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Original Article

Evaluation of the effectiveness of intermittent fasting versus caloric restriction in weight loss and improving cardiometabolic health: A systematic review and meta-analysis

Samah O. Alfahl, MD

Department of Family and Community Medicine and Medical Education, Medical College, Taibah University, Saudi Arabia

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الملخص

أهداف البحث: هدفنا إلى إجراء مراجعة منهجية وتحليل تلوي لاستكشاف آثار الأنظمة الغذائية المقيدة بالطاقة والصيام المتقطع على وزن الجسم وعوامل القلب والأيض.

طريقة البحث: تم استخدام منهجية متوافقة مع "بريزما"، وتم إجراء بحث منهجي في "بيميد" ومكتبة "كوشرين المركزية" للتجارب العشوائية الخاضعة للتحكم، لتحديد التجارب العشوائية الخاضعة للتحكم ذات الصلة من بداية قاعدة البيانات حتى ٢٧ سبتمبر ٢٠٢٣. كما تم إجراء البحث البيبليوغرافي والبحث في الأدبيات الرمادية لتحديد الأدبيات غير المنشورة. تم تجميع أحجام التأثير باستخدام نماذج التأثيرات العشوائية في حزمة "آر ميتا" وتم الإبلاغ عنها على أنها فروق متوسطة. تم تقييم جودة الدراسات المشمولة باستخدام أداة تقييم مخاطر التحيز "كوشرين".

النتائج: تم تحديد إجمالي ٢٩٣١ سجلا من خلال البحث في قاعدة البيانات، وقمنا بتضمين ١٦ تجربة عشوائية محكومة بعد مرحلتين من الفحص، مع منشور إضافي واحد من البحث البيبليوغرافي، مما أدى إلى إجمالي ١٧ منشورا. نشرت جميع التجارب بين عامي ٢٠١١ و ٢٠٢٢م، وشملت ١٢٥٨ مشاركا (النطاق: ٢٤-٢٠٩). كشف التحليل المجمع للنتائج أن الصيام المتقطع أدى إلى انخفاض أكثر أهمية في مؤشر كتلة الجسم مقارنة بنظام بالنظام المقيد بالطاقة، مما أظهر نتائج ذات دلالة إحصائية أظهر الصيام المتقطع انخفاضا أكبر قليلا في الوزن ومستويات الدهون الثلاثية وجلوكوز البلازما الصائم وضغط الدم الانبساطي مقارنة بنظام بالنظام المقيد بالطاقة، على الرغم من عدم أهميته إحصائيا. ومع ذلك، لوحظ انخفاض مماثل في مستويات ضغط الدم الانقباضي والكوليسترول الضار والكوليسترول الجيد بين الصيام المتقطع والصيام المتقطع، مما يشير إلى عدم وجود فرق كبير. عانت مجموعة الصيام المتقطع من تواتر أعلى للصداع مقارنة بمجموعة الصيام المتقطع، في حين أبلغت مجموعة الصيام المتقطع عن حدوث أكبر للدوخة مقارنة بمجموعة الصيام المتقطع.

الاستنتاجات: يبدو أن الصيام المتقطع مفيد قليلا لوزن الجسم وعوامل التمثيل الغذائي للقلب ومستويات الجلوكوز في البلازما.

الكلمات المفتاحية: فقدان الوزن؛ الصيام المتقطع؛ الأنظمة الغذائية المقيدة بالطاقة؛ مستوى الجلوكوز في البلازما؛ عامل التمثيل الغذائي للقلب

Abstract

Background: Dietary interventions, particularly intermittent fasting (IF) and energy restriction (ER), have emerged as effective strategies for managing weight.

Objective: We aimed to conduct a systematic review and meta-analysis exploring the effects of IF and ER on body weight and cardiometabolic factors.

Methods: PRISMA compliant methods were used, and PubMed and the Cochrane CENTRAL Library were systematically searched for relevant randomized controlled trials (RCTs) from database inception to September 27, 2023. A bibliographic and gray literature search was also performed to identify unpublished literature. Effect sizes were pooled with random effects models in the R package “meta” and are reported as mean differences with 95 % confidence intervals. The quality of the included studies was assessed with The Cochrane Risk of Bias assessment tool.

Results: A total of 2931 records were identified through a database search. The study included 17 publications: 16 RCTs identified after two stages of screening and an additional publication identified from a bibliographic search. All trials were published between 2011 and 2022, and included a total of 1258 participants (24–209 per study). Pooled analysis revealed that IF led to a more significant decrease in BMI than ER (−0.44 [-0.88 to −0.01]; $p < 0.01$). Additionally, IF resulted in a slightly greater, but statistically nonsignificant, decrease in weight, triglyceride levels, fasting plasma glucose, and

E-mail: Sfahl@taibahu.edu.sa

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diastolic blood pressure than ER. However, similar decreases in SBP, LDL, and HDL levels were observed between IF and ER, which showed no major differences. The ER group experienced a higher frequency of headaches than the IF group, whereas the IF group reported a greater occurrence of dizziness than the ER group.

Conclusion: IF appears to be slightly advantageous over ER in terms of body weight, cardiometabolic factors, and plasma glucose levels.

