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The impact of intermittent fasting on body composition and cardiometabolic outcomes in overweight and obese adults: a systematic review and meta-analysis of randomized controlled trials

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Abstract

Background Obesity is a global health crisis, projected to affect over 1.53 billion adults by 2035. Intermittent fasting (IF) has emerged as a potential alternative to continuous energy restriction (CER) for weight management and metabolic improvement. However, previous meta-analyses have reported inconsistent results. These knowledge gaps hinder the clinical translation of IF, and a rigorous synthesis of randomized controlled trials (RCTs) is necessary to clarify their effects on body composition and cardiometabolic health in overweight and obese populations.

Methods This PRISMA-guided systematic review and meta-analysis searched PubMed, Embase, and Web of Science up to March 2025. We included 15 randomized controlled trials ($n=758$) comparing IF diets with control diets in overweight/obese adults. Primary outcome indicators included total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL), fasting plasma glucose (FPG), hemoglobin A1C (HbA1c), systolic blood pressure (SBP), diastolic blood pressure (DBP), body weight (BW), body mass index (BMI), waist circumference (WC), and waist-to-hip ratio (WHR). Data were pooled using a random-effects model and analyzed in subgroups by intervention duration and IF form.

Results IF significantly reduced BW (MD: -3.73 kg, 95% CI: -5.29, -2.17) and BMI (MD: -1.04 kg/m^2, 95% CI: -1.39, -0.70) in overweight/obese adults, while effectively improving lipid profiles, including TC (MD: -6.31 mg/dl, 95% CI: -12.36, -0.26) and LDL (MD: -5.44 mg/dl, 95% CI: -12.36, -0.26). However, short-term IF (≤ 12 weeks) may have resulted in a temporary elevation of TG (MD: 13.22 mg/dl, 95% CI: 3.39, 23.05), whereas long-term intervention (> 12 weeks) optimized lipid metabolism benefits. In addition, IF significantly reduced DBP (MD: -3.30 mmHg, 95% CI: -5.47, -1.13) but had no significant effect on SBP, FPG and HbA1c. Subgroup analyses showed that alternate day fasting (ADF) was superior to time-restricted eating (TRE) in terms of weight loss and improvement in LDL. The findings suggest that the metabolic effects of IF are time-dependent, and that its clinical use needs to be combined with individualized

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regimens and long-term adherence strategies. Limitations include the short intervention period (≤ 12 weeks) and high heterogeneity of most studies, and standardized long-term trials are needed to validate the sustained benefits and safety.

Conclusions As a non-pharmacological intervention, IF demonstrates significant value for weight management and metabolic improvement. Its advantages in adherence and metabolic regulation position it as a promising therapeutic approach. However, its long-term efficacy and safety warrant further validation through additional high-quality clinical studies. Future efforts should focus on developing precise, sustainable, and personalized IF protocols within a personalized medicine framework to achieve comprehensive cardiometabolic health optimization.

Registration PROSPERO CRD420251036588.

Keywords Intermittent fasting, Obesity, Overweight, Body composition, Lipid profiles

Introduction

Obesity has become a global public health problem. According to the *World Obesity Atlas 2024* published by the World Obesity Federation, it is predicted that by 2035, more than 1.77 billion adults will be overweight globally (1.53 billion of whom will meet the criteria for obesity), representing 54% of the total adult population [1, 2]. This figure means that at least one in two adults is at risk of being overweight or obese. Obesity is strongly associated with a number of chronic diseases, such as cardiovascular disease, diabetes mellitus, and metabolic dysfunction-associated steatotic liver disease (MASLD) [3–6]. Research indicates that approximately 60% of patients with type 2 diabetes are overweight or obese [7]. Obesity increases the risk of developing type 2 diabetes by promoting insulin resistance. Obesity is not only a risk factor for type 2 diabetes but also a significant risk factor for cardiovascular diseases [8]. According to the Clinical Consensus Statement of the European Society of Cardiology (ESC) [9], obesity is strongly associated with a variety of manifestations of cardiovascular disease, including atherosclerosis, heart failure, thrombophilia, arrhythmia, and sudden cardiac death. Obesity greatly increases the risk of cardiovascular disease through several mechanisms, such as inducing structural and functional changes in the heart (e.g., left ventricular hypertrophy and heart failure), activating inflammatory and immune processes, altering hemodynamics, and affecting adipokine levels.

In recent years, weight loss through dietary approaches has become increasingly popular [10–12]. Intermittent fasting (IF), as an emerging model of dietary intervention, has attracted much attention in terms of weight management and metabolic improvement [13]. IF is a dietary pattern that restricts food intake on a regular basis. By maintaining a zero or very low calorie intake for a specific period of time, it stimulates the body's metabolic adaptive mechanisms, leading to improved health. It has attracted considerable attention as an alternative to traditional continuous energy restriction (CER) for weight loss. Common intermittent fasting regimens mainly include two types: Intermittent Energy Restriction (IER) and Time - Restricted Eating (TRE). The implementation of IER involves a significant reduction in energy intake during specific fasting periods, while maintaining normal eating habits during non-fasting periods. The purpose of such periodic adjustments is to induce the body to utilize stored fat as a source of energy, thus potentially achieving the goals of weight control, improved metabolic health, and prevention of related diseases [14]. IER involves alternating between short-term energy restriction (75–100%) and normal eating cycles. Alternate Day Fasting (ADF), as one form of IER, refers to a dietary regimen defined by alternating "fasting days" and "feeding days". On "feeding days", food can be consumed freely; while on "fasting days", food intake is either completely restricted or significantly reduced [15]. The 5:2 fasting (Twice - Weekly Fasting), also known as fasting twice a week, is another form of IER. This dietary approach follows a weekly cycle, requiring individuals to control calorie intake on any two chosen days of the week, while maintaining a normal diet without deliberately restricting food types on the remaining five days. The 5:2 model is easier to stick to over the long term than traditional diets because it allows for normal eating most of the time [16]. Studies have shown [17] that the 5:2 IER regimen results in potentially beneficial changes in fasting blood glucose and fasting subjective appetite ratings within 2 weeks.

