32] Trepanowski JF, Kroeger CM, Barnosky A, Klempel M, Bhutani S, Hoddy KK, et al. Effects of alternate-day fasting or daily calorie restriction on body composition, fat distribution, and circulating adipokines: secondary analysis of a randomized controlled trial. Clin Nutr 2018 Dec;37(6):1871–8. https://doi.org/10.1016/j.clnu.2017.11.018.

[33] Schübel R, Nattenmüller J, Sookthai D, Nonnenmacher T, Graf ME, Riedl L, et al. Effects of intermittent and continuous calorie restriction on body weight and metabolism over 50 wk: a randomized controlled trial. Am J Clin Nutr 2018 Nov; 108(5):933–45. https://doi.org/10.1093/ajcn/nqy196.

[34] Wei X, Lin B, Huang Y, Yang S, Huang C, Shi L, et al. Effects of time-restricted eating on nonalcoholic fatty liver disease. JAMA Netw Open 2023 Mar 17;6(3). https://doi.org/10.1001/jamanetworkopen.2023.3513.

[35] De Oliveira Maranhão Pureza IR, da Silva Junior AE, Silva Praxedes DR, Lessa Vasconcelos LG, de Lima Macena M, Vieira de Melo IS, et al. Effects of time-restricted feeding on body weight, body composition and vital signs in low-income women with obesity: a 12-month randomized clinical trial. Clin Nutr 2021 Mar;40 (3):759–66. https://doi.org/10.1016/j.clnu.2020.06.036.

[36] Castela I, Rodrigues C, Ismael S, Barreiros-Mota I, Morais J, Araújo JR, et al. Intermittent energy restriction ameliorates adipose tissue-associated inflammation in adults with obesity: a randomised controlled trial. Clin Nutr 2022 Aug;41(8): 1660–6. https://doi.org/10.1016/j.clnu.2022.06.021.

[37] Keenan SJ, Cooke MB, Hassan EB, Chen WS, Sullivan J, Wu SX, et al. Intermittent fasting and continuous energy restriction result in similar changes in body composition and muscle strength when combined with a 12 week resistance training program. Eur J Nutr 2022 Jan 27;61(4):2183–99. https://doi.org/10.1007/s00394-022-02804-3.

[38] Teong XT, Liu K, Vincent AD, Bensalem J, Liu B, Hattersley KJ, et al. Intermittent fasting plus early time-restricted eating versus calorie restriction and standard care in adults at risk of type 2 diabetes: a randomized controlled trial. Nat Med 2023 Apr;29(4):963–72. https://doi.org/10.1038/s41591-023-02287-7.

[39] Harvie M, Wright C, Pegington M, McMullan D, Mitchell E, Martin B, et al. The effect of intermittent energy and carbohydrate restrictionv. Daily Energy restriction on weight loss and metabolic disease risk markers in overweight women. Br J Nutr 2013 Apr 16;110(8):1534–47. https://doi.org/10.1017/s0007114513000792.

[40] Gray KL, Clifton PM, Keogh JB. The effect of intermittent energy restriction on weight loss and diabetes risk markers in women with a history of gestational diabetes: a 12-month randomized control trial. Am J Clin Nutr 2021 Aug;114(2): 794–803. https://doi.org/10.1093/ajcn/nqab058.

[41] Keenan S, Cooke MB, Chen WS, Wu S, Belski R. The effects of intermittent fasting and continuous energy restriction with exercise on cardiometabolic biomarkers, dietary compliance, and perceived hunger and mood: secondary outcomes of a randomized, controlled trial. Nutrients 2022 Jul 26;14(15):3071. https://doi.org/10.3390/nu14153071.

[42] Harvie MN, Pegington M, Mattson MP, Frystyk J, Dillon B, Evans G, et al. The effects of intermittent or continuous energy restriction on weight loss and metabolic disease risk markers: a randomized trial in young overweight women. Int J Obes 2010 Oct 5;35(5):714–27. https://doi.org/10.1038/ijo.2010.171.

[43] Maruthur NM, Pilla SJ, White K, Wu B, Maw MT, Duan D, et al. Effect of isocaloric, time-restricted eating on body weight in adults with obesity. Ann Intern Med 2024 May;177(5):549–58. https://doi.org/10.7326/m23-3132.

[44] Liu L, Chen W, Wu D, Hu F. Metabolic efficacy of time-restricted eating in adults: a systematic review and meta-analysis of randomized controlled trials. J Clin Endocrinol Metabol 2022 Oct 3;107(12):3428–41. https://doi.org/10.1210/clinem/dgac570.

[45] Saleh SAK, Santos HO, Găman M-A, Cerqueira HS, Zaher EA, Alromaih WR, et al. Effects of intermittent fasting regimens on glycemic, hepatic, anthropometric, and clinical markers in patients with non-alcoholic fatty liver disease: systematic review and meta-analysis of randomized controlled trials. Clinical Nutrition ESPEN 2024 Feb;59:70–80. https://doi.org/10.1016/j.clnesp.2023.11.009.

[46] Zeng L, Li H, Liu M, Rao WM, He QQ. Effects of intermittent fasting on cardiometabolic risk factors in patients with metabolic syndrome: a systematic review and meta-analysis of randomized controlled trials. PubMed 2022;31(4): 642–59. https://doi.org/10.6133/apjcn.202212_31(4).0008.