Keywords: Cardiometabolic factor; Energy-restricted diets; Intermittent fasting; Plasma glucose levels; Weight loss

Introduction

Dietary interventions have emerged as effective strategies for weight management, among which intermittent fasting (IF) and energy restriction (ER) are widely used techniques. IF is a frequently used and effective dietary intervention involving regular periods with no caloric intake.[1] This approach is simple to follow, and promotes weight loss and overall health.[2] IF has two main types. The first type is a time-restricted diet followed daily. Variations include 16-h fasts with 8-h feeding times (16:8), or 12:12, 14:10, 18:6, or 20:4 schedules. The second type is alternate-day fasting (ADF), which consists of a 24-h fast followed by a 24-h eating period. ADF can be performed several times per week; for example, a 5:2 strategy consists of two fasting days followed by five non-restrictive days.[1,3] Beyond weight loss, IF helps restore hormonal equilibrium by elevating SBH and decreasing androgens in obese premenopausal women. Furthermore, IF significantly improves glycemic control and insulin sensitivity; decreases cardiovascular risk by decreasing resting heart rate, BP, fat mass, total cholesterol, triglycerides, and LDL cholesterol; and also positively influences markers of oxidative stress and inflammation in obese patients with asthma.[4,5]

ER is another compelling caloric restriction approach characterized by controlled caloric intake without inducing malnutrition, by prioritizing adequate nutrition while limiting overall energy intake.[6,7] A calorie-restricted diet rich in fiber, with >50 % total energy intake from carbohydrates and limited fat, has been generally accepted and is recommended by guidelines,[7] because of its ability to consistently decrease the biological rate of aging, improve metabolic health, maintain glucose homeostasis, and facilitate obesity management.[7–9]

ER is the primary treatment modality for individuals with overweight and obesity.[10] Some randomized controlled trials (RCTs) have indicated that ER has positive effects on various cardiometabolic risk factors—such as anthropometric measurements, body composition, blood pressure, HDL-cholesterol, LDL-cholesterol, triglycerides, insulin resistance, glucose control, metabolic syndrome, and chronic inflammatory tone—and also increases adiponectin levels, thereby aiding in healthy weight loss. These findings indicate the profound effects of controlled energy intake in enhancing overall health and mitigating cardiovascular risk factors.[11,12]

Parvaresh et al.[13] have reported that IF has superior efficacy to ER in the management of body weight, waist circumference, blood pressure, and fasting plasma glucose. Several studies[14,15] have additionally indicated that IF excels in lipid and glycemic control. However, other research[16,17] has suggested no significant differences between treatment groups, indicating comparable efficacy. Therefore, determining the differences in effectiveness between IF and ER is important.

Although both IF and ER have gained attention as potential strategies for weight management and improving metabolic health, their relative efficacy remains unclear. To our knowledge, a comprehensive, up-to-date systematic review directly comparing the effects of IF and ER is currently lacking in the literature.

To address this knowledge gap, we aimed to conduct a systematic review and meta-analysis of RCTs comparing the effects of IF and ER.

Materials and Methods

This meta-analysis is reported according to Preferred Reporting Items for Systematic Review (PRISMA) guidelines.

Eligibility criteria

The research question was framed in Population, Intervention, Comparison, Outcome, Study Design (PICOS) format to explore study eligibility for inclusion. Published and unpublished RCTs evaluating IF versus ER were included, regardless of the use of other therapies, and participants' age, sex, country, and ethnic group. Non-human RCTs, in vitro research, phase I clinical trials, case reports, editorials, conference proceedings, commentaries, expert opinions, reviews, RCTs not reporting original data, non-RCTs, non-English publications, and duplicate publications were excluded.

Search strategy

A comprehensive literature search was performed in the PubMed and Cochrane Central Register of Controlled Trials Library electronic databases, to identify relevant RCTs from database inception until September 27, 2023. The search terms were "intermittent fasting" OR "fasting" OR "alternate day fasting" AND "caloric restriction" OR "dietary restriction" OR "ER." Detailed search strategies are listed in Supplementary Table 1 and Supplementary Table 2. Additional reference lists from review articles, Google Scholar, and bibliographies were also manually searched to identify published and unpublished trials. No date restrictions were applied, but the English language restriction was used in electronic searches for RCTs.

Study selection

Two reviewers independently performed first-pass screening by reviewing the titles and abstracts of all retrieved records to identify articles potentially meeting the predefined eligibility criteria. For eligible titles, the full texts were downloaded and reviewed independently by two reviewers in the second-pass screening, to determine relevant inclusion in the final analysis. Disagreements between reviewers during both screening stages were resolved through discussion with a third reviewer.

Data extraction and management

Two reviewers independently performed the data extraction. All relevant data were extracted from the included RCTs with data extraction templates. Disagreements during data extraction were resolved through discussion with a third reviewer. The following details were extracted: study identification, authors details, study objectives, study design, intervention setting, study population, measures, and main findings (changes in body weight, BMI, waist circumference, cholesterol levels, triglycerides, and blood pressure). Efficacy data reported in the final weeks of follow-up were collected.