The core of TRE is to condense daily eating into a fixed time window (usually 8–12 h), for example, choosing to eat from 10 a.m. to 6 p.m. (an 8 - hour window) and fasting for the remaining 16 h. Numerous studies have shown [18–21] that intermittent fasting can not only effectively reduce body weight but also improve metabolic indicators such as blood glucose and blood lipids, with potential benefits for cardiovascular and metabolic health.

Despite the large number of studies that have explored the use of IF in obesity, there are still significant inconsistencies and gaps in the available evidence. On the one hand, there is disagreement between different studies regarding the effectiveness of intermittent fasting in terms of weight loss and improvement in metabolic

markers, with one study finding [22] that intermittent fasting was superior to CER in improving triglyceride (TG) levels, with a mean reduction of 10.16 (95% CI: -18.88, -1.45), whereas one study found that short-term IF may increase glycan TG levels [23], which is in contradiction to the commonly belief that IF helps to improve metabolic markers. On the other hand, we still know very little about the effectiveness and safety of intermittent fasting duration. In addition, despite the existence of multiple modes of intermittent fasting, there is no conclusive evidence as to which mode is the most effective and safe. This diversity in modalities not only adds to the complexity of research, but also makes clinicians and patients face confusion when choosing an intermittent fasting regimen. Therefore, this study aimed to provide a comprehensive assessment of existing randomized controlled trials on the use of intermittent fasting in obese adults through a systematic review and meta-analysis approach. By integrating the latest evidence and filling in knowledge gaps, we hope to clarify the effects of intermittent fasting in terms of weight loss, improvement of metabolic markers, and cardiovascular health, and to explore the differences between different modes of intermittent fasting. Ultimately, we hope to provide clinicians and patients with the latest evidence and recommendations on the use of intermittent fasting in obese adults to guide clinical practice and personal health management.

Methods

The current meta - analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta - Analyses (PRISMA) guidelines [24] and the Cochrane Handbook for Systematic Reviews of Interventions. The current systematic review and meta - analysis has been registered in the International Prospective Register of Systematic Reviews (PROSPERO registration ID: CRD420251036588).

Search strategy

A comprehensive search was conducted in three major electronic databases, namely PubMed, Embase, and Web of Science, from their inception to March 2025. The keywords used for searching intermittent fasting interventions included: “Intermittent Fasting” or “Intermittent Energy Restriction” or “Time - Restricted Eating” or “Alternate Day Fasting” or “Twice - Weekly Fasting” or “continuous energy restriction” or “5:2 diet” or “fasting - mimicking diet” or “time - restricted feeding”, and obesity, including “obesity” or “overweights” or “obesities” or “obeses” or “overweight”. The search was restricted to English - language articles, human participants, and the details specified in Supplementary Table 1. All retrievals were performed by the same author (Bingjie Wang).

Study selection and inclusion and exclusion criteria

All initial records were exported to EndNote software (version 20) for screening, and duplicates were excluded. The selection process was first conducted based on titles/abstracts, and then full - texts were screened according to the inclusion and exclusion criteria. The inclusion criteria were defined based on the PICOS standards, including population, intervention, comparison, outcome, and study design. Studies were included for participants with an average age ≥ 18 years and a body mass index ≥ 25 kg/m^2. Regardless of their biological sex and health status (with or without comorbidities). In the intervention, IF refers to various forms of fasting patterns including IER, ADF, 5:2 or 4:3 diets, TRF, and TRE, CON refers to maintaining daily eating habits, and the exercise group is considered CON. The primary outcome must include at least one of the following: total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL), fasting plasma glucose (FPG), hemoglobin A1C (HbA1c), systolic blood pressure (SBP), diastolic blood pressure (DBP), body weight (BW), body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), body weight (BW), body mass index (BMI), waist circumference (WC), waist-to-hip ratio (WHR), and no secondary outcomes. For study design, randomized clinical trials or randomized controlled trials with parallel groups were included. In addition, the studies must: be available in full - text, be peer - reviewed, and be written in English. Exclusion criteria: non - original research, animal studies, and non - randomized trials. In addition, studies that compared with a CR group and had no overweight or obese participants, or used a Mediterranean diet as the comparison group were also excluded. If a study included IF, CR, and CON, only the comparison between IF and CON was included, and the exercise group was considered as CON.

Data extraction and synthesis

Data extraction was conducted by two independent authors (Bingjie Wang and Chen Wang), and any disagreements were resolved by discussion with other authors. The research data include the first author, year of publication, study design, and number of groups. Participant characteristics include sample size, biological sex, age, body mass index, and health status. Intervention characteristics include IF and CON dietary patterns, duration, and protocols. Finally, all outcome indicators are extracted. Data for quantitative analysis were extracted, including mean post-change values, associated standard deviation (SD) and sample size for each group. In the case of medians and ranges or 95% CIs, mean and SD values were calculated utilizing the method developed by Hozo et al. [25]. To assess the clinical significance of the data, TC and FPG data are converted to the

same units using relevant formulas (detailed conversion methodology provided in Additional file 1: Supplement Formula).

