Original Article

Efficacy of intermittent fasting on blood glucose and weight in type 2 diabetes and prediabetes: A comparison with ad libitum and continuous energy restriction diets

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Background and Objectives: This study aimed to evaluate the effects of intermittent fasting (IF) on glycated hemoglobin (HbA1c), fasting blood glucose (FBG), body weight (BW), and body mass index (BMI) in patients with type 2 diabetes mellitus (T2DM) and prediabetes. **Methods and Study Design:** A systematic search of PubMed, Cochrane Library, Embase, Scopus, and Web of Science was conducted for randomized controlled trials on IF in T2DM and prediabetes published before September 30, 2025. Meta-analysis was performed using RevMan 5.3 and Stata 17.0. **Results:** Fourteen studies (sixteen arms), involving 899 patients, were included. Four studies (five arms) compared IF with ad libitum diet (316 patients), and ten studies (eleven arms) compared IF with continuous energy restriction diets (CERD) (583 patients). Meta-analysis showed that IF was more effective than the ad libitum diet in reducing HbA1c, BW, BMI and FBG (Standardized Mean Difference (SMD) (Hedges's g) -0.64, 95% Confidence Interval (CI) -1.04, -0.24; $p<0.05$), (SMD (Hedges's g) -0.30, 95% CI -0.55, -0.05; $p<0.05$), (SMD (Hedges's g) -0.26, 95% CI -0.51, 0.00; $p=0.05$), (SMD (Hedges's g) -0.39, 95% CI -0.64 to -0.15; $p<0.05$). IF demonstrated effects similar to CERD ($p>0.05$) in terms of HbA1c, BW, BMI, and FBG. Among 14 studies, dropout rates were 21.5% (IF), 26.2% (CERD), and 15.9% (ad libitum). CERD showed a significantly higher dropout rate than ad libitum, whereas no significant differences were observed between IF and CERD or between IF and ad libitum. **Conclusions:** Intermittent fasting is a effective dietary approach for patients with T2DM and prediabetes.

Key Words: intermittent fasting, type 2 diabetes, prediabetes, fasting blood glucose, weight

INTRODUCTION

Type 2 diabetes mellitus (T2DM) and pre-diabetes are chronic metabolic diseases that are highly prevalent worldwide and are one of the greatest public health threats of the 21st century, affecting approximately 1 billion adults worldwide.[1, 2] Prediabetes is a state between diabetes and normal blood sugar and is considered to be a necessary stage of diabetes, genetic factors, overweight or obesity, dyslipidemia, and poor lifestyle factors can cause abnormal blood sugar metabolism. Current estimates suggest that impaired fasting glucose and impaired glucose tolerance, these pre-diabetic states, represent a patient's hyperglycemic status.[3] T2DM is associated with poor dietary habits and sedentary behavior, significantly harming human health.[4, 5] Currently, approximately 529 million adults globally have diabetes, and it is projected that by 2045, the prevalence of T2DM will reach 12%.[6] The risk factors for diabetes include genetics, diet, and lifestyle,[7] with obesity being an independent risk factor and a key mechanism in the development of the disease.[8] According to the U.S. Centers for Disease Control and Prevention, the risk of diabetes among American adults is 40%, and a modest 5% weight loss can significantly aid in blood glucose control.[9] Additionally, lack of physical activity is a major contributing factor to T2DM.[10] Lifestyle interventions, such as a balanced diet, regular exercise, and weight management, are essential for managing diabetes.

Dietary interventions such as intermittent fasting (IF) and continuous energy restriction diets (CERD) are

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essential components in the management of T2DM and prediabetes.[11] Therefore, individualized dietary plans are recommended for patients with T2DM or prediabetes to optimize glycemic control and achieve long-term metabolic health.[12] CERD has been shown to be effective for improving glycemic parameters and other metabolic outcomes.[13] Because energy restriction will induces pronounced hunger and discomfort—including dizziness, fatigue, and reduced energy—most individuals find it difficult to sustain prolonged CERD, and some may even develop disordered eating patterns or experience weight regain after initial loss. Although short-term energy restriction is generally well tolerated and confers clear metabolic benefits, long-term adherence remains poor. Consequently, intermittent fasting has emerged as a more feasible alternative, offering structured cycles of fasting and ad libitum feeding while delivering metabolic and anti-inflammatory improvements comparable to continuous caloric restriction, often independent of weight loss.[14,15]