Methodological quality assessment in the included RCTs

Two reviewers independently used the Cochrane collaboration's Risk of Bias assessment tool,[18] which comprises of six domains: selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias. Further results are presented as low risk of bias, unclear risk of bias, or high risk of bias, according to recommendations from the Cochrane handbook.[18]

Statistical analysis

All the analyses were performed in R software 4.2.2. Efficacy estimates are expressed as mean changes and 95 % confidence interval (CI) from baseline. Standard deviations (SD) were calculated from the standard error or 95 % CI and were imputed if not reported, according to the Cochrane Handbook for Systematic Review of Interventions.[19] Higgins' I^2 statistic and Cochran's Q test were used to assess potential statistical heterogeneity among trials. The meta-analysis was conducted with a random-effect model (restricted maximum likelihood method) based on low heterogeneity (<50 %) or high heterogeneity (>50 %). A funnel plot was generated to address the publication bias for the outcomes reported in at least ten studies in the meta-analysis.[20] Further sensitivity analyses were conducted to estimate the influence of individual study variation on overall outcomes.

Results

Study characteristics

A total of 2931 records were initially identified through database searching. After removal of 13 duplicate articles, the remaining 2918 records underwent primary screening.

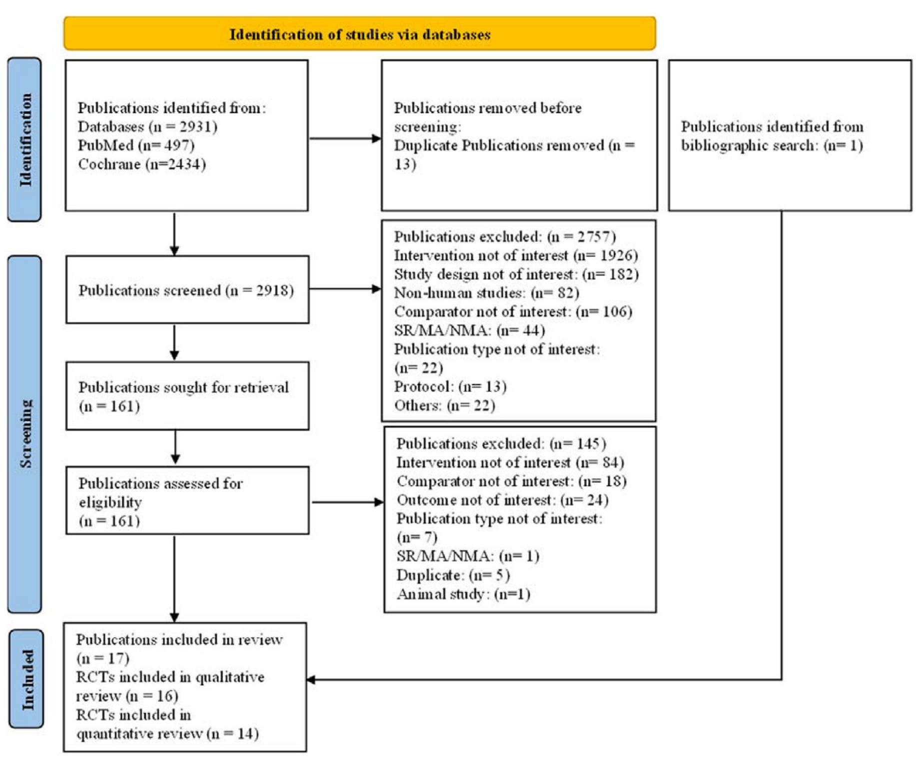

Figure 1: PRISMA flowchart of literature search and study selection. *17 publications from 16 RCTs were included (two different publications reported the data from one RCT).

Table 1: Baseline characteristics of included RCTs.

Author ID	Country	Blinded/ open label	Study duration	No. participants	Fasting duration	Setting	Type of center	Age group (years)
Catenacci et al., 2016[21]	U.S.A.	Open	32 weeks	29	Alternate day fasting	Community	Single	18−55
Conley et al., 2018[22]	Australia	Blinded	6 months	24	Alternate days (2 days per week)	Community	Single	55−75
Corley et al., 2019[a 23]	New Zealand	NR	6 weeks	NR	NR	NR	NR	NR
He et al., 2022[14]	China	Open	3 months	169	16 h fast every day	Community	Single	18−65
Isenmann et al., 2021[25]	Germany	Open	14 weeks	42	16 h fast every day	Community	Single	20−40
Keenan et al., 2022[15]	Australia	Open	12 weeks	34	Alternate days (2 days per week)	Community	Single	18−45
Liu et al., 2019[16]	Australia	Open	10 weeks	88	24 h fast (3 alternate days per week)	Community	Single	49−51
Hutchison et al., 2018[#24]	Australia	NR	10 weeks	88	24 h fast (3 alternate days per week)	NR	Single	Mean (SD): 50 (1)
Liu et al., 2022[17]	China	Open	12 months	139	16 h fast every day	Community	Single	18−75
Lowe et al., 2020[26]	U.S.A.	Open	12 weeks	141	16 h fast every day	Community	NR	Mean (SD): 46.5 (10.5)
Parvaresh et al., 2019[13]	Iran	Open	8 weeks	69	Alternate day fasting	Community	Single	25−60
Razavi et al., 2021[27]	Iran	Open	4 months	80	Alternate day fasting	Hospital	Single	25−60
Templeman et al., 2012[28]	United Kingdom	Open	8 weeks	37	Alternate day fasting	Community	NR	18−65
Teong et al., 2023[29]	Australia	Open	18 months	209	20 h fast on three consecutive days per week	NR	NR	58 (10)
Tivya S et al., 2021[a 30]	Malaysia	Open	12 weeks	37	Alternate days (2 days per week)	Hospital	Single	Mean (SD): 38.9 (5.9)
Trepanowski et al., 2017[31]	U.S.A.	Open	12 months	100	Alternate day fasting	Community	Single	18−64
Varady et al., 2011[31]	U.S.A.	Open	12 weeks	60	Alternate day fasting	Community	Single	35−65

[a] RCTs not included in the meta-analysis.
[b] Study associated with Liu et al., 2019 (not included in meta-analysis).