Risk of bias assessment

The risk of bias of the included studies was assessed using the Risk of Bias Tool provided by the Cochrane Collaboration, which was conducted using Rob 1.0 in the Reviewer Manager (RevMan) software (version number RevMan 5.4) [26]. The assessment mainly includes the following six aspects: (1) Random Sequence Generation: Assess whether the randomization method is adequate to ensure baseline comparability between groups. (2) Allocation Concealment: Assess the concealment of the random allocation scheme to prevent selection bias. (3) Blinding: Assess whether researchers and participants are blinded, and the extent to which blinding is implemented, including: blinding of participants; blinding of researchers; blinding of outcome assessors. (4) Incomplete Outcome Data: Assess whether there are losses to follow-up, withdrawals, or missing data, and whether appropriate handling (such as intention-to-treat analysis) has been conducted. (5) Selective Reporting: Assess whether the study has a predefined protocol and reports all predetermined outcome measures to prevent selective reporting bias. (6) Other Bias: Assess whether there are other potential sources of bias, such as baseline imbalance, conflicts of interest, etc. The risk of bias was assessed by two independent authors (Bingjie Wang and Chen Wang), and any disagreement was resolved by discussion with the other authors.

Meta-analysis

When studies report the same outcome in the same or different units, calculate the pooled standard mean difference (MD) and its 95% confidence interval. The I^2 statistic is used to assess heterogeneity among the included studies, with values < 25% indicating low heterogeneity, 25–75% indicating moderate heterogeneity, and > 75% indicating high heterogeneity. Publication bias is assessed using visual interpretation of funnel plots. When there are nine or more trials reporting results for an outcome measure, sensitivity analysis is conducted by removing individual studies. Finally, when seven or more trials report results for an outcome measure, several subgroup analyses are performed based on intervention duration and IF mode.

Results

Study selection

The database search yielded 978 studies from PubMed, Embase, and Web of Science. After removing 272 duplicates, 477 studies were screened based on titles and abstracts, and subsequently, the eligibility of 229 articles was assessed through full-text screening. Finally, after excluding 214 studies for the reasons shown in Figs. 1 and 15 studies met the inclusion criteria. Among the included studies, 7 studies contained experimental groups other than IF and CON [27–33].

Characteristics of participants and interventions

A total of 758 participants were included (Table 1). All participants were overweight or obese adults. Except for four studies with only female participants [28, 34–36] and one study with only male participants [37], the remaining studies included both males and females. The duration of the interventions ranged from 6 to 16 weeks. Most studies used TRE [27, 34, 35, 37–40], while others used ADF [30, 31, 33], the 5:2 diet [28, 41], the 4:3 diet [42], or IER [29, 32]. Additionally, one study combined TRE with a resistance and endurance circuit training program [34], and another study combined TRE with Nordic walking [39]. The overall quality of the included studies is summarized in Table 1.

Meta-analysis

Lipid profiles

IF decreased TC [MD: -6.31 mg/dl (95% CI: -12.36, -0.26), $P = 0.04$; 10 experiments], LDL [MD: -5.44 mg/dl (95% CI: -10.74, -0.13), $P = 0.04$, 12 experiments], increased TG [MD: 8.56 mg/dl (95% CI: 0.50, 16.62), $P = 0.04$, 11 experiments], did not significantly increase or decrease HDL [MD: -0.89 mg/dl (95% CI: -4.54, 2.76), $P = 0.63$, 11 experiments], TC ($I^2 = 51\%$, $P = 0.03$), LDL ($I^2 = 62\%$, $P = 0.002$) and TG ($I^2 = 61\%$, $P = 0.005$) had moderate heterogeneity, and HDL ($I^2 = 84\%$, $P < 0.00001$) had high heterogeneity. However, sensitivity analyses showed a change in the significance of HDL ($I^2 = 46\%$, $P = 0.05$) after exclusion of the S. Bhutani [33] study, which consisted of a 4-week tightly controlled feeding period followed by 8 weeks of self-selected diets, a phased intervention that may have led to fluctuations in adherence and weakened the long-term effect of ADF on HDL. Subjects in the ADF group included in this study were predominantly female (24/25), and the metabolic response to ADF in women may differ from other studies with a higher gender preponderance due to hormone levels. Second, with a high dropout rate of 36% (9/25) in the ADF group, the final data may have been biased in favor of a more tolerant subgroup, resulting in a magnitude of HDL change that deviates from the true effect. Visual interpretation of funnel plots suggests possible publication bias. (Figures S3-S11)

Body composition

IF decreased BW [MD: -3.73 kg (95% CI:-5.29, -2.17), $P < 0.00001$, 8 experiments], BMI [MD: -1.04 kg/m^2 (95% CI: -1.39, -0.70), $P < 0.0001$, 7 experiments], and did not significantly decrease or increase WC [MD:-2.42 cm