Intermittent fasting encompasses several approaches.[16,17] One category is alternate-day fasting (ADF), which involves a 36-hour fasting period every other day, followed by a 12-hour period of unrestricted eating. A modified version, modified alternate-day fasting (MADF), typically includes 3–5 fasting days per week, alternating with regular eating days, with caloric intake during fasting days limited to 0–40% of daily needs (approximately 0–600 kcal/day). The 5:2 or 5:3 diet includes two or three fasting days per week with similar caloric restriction, and unrestricted eating on the remaining days. Another popular form is time-restricted feeding (TRF), which confines food intake to a specific window each day—typically 8 hours—without restricting caloric intake during this period. The remaining 16 hours are fasting. TRF can be further subdivided into early TRF, with an eating window from 6 a.m. to 3 p.m., and midday TRF, with eating from 11 a.m. to 8 p.m. fasting-mimicking diet (FMD) is a periodic, low-calorie and specific macronutrient–restricted dietary approach designed to mimic the metabolic effects of prolonged fasting while allowing limited food intake. It is typically implemented in short cycles of several consecutive days with markedly reduced energy intake, followed by a return to habitual eating. Despite the diversity of IF regimens and their growing popularity, evidence regarding their efficacy in individuals with T2DM and prediabetes remains incomplete.

Several meta-analyses have examined the effects of IF on body weight and glucose metabolism. Schroor et al. analyzed 28 studies and found no differences in glucose or insulin control between IF and continuous energy restriction; however, their analysis focused on apparently healthy adults rather than dysglycemic populations.[18] Borgundvaag et al. evaluated seven trials in individuals with T2DM and reported weight loss with IF but no clear glycaemic advantage over standard diets; this review was limited by an early search cutoff (August 2020) and the absence of an active comparator such as CERD.[19] Similarly, Sharma et al. included 11 studies and found no glycaemic differences between IF and caloric restriction, but their review also had an early cutoff (April 2022) and did not compare IF with ad libitum diets.[20] In the meta-analysis by Khalafi et al., normal diet and calorie restriction were combined into a single comparator despite representing distinct physiological conditions–ad libitum intake versus active energy restriction—potentially affecting interpretation of IF's metabolic effects.[21]

Prior reviews have either relied on isolated pairwise comparisons (e.g., IF vs. CERD or IF vs. ad libitum) or pooled CERD and ad libitum diets into a single comparator group–approaches that obscure the distinct effects of negative versus active controls or lack comprehensive comparison. Additionally, evidence in individuals with T2DM and prediabetes has been limited by small sample sizes and narrow outcome measures. By integrating IF, CERD, and ad libitum comparisons within a unified analytical framework, this study addresses these limitations and offers a more comprehensive evaluation of the comparative efficacy of intermittent fasting.

Therefore, this meta-analysis synthesizes randomized controlled trials (RCTs) to compare the effects of IF, CERD, and ad libitum diets on glycated hemoglobin (HbA1c), fasting blood glucose (FBG), body weight (BW), and body mass index (BMI) in patients with T2DM and prediabetes. The goal is to provide more robust and clinically relevant evidence for the application of IF as a therapeutic strategy in these high-risk populations.

METHODS

Registration information

This study was designed and conducted as a systematic review with pairwise meta-analyses, registered a priori in the International Prospective Register of Systematic Reviews (PROSPERO) under ID CRD 42024572320. The methodology adhered strictly to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[22]

Search strategy

The search was conducted for RCTs published from the inception of the databases to September 30, 2025, focusing on the effects of intermittent fasting on T2DM and prediabetes patients with continuous energy restriction or ad libitum diet as control groups. Five databases were searched: PubMed, Cochrane Library, Embase, Scopus, and Web of Science. Additionally, relevant systematic reviews and references from included studies were tracked to identify any additional studies. Search strategies combined medical subject headings and keywords, adjusted according to the search logic of each database. Search terms included "fasting", " intermittent fasting", " intermittent energy restriction", "intermittent calorie restriction", "periodic fasting", "alternate-day fasting", "zero-calorie alternate-day fasting", "modified alternate-day fasting", "time-restricted feeding", "5:2diet", "time-restricted eating", "diabetes", "diabetes mellitus", "type 2 diabetes", "prediabetes", and "randomized controlled trials" (Supplementary Table 1-5).

Inclusion and exclusion criteria

For the purposes of this systematic review and meta-analysis, prediabetes was defined by the following criteria: FBG levels between 5.6 and 6.9 mmol/L, HbA1c levels ranging from 5.7% to 6.4%, and 2-hour glucose (2hG) levels between 7.8 and 11 mmol/L. T2DM was defined as FBG ≥7.0 mmol/L, HbA1c ≥6.5%, or 2hG ≥11.1 mmol/L.[23-25]

Included studies must meet the following criteria:

(1) Randomized controlled trials from the date of database establishment to September 30, 2025: PubMed, Cochrane Library, Embase, Scopus, and Web of Science.

(2) Adults with T2DM or prediabetes.

(3) Intervention: Intermittent fasting regimens (e.g. ADF, MADF, TRF, 5:2 diet, FMD).