[47] Yao K, Su H, Cui K, Gao Y, Xu D, Wang Q, et al. Effectiveness of an intermittent fasting diet versus regular diet on fat loss in overweight and obese middle-aged and elderly people without metabolic disease: a systematic review and meta-analysis of randomized controlled trials. J Nutr Health Aging 2024 Mar;28(3):100165. https://doi.org/10.1016/j.jnha.2024.100165.

[48] Park J, Seo Y-G, Paek Y-J, Song HJ, Park KH, Noh H-M. Effect of alternate-day fasting on obesity and cardiometabolic risk: a systematic review and meta-analysis. Metabolism 2020 Oct;111:154336. https://doi.org/10.1016/j.metabol.2020.154336.

[49] Harris L, Hamilton S, Azevedo LB, Olajide J, De Brún C, Waller G, et al. Intermittent fasting interventions for treatment of overweight and obesity in adults: a systematic review and meta-analysis. JBI Database of Systematic Reviews and Implementation Reports 2018 Feb;16(2):507–47. https://doi.org/10.11124/jbisrir-2016-003248.

[50] Borgundvaag E, Mak J, Kramer CK. Metabolic impact of intermittent fasting in patients with type 2 diabetes mellitus: a systematic review and meta-analysis of Interventional Studies. J Clin Endocrinol Metabol 2020 Dec 15;106(3):902–11. https://doi.org/10.1210/clinem/dgaa926.

[51] Schroor MM, Joris PJ, Plat J, Mensink RP. Effects of intermittent energy restriction compared with those of continuous energy restriction on body composition and cardiometabolic risk markers – a systematic review and meta-analysis of randomized controlled trials in adults. Adv Nutr 2024 Jan;15(1):100130. https://doi.org/10.1016/j.advnut.2023.10.003.

[52] Enríquez Guerrero A, San Mauro Martín I, Garicano Vilar E, Camina Martín MA. Effectiveness of an intermittent fasting diet versus continuous energy restriction on anthropometric measurements, body composition and lipid profile in overweight and obese adults: a meta-analysis. Eur J Clin Nutr 2020 Dec 9;75(7):1024–39. https://doi.org/10.1038/s41430-020-00821-1.

[53] Elsworth RL, Monge A, Perry R, Hinton EC, Flynn AN, Whitmarsh A, et al. The effect of intermittent fasting on appetite: a systematic review and meta-analysis. Nutrients 2023 Jun 1;15(11):2604. https://doi.org/10.3390/nu15112604.

[54] Silverii GA, Cresci B, Benvenuti F, Santagiuliana F, Rotella F, Mannucci E. Effectiveness of intermittent fasting for weight loss in individuals with obesity: a meta-analysis of randomized controlled trials. Nutr Metabol Cardiovasc Dis 2023 Aug;33(8):1481–9. https://doi.org/10.1016/j.numecd.2023.05.005.

[55] Chang Y, Du T, Zhuang X, Ma G. Time-restricted eating improves health because of energy deficit and Circadian Rhythm: a systematic review and meta-analysis. iScience 2024 Feb;27(2):109000. https://doi.org/10.1016/j.isci.2024.109000.

[56] Cook F, Langdon-Daly J, Serpell L. Compliance of participants undergoing a '5-2' intermittent fasting diet and impact on body weight. Clinical Nutrition ESPEN 2022 Dec;52:257–61. https://doi.org/10.1016/j.clnesp.2022.08.012.

[57] Staudacher HM, Irving PM, Lomer MC, Whelan K. The challenges of control groups, placebos and blinding in clinical trials of dietary interventions. Proc Nutr Soc 2017 Jun 20;76(3):203–12. https://doi.org/10.1017/s0029665117000350.

[58] Yurkewicz M, Cordas M, Zellers A, Sweger M. Diabetes and sports. Am J Lifestyle Med 2016 Jul 8;11(1):58–63. https://doi.org/10.1177/1559827615583648.

[59] Yuan X, Wang J, Yang S, Gao M, Cao L, Li X, et al. Effect of intermittent fasting diet on glucose and lipid metabolism and insulin resistance in patients with impaired glucose and lipid metabolism: a systematic review and meta-analysis. International Journal of Endocrinology 2022 Mar 24;2022:1–9. https://doi.org/10.1155/2022/6999907.

[60] Sharma SK, Mudgal SK, Kalra S, Gaur R, Thakur K, Agarwal R. Effect of intermittent fasting on glycaemic control in patients with type 2 diabetes mellitus: a systematic review and meta-analysis of randomized controlled trials. Eur Endocrinol 2023;19(1):25. https://doi.org/10.17925/ee.2023.19.1.25.

[61] Xiaoyu W, Yuxin X, Li L. The effects of different intermittent fasting regimens in people with type 2 diabetes: a network meta-analysis. Front Nutr 2024 Jan;25:11. https://doi.org/10.3389/fnut.2024.1325894.

[62] Wang X, Yang Q, Liao Q, Li M, Zhang P, Santos HO, et al. Effects of intermittent fasting diets on plasma concentrations of inflammatory biomarkers: a systematic review and meta-analysis of randomized controlled trials. Nutrition 2020 Nov: 79–80. https://doi.org/10.1016/j.nut.2020.110974. 110974.

[63] Mulas A, Cienfuegos S, Ezpeleta M, Lin S, Pavlou V, Varady KA. Effect of intermittent fasting on circulating inflammatory markers in obesity: a review of human trials. Front Nutr 2023 Apr;17:10. https://doi.org/10.3389/fnut.2023.1146924.