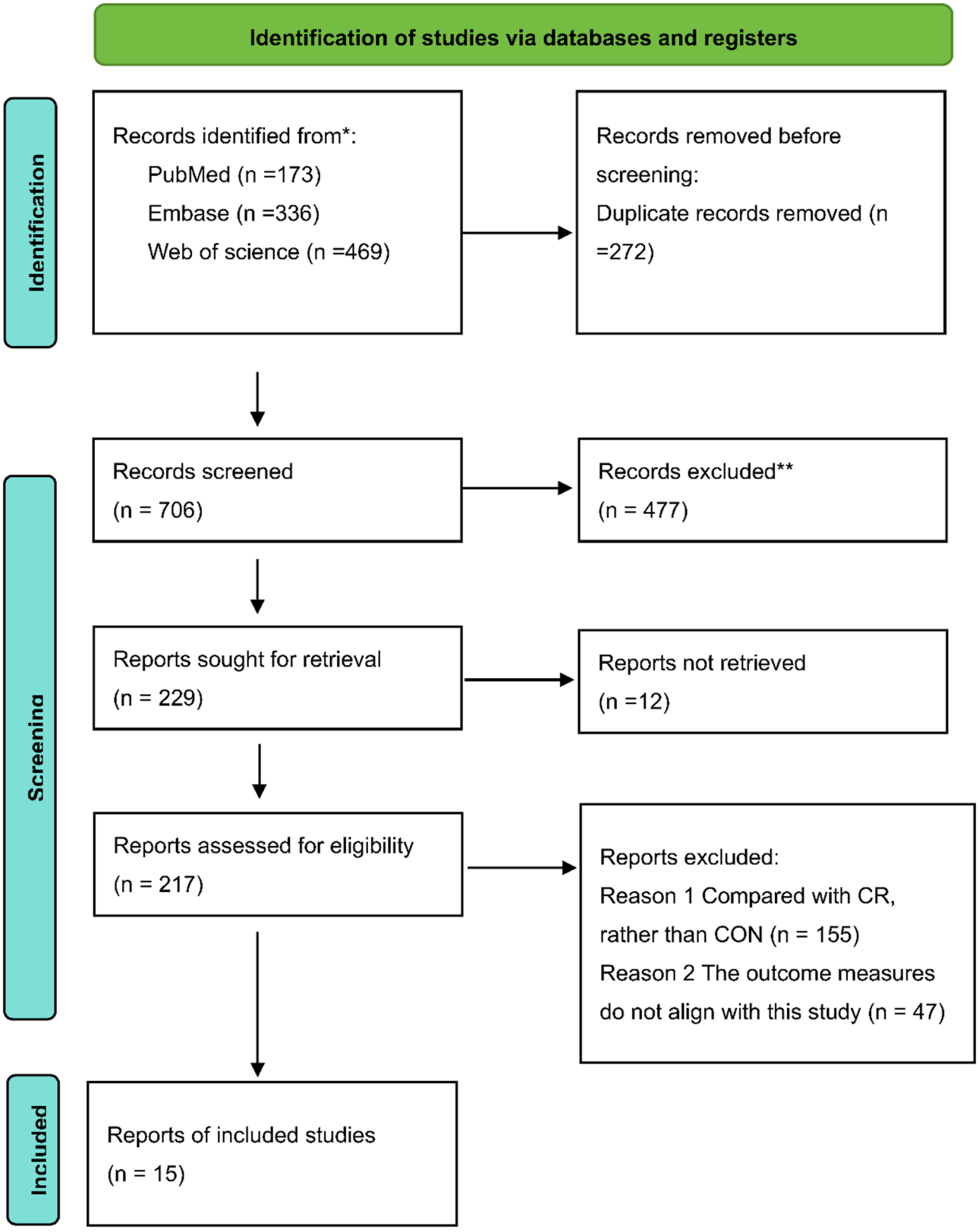

Fig. 1 Flow diagram of systematic literature search

Table 1 Characteristics of participants and interventions

Author	Year	Body form	Age	BMI	Sample size	Duration (Weeks or months)	IF form	Outcomes
J. S. Quist [38]	2024	Overweight	IF: 56.00 ± 8.89	IF:33.80 ± 5.20	IF: 50	3 months	TRE	BW, FPG, LDL, HbA1c
		Obesity	CON: 59.00 ± 9.64	CON:33.90 ± 6.40	CON: 50			
P. Keawtep [28]	2024	Overweight	IF: 52.87 ± 3.88	IF:28.28 ± 2.78	IF: 23	3 months	5: 2	TC, TG, BMI, BW, WHR,
		Obesity	CON: 53.61 ± 2.81	CON:29.18 ± 2.85	CON: 23			
B. Jóźwiak [34]	2024	Overweight	ND	IF:26.95 ± 10.64	IF: 28	12 weeks	TRE	TC, LDL, HDL, SBP, DBP, BMI, WC, WHR,
		Obesity		CON:26.35 ± 11.46	CON: 34			
Czerwińska-Ledwig, O [39].	2024	Overweight	ND	IF: 29.41 ± 4.53	IF: 13	12 weeks	TRE	TC, TG, LDL, HDL
		Obesity		CON: 28.43 ± 5.57	CON: 13			
Rizvi, Z. A. [27]	2024	Overweight	IF: 48.00 ± 8.34	IF: 29.95 ± 3.47	IF: 30	12 weeks	TRE	TC, TG, LDL, HDL, BMI, WC
		Obesity	CON: 48.50 ± 6.67	CON: 31.04 ± 4.68	CON: 30			
Skarstad, Hanna M. S. [35]	2024	Overweight	IF: 32.20 ± 3.80	IF: 29.90 ± 5.50	IF: 17	5 weeks	TRE	TC, TG, LDL, HDL, HbA1c, SBP, DBP, BW
		Obesity	CON: 30.10 ± 2.90	CON: 28.50 ± 5.30	CON: 15			
A. Obermayer [42]	2023	Obesity	IF: 65.00 ± 6.00	IF: 33.50 ± 4.70	IF: 22	12 weeks	4:3	HbA1c
			CON: 61.00 ± 7.00	CON: 35.00 ± 4.30	CON: 24			
M. B. Cooke [29]	2022	Overweight	IF: 37.00 ± 5.90	IF: 30.00 ± 3.90	IF: 8	16 weeks	IER	TC, TG, LDL, HDL, FPG, HbA1c, WC, WHR
		Obesity	CON: 32.00 ± 8.30	CON: 32.00 ± 4.40	CON: 9			
Domaszewski [37]	2022	Overweight	ND	IF: 28.00 ± 1.65	IF: 23	6 weeks	TRE	BW, BMI, WC
				CON: 28.38 ± 1.72	CON: 23			
Guo, Y. [17]	2021	Overweight	IF: 40.20 ± 5.70	IF: 28.00 ± 8.21	IF: 23	8 weeks	5:2	TC, TG, LDL, HDL, BW, BMI, WC
		Obesity	CON: 42.70 ± 4.10	CON: 27.70 ± 2.66	CON: 23			
Lisa S. Chow [40]	2020	Overweight	IF: 46.50 ± 12.40	IF: 33.80 ± 7.60	IF: 11	12 weeks	TRE	TG, LDL, HDL
		Obesity	CON: 44.20 ± 12.30	CON: 33.40 ± 7.80	CON: 9			