After evaluation of titles and abstracts, 2757 articles were excluded, thus leaving 161 for full-text assessment. Of these, 145 were excluded because of irrelevance, insufficiency, or ambiguity (Supplementary Table 3). An additional study was identified through bibliographic searching, thus yielding a total of 17[13−17,21−32] publications from 16[13−17,21−23,25−32] RCTs. Among these, 14[13−17,21,22,25−29,31,32] RCTs provided quantitative data used in the meta-analysis (Figure 1).

All included trials were published between 2011 and 2022. These RCTs included a total of 1258 (range: 24−209) participants; all were parallel design, single center RCTs. Most trials were conducted in Australia (n = 5), followed by the United States of America (n = 4). Two RCTs each were from China and Iran, and one study each was from Malaysia, New Zealand, Germany, and the United Kingdom. Most trials were community based (n = 12), whereas only two RCTs were hospital based, and the remaining RCTs did not report the setting. The mean age of the included participants at baseline was 50.14 years (range: 18−75 years) (Table 1).

Quality assessment of included RCTs

The overall risk of bias of the eligible RCTs was assessed with the Cochrane Risk of Bias tool (Figure 2). All RCTs except Conley et al.[22] had an overall high risk of bias, because of their open-label nature. Although Conley et al.[22] was a blinded study, it nonetheless had high risk of bias because of unclear randomization processes and the presence of attrition bias. In terms of randomization techniques, half the RCTs explicitly indicated the methods used, whereas the other half did not clearly describe the randomization processes, thus indicating a chance of selection bias. A substantial proportion of RCTs did not clearly indicate allocation concealment, thus indicating a potential for selection bias. Almost half the RCTs reported incomplete outcome data, thus potentially indicating attrition bias. Notably, we found no evidence of selective reporting in the included RCTs, thereby eliminating the possibility of reporting bias.

Meta-analysis

Body weight and BMI

Eleven RCTs[13,14,16,17,21,22,25−29] were analyzed to compare the effects of IF and ER on baseline weight change. The random effects model (Figure 3) illustrated the effectiveness of IF, revealing a slightly greater, though statistically nonsignificant, weight decrease than observed for ER (MD

[95 % CI]: −0.41 [−1.25 to 0.42]; p = 0.33). Furthermore, sensitivity analysis demonstrated that none of the included studies affected the overall estimate for this outcome (Supplementary Fig. 3). Additionally, we reported the effects of IF on BMI by analyzing data from seven RCTs[13,14,17,21,25,27,28] reporting BMI changes from baseline. The efficacy of IF in altering BMI levels was displayed with a random effects model (Figure 4). Notably, IF exhibited a significantly greater decrease in BMI than ER (MD [95 % CI]: −0.44 [−0.88 to −0.01]; p = 0.04). Furthermore, sensitivity analyses demonstrated that one study (Templeman et al., 2012) that compared IF (alternate day fasting) and ER (consumption of 75 % energy needs) significantly affected the overall estimate (Supplementary Fig. 4).

Authors	Random sequence generation (Selection bias)	Allocation concealment (Selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Overall bias
Catenacci et al, 2016	?	?	−	−	+	+	−
Conley et al, 2018	?	+	+	?	−	+	−
He et al, 2022	+	+	−	−	−	+	−
Isenmann et al, 2021	?	?	?	?	+	+	−
Keenan et al, 2022	+	−	?	?	+	+	−
Liu et al, 2019	+	?	?	?	+	+	−
Liu et al, 2022	?	?	−	?	−	+	−
Lowe et al, 2020	?	?	−	+	+	+	−
Parvaresh et al, 2019	+	+	−	+	−	+	−
Razavi et al, 2021	+	?	?	−	+	+	−
Templeman et al, 2012	+	+	−	+	−	+	−
Teong et al, 2023	+	?	−	+	+	+	−
Tivya et al, 2021	?	?	?	?	−	+	−
Trepanowski et al, 2017	+	?	−	+	−	+	−
Varady et al, 2011	?	?	?	?	+	+	−

Figure 2: Assessment of risk of bias in the included RCTs with the Cochrane domain-based quality assessment tool.