K. Gabel [30]	2019	Overweight	IF: 43.00 ± 3.00	IF: 34.00 ± 1.00	IF: 34	6 months	ADF	TC, TG, LDL, HDL, SBP, DBP, BW, BMI
		Obesity	CON: 41.00 ± 3.00	CON: 35.00 ± 1.00	CON: 31			
J. F. Trepanowski [15]	2018	Overweight	IF: 46.00 ± 2.00	IF: 34.00 ± 1.00	IF: 25	12 weeks	ADF	TC, TG, LDL, HDL, FPG, BW
		Obesity	CON: 44.00 ± 2.00	CON: 34.00 ± 1.00	CON: 25			
R. Schübel [32]	2018	Overweight	IF: 49.40 ± 9.00	IF: 32.00 ± 3.80	IF: 49	12 weeks	IER	LDL, HDL, TG, FPG
		Obesity	CON: 50.70 ± 7.10	CON: 31.10 ± 3.60	CON: 52			
S. Bhutani [33]	2013	Obesity	IF: 42.00 ± 2.00	IF: 35.00 ± 1.00	IF: 25	12 weeks	ADF	TC, TG, LDL, HDL, FPG, SBP, DBP, BW, BMI
			CON: 49.00 ± 2.00	CON: 35.00 ± 1.00	CON: 16			

Abbreviations: TC total cholesterol, TG triglyceride, LDL low-density lipoprotein, HDL high-density lipoprotein, FPG fasting plasma glucose, HbA1c Hemoglobin A1C, SBP systolic blood pressure, DBP diastolic blood pressure, BW body weight, BMI body mass index, WC waist circumference, WHR, Waist-to-Hip Ratio.

IF intermittent fasting, CON control.

TRE, time-restricted eating, ADF alternate day fasting, IER intermittent energy restriction, 5:2 twice-weekly fasting, 4:3 intermittent fasting.

ND not-described

(95%CI: -5.24, 0.39), $P = 0.09$, 5 experiments] and WHR [MD: -0.02(95% CI: -0.09, 0.04), $P = 0.50$, 3 experiments], BMI ($I^2 = 0\%$, $P = 0.73$), WC ($I^2 = 15\%$, $P = 0.32$) with low heterogeneity, BW ($I^2 = 38\%$, $P = 0.12$), WHR ($I^2 = 71\%$, $P = 0.03$) with medium heterogeneity. Visual interpretation of funnel plots suggests possible publication bias. (Figures S12-S19)

Blood pressure

IF did not significantly increase or decrease SBP [MD: -1.51 mmHg (95% CI: -3.46, 0.45), $P = 0.13$, 4 experiments], but decreased DBP [MD: -3.30 mmHg [95% CI: -5.47, -1.13), $P = 0.003$, 4 experiments], SBP ($I^2 = 22\%$, $P = 0.28$) had low heterogeneity and DBP ($I^2 = 63\%$, $P = 0.04$) had moderate heterogeneity. Visual interpretation of funnel plots suggests possible publication bias. (Figures S20-S23)

Glycemic markers

IF did not significantly reduce FPG [MD: -3.36 mg/dl (95% CI: -9.02, 2.31), $P = 0.25$, 5 experiments], HbA1c [MD: -0.64 mg/dl (95% CI: -2.04, 0.77), $P = 0.37$, 4 experiments], HbA1c ($I^2 = 19\%$, $P = 0.30$) had low heterogeneity, but FPG ($I^2 = 94\%$, $P < 0.00001$) had high heterogeneity. However, sensitivity analyses showed a change in the significance of FPG ($I^2 = 46\%$, $P = 0.14$) after exclusion of the S. Bhutani [33] study, where the intervention was implemented in phases, with strict dietary control for the first 4 weeks, followed by an autonomous diet for the next 8 weeks, a phased design that may have led to fluctuations in adherence and weakened the sustained effect of the ADF on glycemic regulation, and the autonomous dietary phase may have been be accompanied by an increase in calorie or carbohydrate intake, partially offsetting the improvement in insulin sensitivity associated with fasting and resulting in weak changes in FPG. The ADF group was predominantly female (24/25), and estrogen levels may have influenced changes in FPG by modulating hepatic gluconeogenesis and insulin signaling pathways, leading to differences in results from other gender-balanced studies. The dropout rate was as high as 36% (9/25) in the ADF group. The final completers may be a subgroup with greater metabolic adaptability, with smaller than expected FPG changes, deviating from the results of other studies. Visual interpretation of funnel plots suggests possible publication bias. (Figures S24-S28)

Subgroup analyses

Lipid profiles

To further explore the effect of intervention time on TC levels, the present study used a predefined subgroup analysis strategy, starting with 12 weeks as the intervention time point. Given that the subgroups of intervention time > 12 weeks TC [MD: -3.06 mg/dl (95% CI: -8.09,1.96), $P = 0.23$; 3 experiments] and ≤ 12 weeks TC [MD: -7.33 mg/dl (95% CI: -16.17,1.51), $P = 0.10$; 7 experiments] did not have statistically significant results, we further analyzed the subgroups with 8 weeks as the intervention time point. The results were not statistically significant, and we further performed an exploratory subgroup analysis with 8 weeks as the intervention time point. Subgroup analysis based on intervention time showed that intervention time greater than 8 weeks significantly decreased TC [MD: -8.06 mg/dl (95% CI -14.47, -1.65), $P = 0.01$, 8 experiments], intervention time less than or equal to 12 weeks significantly decreased LDL [MD: -7.34 mg/dl (95% CI: -14.11, -0.58), $P = 0.03$, 9 experiments] and increased TG [MD: 13.22 mg/dl (95% CI: 3.39, 23.05), $P = 0.008$, 8 experiments]. Subgroup analysis according to IF form showed that ADF significantly decreased TC [MD: -5.11 mg/dl (95% CI: -9.57, -0.66), $P = 0.02$, 4 experiments] and LDL [MD: -8.88 mg/dl (95%CI: -12.06, -5.71), $P < 0.00001$, 5 experiments]. No IF form significantly increased or decreased TG. (Figures S29-S35)

Body composition

Subgroup analyses according to intervention duration showed that intervention duration less than or equal to 12 weeks and greater than 12 weeks reduced BW and BMI, but intervention duration greater than 12 weeks more significantly reduced BW [MD: -4.67 kg (95% CI: -7.68, -1.67), $P = 0.002$, 3 experiments] and BMI [MD: -1.42 kg/m^2 (95% CI: -2.66, -0.18), $P = 0.02$, 2 experiments]. Subgroup analysis according to the IF form showed that ADF significantly reduced BW [MD:-4.43 kg (95% CI: -6.27, -2.58), $P < 0.00001$, 3 experiments], for BMI, both ADF and TRE had a significant effect on BMI reduction, but the results of ADF for BMI [MD: -1.00 kg/m^2 (95% CI: -1.38, -0.62), $P < 0.00001$, 2 experiments] results were highly statistically significant, whereas TRE was statistically significant for BMI [MD: -1.02 kg/m^2 (95% CI: -1.98, -0.07), $P = 0.03$, 3 experiments] results, but with a larger P-value relative to the ADF, and with slightly weaker statistical significance. However, because the number of studies, sample sizes, and inter-study heterogeneity may differ between the two groups, it is not possible to state with absolute certainty which is more effective, ADF or TRE, solely on the basis of the available data. (Figures S36-S39)

Discussion

A systematic review and meta-analysis of randomized controlled trials of IF showed that IF effectively lowered TC and LDL, and reduced BW, BMI, and DBP compared to CON. IF could be an effective approach for long-term weight loss and improved cardiometabolic health in overweight or obese adults.