Triglycerides and total cholesterol

Nine RCTs[13−17,21,22,27,29] provided data on the effects of IF versus ER on triglyceride levels from baseline. The random effects model indicated the efficacy of IF in changing blood triglyceride levels (Figure 5), thus demonstrating a slightly greater, but statistically nonsignificant, decrease in the IF group than the ER group (MD [95 % CI]: −0.09 [−0.19 to 0.01]; p = 0.09). Furthermore, sensitivity analysis demonstrated that two studies (Templeman et al., 2012 and Teong et al., 2023) that compared IF (alternate day fasting/20 h fast on three consecutive days per week) with ER (consumption of 75 %/70 % energy needs) significantly affected the overall estimate (Supplementary Fig. 5). Similarly, total cholesterol levels were reported by eight RCTs.[13−17,22,27,29] The efficacy of IF in changing total cholesterol levels from baseline was illustrated with a random effects model (Figure 6). IF resulted in a greater decrease in total cholesterol levels than ER, although these results were statistically nonsignificant (MD [95 % CI]: −0.07 [−0.26 to 0.13]; p = 0.51). Furthermore, sensitivity analysis demonstrated that two studies (Templeman et al., 2012 and Teong et al., 2023) that compared IF (alternate day fasting/20 h fasting on three consecutive days per week) with ER (consumption of 75 %/70 % energy needs) significantly affected the overall estimate (Supplementary Fig. 6).

LDL and HDL

The effects of IF versus ER on LDL levels from baseline were analyzed across eight RCTs.[13−17,22,28,29] The efficacy of IF was displayed with a random effects model (Figure 7), which revealed similar decreases in LDL levels between the IF and ER groups (MD [95 % CI]: −0.02 [−0.16 to 0.12]; p = 0.80). Furthermore, sensitivity analysis demonstrated

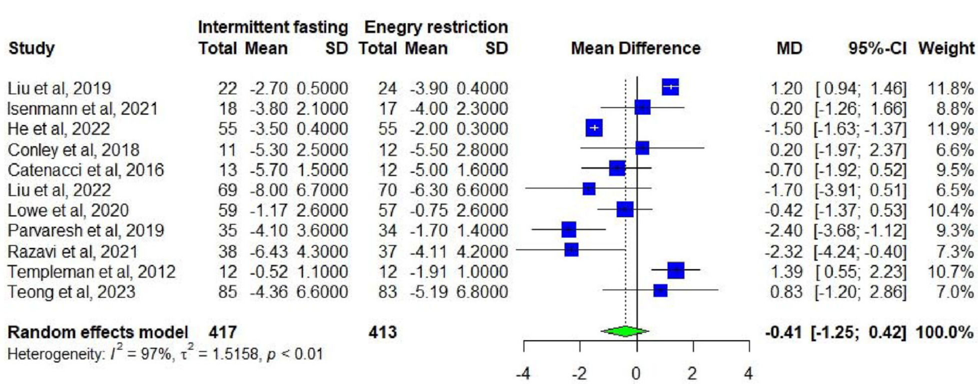

Figure 3: Changes in weight from baseline.

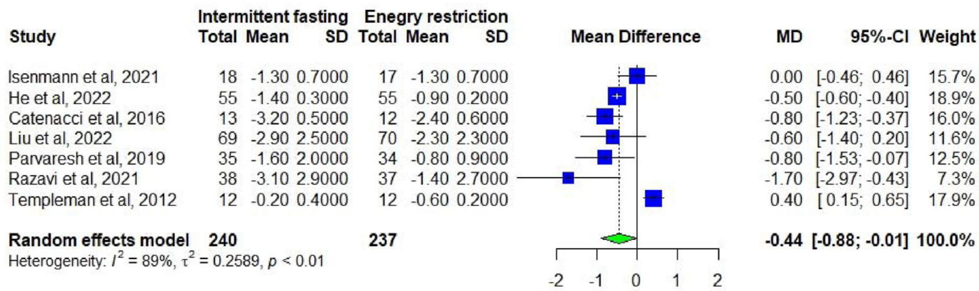

Figure 4: Changes in BMI from baseline.

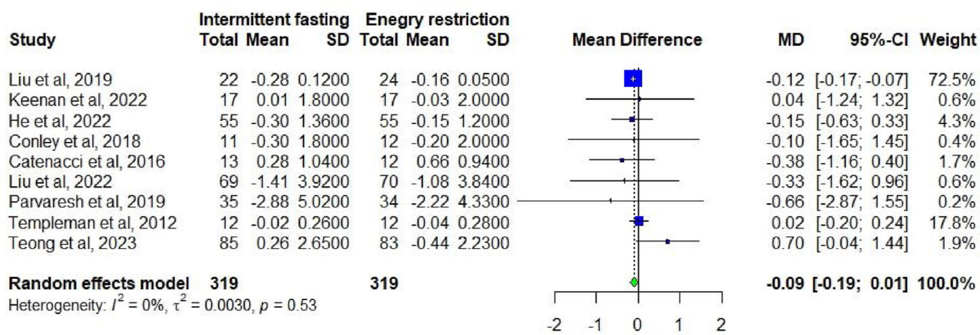

Figure 5: Changes in triglycerides levels from baseline.