Lipid profiles

The relationship between excessive obesity and cardiovascular metabolic diseases, such as dyslipidemia, has been widely explored. The underlying mechanisms may involve multiple pathophysiological pathways, including chronic inflammation, insulin resistance, and adipose tissue dysfunction [43–45]. Current evidence [11] suggests that weight loss achieved through dietary interventions is effective in ameliorating dyslipidemia in people who are overweight or obese, and that this benefit persists over long-term follow-up. Previous meta-analyses have shown [46] that IF can significantly reduce TC, LDL, and TG without affecting HDL levels. However, this study found that IF increased TG compared to CON, and according to the subgroup analysis, the duration of intervention less than or equal to 12 weeks was the main reason for its increase. This may be due to the fact that during the initial period of fasting, the body has not yet fully adapted to this new eating pattern, and the drastic reduction in energy intake causes the body to mobilize stored fat for energy, resulting in an increase in free fatty acids and TG in the blood [47]. Short-term IF may promote the release of free fatty acids (FFA) from adipose tissue through activation of the sympathetic nervous system and adipose catabolic hormones, whereas the liver, after ingesting an excessive amount of FFA may result in the re-esterification of FFA to TG and accumulation in the circulation due to the fact that its lipid oxidizing capacity has not yet fully adapted or increased carbohydrate intake during refeeding [48]. Also, the body may absorb and store energy more efficiently when feeding, which may lead to a temporary elevation of TG levels [47]. In addition, the regulatory effects of IF on the intestinal flora may have a time-dependent effect. Some animal experiments have shown that IF needs to be sustained for at least 8 weeks to significantly improve lipid metabolism via the "gut flora-metabolite-platelet" axis, and short-term interventions may be insufficient to inhibit hepatic TG synthesis due to insufficient accumulation of flora metabolites [48]. Individual differences may also contribute to the increase in TG, and there may be differences in the responses to IF in different individuals. IF response may vary, including the effects of age, gender, genetics, and other factors. Notably, the metabolic benefits of IF showed a trend toward attenuation with prolonged duration of intervention, which may be related to decreased long-term adherence, partial rebound in body weight, and increased compensatory energy intake [46]. Short-term IF may need to be implemented with caution in populations at risk for dyslipidemia. Clinicians should be concerned about patients' baseline TG levels and dietary composition during the refeeding period, and low-carbohydrate or low-glycemic index foods are recommended to reduce hepatic TG synthesis. Future studies need to further clarify the time-course pattern of TG changes in IF interventions and provide a basis for the development of individualized intervention protocols by dynamically monitoring biomarkers such as FFA and intestinal flora metabolites.

Body composition

Weight loss is the most visual indicator of weight loss effectiveness. Changes in body weight are widely used in weight loss research and practice to assess the effectiveness of weight loss interventions because they are easy to measure and directly reflect changes in body composition. A systematic study evaluating weight loss interventions combining diet and physical activity found that weight change was measured in all studies and that weight loss was consistent with improvements in body composition [49]. Weight loss is usually accompanied by a reduction in body fat, which is one of the core goals of weight loss. The meta-analysis showed that IF significantly reduced BW and BMI, but the improvement in WC and WHR did not reach statistical significance. The significant reduction in BW and BMI by IF may be related to IF-induced negative energy balance, enhanced fat oxidation and improved insulin sensitivity. Based on subgroup analysis, ADF and TRE may have significant effects in reducing BMI, and the 5:2 diet did not show a significant difference in BMI from the control group in this analysis. As for BW, only ADF showed a more significant effect in reducing BW. This difference may be related to the more stringent energy restriction of ADF, whose cyclical deep caloric deficit is more likely to trigger fat mobilization; in contrast, TRE, although synchronized to optimize glucose-lipid metabolism through circadian rhythms, may limit the depth of fat mobilization with its shorter daily fasting window. In addition, the lower frequency of weekly food restriction on the 5:2 diet may have attenuated the overall negative energy balance. A meta-analysis has shown [50] that ADF is more effective in reducing WC than other forms of IF; however, the lack of a significant reduction in WC in this study seems to contradict this meta-analysis improvement, and differences in the sensitivity of the measurement methods may affect the reliability of the results [51]. WC and WHR are used as surrogate indices of abdominal fat distribution, and the imaging technique can accurately differentiate between visceral and subcutaneous fat, whereas traditional tape measurements may mask subtle changes in visceral fat due to individual measurement errors or changes in body position. Measurements may mask subtle changes in visceral fat due to individual measurement error or postural changes. Second, insufficient intervention duration may be a key limiting factor. Visceral fat has a high metabolic inertia and its reduction usually lags behind changes in overall adiposity, and the length of the intervention in the included studies may not have

been sufficient to induce a significant remodeling of the abdominal fat depots, especially since the mobilization of visceral fat requires a more sustained negative energy homeostasis and lipid oxidation adaptations [52]. In addition, IF may preferentially mobilize nonabdominal subcutaneous fat [53] whereas visceral fat is less sensitive to catecholamines due to its richness in β3-adrenergic receptors, resulting in a slower rate of catabolism [54]. This adipose depot-specific response with gender differences, such as the propensity of females to store fat in the hips, may further confound the direction of change in the WHR [55]. The lack of improvement in WC and WHR suggests that IF may have a limited role in reducing total body weight while improving metabolic risk associated with central obesity, especially when the intervention cycle is short. For those at high cardiovascular risk, reliance on IF alone may require prolonged intervention time to achieve substantial reduction in visceral fat, or combined resistance training to enhance the efficiency of abdominal fat oxidation. In addition, WC and WHR measurements should be standardized and attention should be paid to the heterogeneity of individualized fat distribution patterns in response to IF. Future studies need to clarify the time-course effects of IF on different fat depots through a longitudinal design combined with body composition analysis and explore the synergistic modulation of abdominal fat metabolism by dietary nutrient rationing.

Blood pressure

The results showed that although IF did not significantly alter SBP, it significantly reduced DBP, a finding that suggests that IF may selectively improve peripheral vascular resistance or autonomic regulation through specific mechanisms, resulting in beneficial effects on diastolic blood pressure, but its modulation of systolic blood pressure was limited [56]. IF-induced energy deficit reduces inflammation and oxidative stress in adipose tissue, which improves vascular endothelial function and reduces peripheral vascular resistance [57]. This mechanism is particularly important for the regulation of DBP, which better reflects peripheral arterial vascular tone during diastole. In addition, IF may indirectly promote vasodilation by modulating gut microbiota-derived metabolites or by inhibiting the activity of the renin-angiotensin system [58]. However, the lack of a significant decrease in SBP may be due to the following reasons. First, SBP is influenced by a number of factors, such as large artery elasticity, cardiac output, and blood volume. The mean reduction of 3.21 kg body weight in this study may not have been sufficient to significantly alter these macroscopic hemodynamic parameters. Second, the duration of intervention in these studies was relatively short, with most studies lasting less than 12 weeks, and improvement in SBP may require a longer period of vascular remodeling or reduction in arterial stiffness [59]. In addition, heterogeneity among studies may affect the generalizability of findings. Although the number of studies was insufficient for subgroup analyses, we hypothesized that ADF may partially counteract the antihypertensive effects of intermittent starvation stress activating the sympathetic nervous system, whereas TRE may be more conducive to BP regulation by aligning the eating window with circadian rhythms.

Glycemic markers

In the present study, we found that IF did not significantly reduce FPG and HbA1c, and although the downward trend in FPG approached statistical significance, the differences were large, suggesting inconsistency between studies, whereas the reduction in HbA1c was small and non-significant, a result that suggests that, although IF may trigger short-term metabolic adaptations through cyclic fasting, it has a limited role in regulating glycemic homeostasis in the long term. The transient decrease in fasting insulin-induced FPG may be related to the inhibition of hepatic gluconeogenesis and the transient enhancement of insulin sensitivity during fasting [60–62]. Fasting reduces the supply of glucose substrates by restricting the duration of eating, thereby decreasing glucose output from the liver. At the same time, the activation of autophagy triggered by fasting may improve glucose uptake by peripheral tissues such as skeletal muscle [63]. However, these effects may be offset by compensatory elevations in counter-regulatory hormones during fasting [64], especially in individuals who have not yet fully adapted to the metabolic transition, and thus it is difficult to significantly disrupt glycemic homeostasis [63]. In addition, HbA1c, which reflects long-term glucose exposure, did not change significantly, further suggesting that, although IF can optimize glycemic fluctuations in the short term, it does not sustainably reverse the core pathological mechanisms of insulin resistance or β-cell dysfunction.

Future implications

The findings of this study provide an important basis for the clinical application of IF. In the future, it is necessary to validate the sustainability of its metabolic benefits through standardized intervention protocols (e.g., clarifying the fasting cycle, energy restriction ratio, and nutritional structure of the refeeding period) in combination with long-term follow-up (> 12 months), and to dynamically monitor the distribution of visceral fat, FFA, and intestinal flora metabolites with the help of imaging techniques and metabolomics to reveal the molecular mechanisms by which IF regulates The molecular mechanism of lipid oxidation. To address the heterogeneity of

the population, stratified studies are needed to develop individualized strategies, such as optimizing the fasting-feeding cycle in hypertriglyceridemic or insulin-resistant populations and exploring the synergistic effects of IF in combination with resistance training or low-carbohydrate diets. For clinical translation, high-quality evidence needs to be accumulated to support guideline development, clarify the safety and indications of IF in special populations (e.g., patients with diabetes, cardiovascular disease), and develop digital management tools (e.g., AI-driven dynamic adjustment of fasting window, real-time monitoring by wearable devices) to improve adherence. Through interdisciplinary integration of mechanism research, precision medicine and behavioral interventions, IF is expected to shift from a universal model to individualized health management, and ultimately achieve comprehensive prevention and control of cardiovascular and metabolic risks.

Limitations

While this meta-analysis provides critical insights into the effects of IF, several limitations warrant consideration. First, the majority of included studies featured short-term interventions (≤ 12 weeks), which may inadequately capture the full spectrum of metabolic adaptations (e.g., sustained improvements in visceral fat reduction or glycemic control) and long-term risks such as weight regain. The lack of follow-up data beyond intervention periods further limits our understanding of the durability of IF's benefits. Second, heterogeneity in IF protocols—including variations in fasting duration (e.g., 16:8 vs. 5:2), energy restriction intensity, and dietary composition during feeding windows—complicates cross-study comparisons and generalizability. Third, reliance on surrogate markers like waist circumference (measured via tape) rather than imaging techniques (e.g., MRI/CT) may underestimate or misrepresent visceral fat dynamics, a key determinant of cardiometabolic risk. Additionally, the predominance of studies in metabolically stable populations limits insights into IF's efficacy and safety in high-risk subgroups, such as those with advanced insulin resistance or cardiovascular comorbidities. Finally, while sex-specific responses were noted, the mechanisms underlying these differences remain unexplored. Future studies should prioritize long-term RCTs (> 12 months) with standardized protocols, imaging-based body composition assessments, and stratified analyses by metabolic phenotype to address these gaps.

Conclusions

IF, as a non-pharmacological intervention, has clear value in weight management and metabolic improvement, and may become a mainstream approach due to its advantages in adherence and metabolic regulation. However, its long-term efficacy and safety require verification by more high-quality studies. In the future, precise and sustainable IF strategies need to be developed within the framework of personalized medicine to achieve comprehensive optimization of cardiometabolic health.

Supplementary Information

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Supplementary Material 1

Author contributions

All authors carried out the screenings and reviews, plus the analysis of the articles. Bingjie Wang drafted the manuscript and Bingjie Wang, Chen Wang, revised the manuscript. All authors read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Human Ethics and Consent to Participate

Not applicable.

Consent for publication

All authors approved the final version of the manuscript, and agreed for all aspects of the work to be published.

Competing interests

The authors declare no competing interests.

Clinical trial number

Not applicable.

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