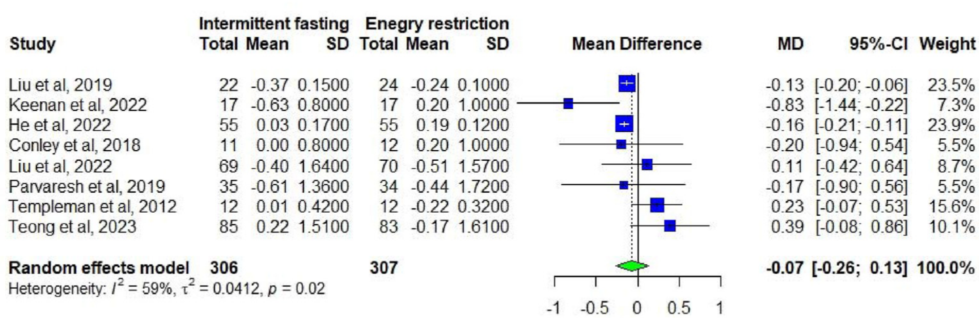

Figure 6: Changes in total cholesterol levels from baseline.

that none of the included studies affected the overall estimate for this outcome (Supplementary Fig. 7) Additionally, HDL levels were assessed in same eight RCTs.[13−17,22,28,29] The efficacy of IF in changing total HDL levels from baseline was illustrated with a random effects model (Figure 8). The results for HDL, similarly to those for LDL, indicated similar decreases between the IF group and the ER group (MD [95 % CI]: −0.01 [−0.02 to 0]; p = 0.03). Furthermore, sensitivity analysis demonstrated that two studies (Liu et al., 2019 and He et al., 2022) that compared IF (24 h fasting/16 h fasting) with ER (consumption of 70 %/75 % energy needs) significantly affected the overall estimate (Supplementary Fig. 8).

Fasting plasma glucose and HbA1C

Eight RCTs[13−17,21,22,29] examined the effects of IF versus ER on changes in fasting plasma glucose levels from baseline. A random effects model (Figure 9) demonstrated that the IF group exhibited a slightly superior decrease in plasma glucose levels to the ER group, although this difference was statistically non-significant (MD [95 % CI]: −0.09 [−0.20 to 0.02]; p = 0.09). Furthermore, sensitivity analysis demonstrated that one study (Templeman et al., 2012) that compared IF (alternate day fasting) and ER (400 kcal/day decrease from estimated energy requirements) significantly affected the overall estimate (Supplementary Fig. 9). Additionally, HbA1C levels were evaluated in only two RCTs.[14,29] The efficacy of IF in changing HbA1C levels from baseline was illustrated with a random effects model (Figure 10), which revealed similar changes between the IF and ER groups (MD [95 % CI]: −0.01 [−0.02 to 0]; p = 0.78). Furthermore, a sensitivity analysis demonstrated that none of the included studies affected the overall estimate for this outcome (Supplementary Fig. 10).

Blood pressure

Seven RCTs[13,14,16,17,22,26,29] compared IF and ER effects on SBP levels from baseline. IF's efficacy was displayed with a random effects model (Figure 11). The RCTs indicated similar decreases in SBP levels between IF and ER (MD [95 % CI]: −0.04 [−1.78 to 1.69]; p = 0.96). Furthermore, sensitivity analysis demonstrated that none of the included studies affected the overall estimate for this outcome (Supplementary Fig. 11). Additionally, these RCTs[13,14,16,17,22,26,29] examined DBP levels, as presented with a random effects model (Figure 12). In contrast to SBP, DBP displayed a slightly greater decrease in the IF

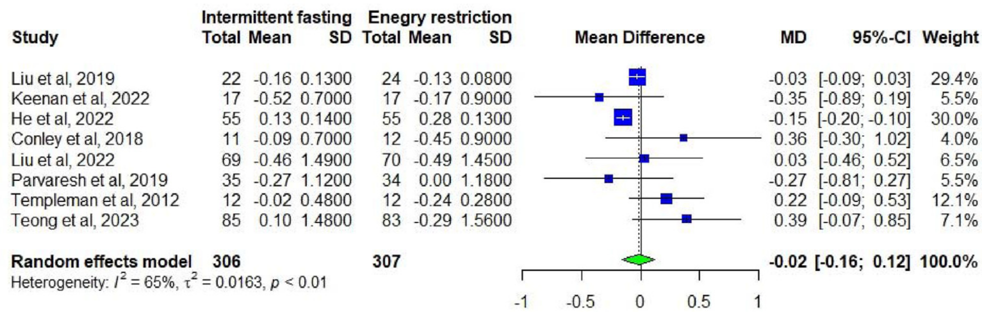

Figure 7: Changes in LDL levels from baseline.

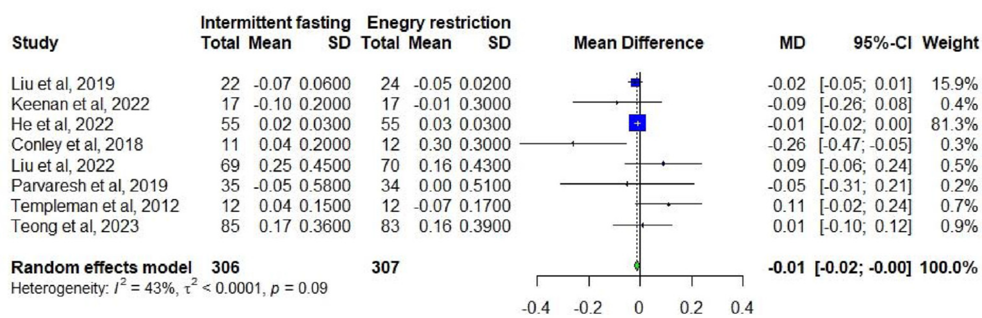

Figure 8: Changes in HDL levels from baseline.

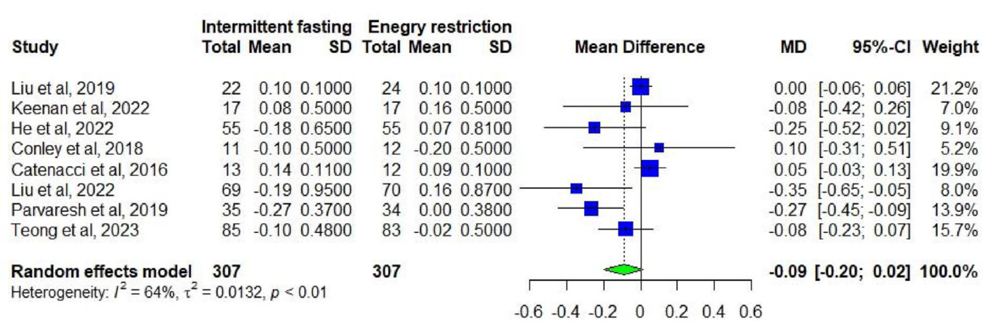

Figure 9: Changes in fasting plasma glucose levels from baseline.

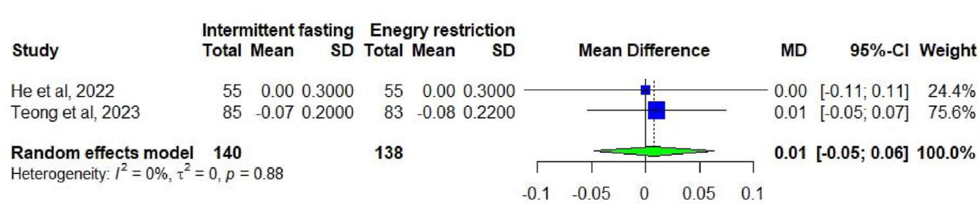

Figure 10: Changes in HbA1C levels from baseline.

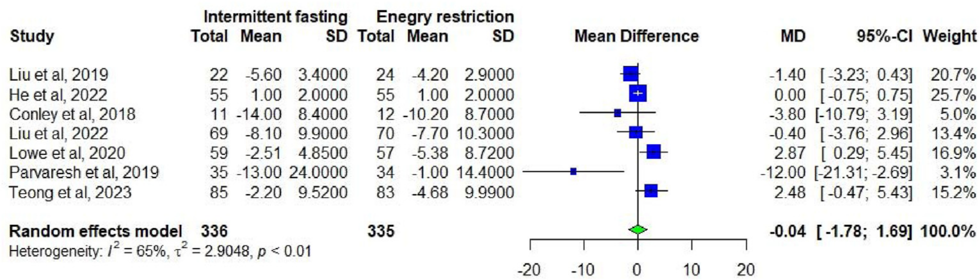

Figure 11: Changes in SBP levels from baseline.

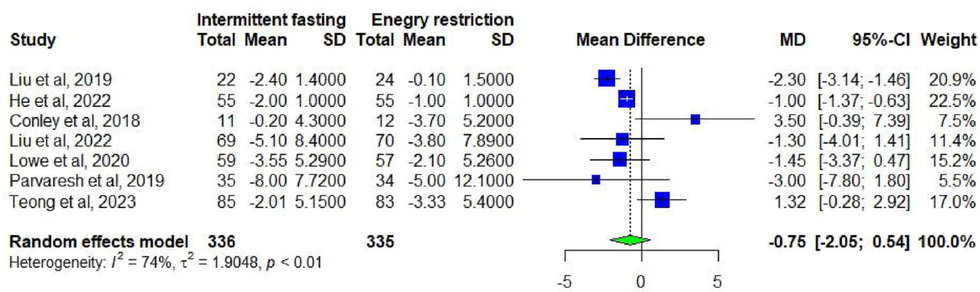

Figure 12: Changes in DBP levels from baseline.

group than the ER group (MD [95 % CI]: −0.75 [−2.05 to 0.54]; p = 0.25); however, the difference was statistically nonsignificant. Furthermore, sensitivity analysis demonstrated that only one study (Teong et al., 2023) that compared IF (alternate day fasting) with ER (consumption of 75 % energy needs) significantly affected the overall estimate (Supplementary Fig. 12).

Safety

Three RCTs documented occurrences of adverse events in populations undergoing either IF or ER. In the study by Teong et al.,[29] the incidence of headache was consistent between arms. However, Liu et al.[17] observed a higher frequency of headaches in the ER group (2.9 %) than the IF group (1.5 %). Interestingly, that study also reported greater occurrence of dizziness in the IF group (8.7 %) than the ER group (7.1 %). In contrast, Conley et al.[22] found no instances of headache or dizziness throughout the duration of their study.

Discussion

We conducted a thorough systematic review and meta-analysis comparing IF and ER regimens in terms of changes in waist circumference, body weight, cardiovascular factors, and lipid profiles. Although IF showed benefits, the observed effects were not statistically significant. A well-studied dietary intervention might have substantial effects on society.

The analysis of body weight changes from baseline revealed notable differences between interventions. In a qualitative study by Tivya et al.,[30] the reported change in body weight revealed a greater decrease in the IF group than the ER group (5.9 % and 2.3 % decreases from baseline, respectively). However, our meta-analysis findings were deemed statistically insignificant, in agreement with the results reported by Zhang et al..[33] However, IF was found to better at maintaining lean body mass by Varady et al..[31] Additionally, nine RCTs[13,14,16,17,22,25,27–29] reported waist circumference. We observed a comparatively greater decrease in waist circumference with IF than ER, yet these findings were statistically nonsignificant (MD [95 % CI]: −0.7 [−1.91 to 0.52]; p = 0.26) (Supplementary Fig. 1). These results are consistent with those described in a previously published review by Zhang et al.[33]

We explored the effects of IF on BMI, and found that IF exhibited a significantly greater decrease in BMI than ER. These findings align with those from a Cochrane review by Allaf et al.[34] and a meta-analysis study by Guerrero et al..[35] However, a separate study by Zhang et al.[33] suggested no differences in BMI. These differences among studies might be attributable to the analysis of fewer RCTs and the inclusion of an intermittent ER arm.

We assessed lipid profiles, including changes in triglycerides, total cholesterol, LDL, and HDL levels. IF exhibited slightly greater efficacy than ER in decreasing triglycerides and total cholesterol; however, these differences were not statistically significant. Moreover, no notable difference in decreasing LDL and HDL levels was observed. These results align with those from previously published reviews by Allaf et al.[34] and Cioffi et al.[36]

We assessed the diabetic profile according to changes in fasting plasma glucose and HbA1C levels. The IF group exhibited a slightly greater decrease in plasma glucose levels than the ER group, although this difference was statistically insignificant. Meanwhile, HbA1C levels showed similar changes between the IF and ER groups. Our findings align with those from a previous review by Silverii et al..[37] Interestingly, another study has reported a (IF) significant decrease in fasting plasma glucose, possibly because of the inclusion of a mixed population of prediabetic and healthy individuals.[38]

Finally, we assessed changes in cardiovascular factors, including SBP and DBP. Similar decreases in SBP were observed between the IF and ER groups. In contrast, although DBP exhibited a slightly greater decrease in the IF group than the ER group, this difference lacked statistical significance. Our findings are in agreement with previously published reviews by Silverii et al.[37] and Allaf et al.[34]

Our meta-analysis has several limitations that require acknowledgment. Primarily, the IF and ER procedures varied across the included studies. To minimize the effects of these differences, we used a random effects model to estimate the pooled effect and used the mean difference rather than standardized mean difference. Although this approach did not resolve the underlying heterogeneity, it incorporated heterogeneity into the confidence intervals of the effect size estimates. Additionally, we performed sensitivity analyses for each outcome to understand the differences in study protocols for IF and ER. However, caution must be exercised in generalizing these results. Furthermore, the inclusion of RCTs with small sample sizes contributed to heterogeneity in the analysis, thereby affecting the overall robustness of our findings. To increase the accuracy and reliability of our meta-analysis, larger-scale RCTs on similar protocols are required.

Another notable limitation was the substantial differences in follow-up times among the included RCTs, some of which lacked adequate follow-up data altogether. This difference in follow-up periods might potentially have affected comprehensive understanding of the interventions' long-term effects. Additionally, all RCTs had high risk of bias because of their open label nature, which might have distorted the efficacy estimates for IF regimens. Furthermore, we evaluated publication bias for only body weight, because it was the only outcome reported in more than ten studies, whereas all other outcomes were reported in fewer than ten studies.[20] Additionally, we did not search EMBASE and CINAHL, because they are paid databases; this limitation might potentially have affected the robustness of our findings. To mitigate this limitation, we performed a comprehensive search strategy in PubMed and Cochrane, which are widely recognized for their extensive coverage of the biomedical literature. Additionally, we conducted supplementary searches in Google Scholar and performed a thorough bibliographic search to identify any additional relevant studies.

In conclusion, our findings indicated that IF is more effective than ER in BMI lowering, yet no significant weight decrease was observed. IF, compared with ER, appears to offer slightly more advantageous or comparable effects on cardiometabolic factors and plasma glucose levels. Also weight loss will stop and very likely the patient will gain weight, if patient stops this dietary modification. Heterogeneity significantly affected the reliability of our findings and emerged as the primary challenge in this review. This limitation must be explicitly acknowledged, because it considerably diminishes the trustworthiness of the results presented. We anticipate that future long-term RCTs including large sample sizes will contribute to more comprehensive evaluation of the clinical effects of IF in dietary interventions.

Conflict of interest

There is no conflict of interest.

Ethical approval

As this systematic review and meta-analysis did not entail data collection from human or animals, there was no question of ethics that arose from the process of research. Thus, this study did not need clearance from an institutional review board. All data in this study were collected from the open source, whereas all studies included in the research had passed through their own ethical clearances. The study was done following the guidelines of systematic review and meta-analysis available in the guidelines of the International Committee of Medical Journal Editors.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jtumed.2025.02.012.

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