(4) Comparison: CERD, Mediterranean diet, or ad libitum diet.

(5) Outcomes: HbA1c, FBG, BW, and BMI.

Studies with the following characteristics were excluded:

(1) Duplicate publications.

(2) Study protocols, conference abstracts, case reports, non-randomized trials, studies with ad libitum diet or CERD as control groups without valid controls.

(3) Studies with omitted or erroneous outcome data.

(4) Studies that do not report relevant outcome measures.

(5) Animal studies.

(6) Studies with insufficient information where necessary summary statistics could not be retrieved or calculated, and where attempts to contact the original authors were unsuccessful or the provided data did not meet the necessary conditions.

(7) Non-peer-reviewed articles and gray literature.

(8) Studies related to religious fasting (e.g., Ramadan) were also excluded.

Data collection

After removing duplicates and manually checking for duplicates using Endnote X9 software, two researchers trained in evidence-based methods independently conducted literature screening and data extraction according to the inclusion criteria. Discrepancies were resolved through discussion between the researchers or by involving a third researcher. The kappa statistic was employed to evaluate the level of agreement between raters. A kappa score of ≤ 0.20 indicated a poor level of agreement, 0.21-0.40 denoted a fair agreement, 0.41–0.60 was considered a moderate agreement, 0.61–0.80 signified a good agreement, and a score ranging from 0.81–1.00 represented an excellent agreement.[26]

The screening process consisted of two stages: an initial screening of titles and abstracts, followed by a full-text review. Data were extracted using Microsoft Excel, including author information, publication year, country, sample size, intervention, control conditions, and outcome indicators (Table 1). To calculate effect sizes, the means and standard deviation (SD) before and after the intervention were used. When necessary, data were extracted from figures. If the required data could not be obtained, corresponding authors were contacted to request the missing information. Additionally, when needed, blood glucose values reported in mg/dL were converted to mmol/L using the formula: mg/dL × 0.06 = mmol/L.

Quality assessment

During the meta-analysis, two researchers independently extracted data from each study, including general information (first author, year, country), participant characteristics, intervention and control diets, and primary outcome measures. Participant characteristics included age and sample size. The primary outcomes were HbA1c, FBG, BW, and BMI. For studies with incomplete or imprecise results, attempts were made to contact the original authors to obtain additional data. Data extraction forms and their content were jointly verified by the two researchers.

Each study's risk of bias was independently assessed using the Cochrane Handbook, and statistical evaluations were conducted using Review Manager software (Review Manager 5.3). During the assessment, the reviewers classified the studies as "low risk," "high risk," or "unclear risk." Studies were deemed to have a low risk of bias if they adequately addressed all aspects of selection, performance, attrition, and reporting bias. Those that did not sufficiently address these outcomes were considered to have a high risk of bias, while studies where a definitive judgment could not be made were categorized as having an unclear risk of bias (Supplementary Table 6).

Data synthesis and statistical analysis

This analysis employed standard pairwise meta-analysis techniques to compare intermittent fasting directly against control diets. Meta-analysis was conducted using Stata 17.0 software. Standardized Mean Difference (SMD), calculated as Hedges's g when measurement units varied, and 95% Confidence Interval (CI) were estimated using a random-effects model. A random-effects model was chosen because there may be heterogeneity among the included clinical trials, which could affect the results. The random-effects model was preferred for analysis to account for potential heterogeneity. The I^2 statistic was used to determine the heterogeneity among the included studies, and its interpretation is as follows: I^2 values of <25%, 50%, 75%, and >75% were defined as low, moderate, high, and considerable heterogeneity, respectively. Publication bias was assessed by visual inspection of funnel plots and by Egger's test. Funnel plots and asymmetry tests were interpreted with caution for outcomes including fewer than 10 studies because of limited statistical power.

Subgroup analyses were conducted according to IF modality, including: (1) TRF, defined as daily restriction of food intake to a fixed eating window without mandated caloric restriction; (2) MADF, typically includes 3–5 fasting days per week, alternating with regular eating days, with caloric intake during fasting days limited to 0–40% of daily needs; and (3) FMD, defined as a cyclic low-calorie, low-protein, and low-carbohydrate dietary regimen followed by a return to habitual eating.[27,28] Differences between subgroups were considered significant at p <0.05.

RESULTS

Study selection and study characteristics

A total of 179981 articles were identified through the electronic database search. After removing duplicates, 75334 records were excluded. The remaining 104647

Table 1. The study procedure

Study	Country	Participants	Intervention	Control	Main outcome
Yang X et al.[29] 2023	China	72 (36, 36) 18-75years	Three-month intervention with repeated 15-day cycles, each including five modified fasting days (~840 kcal/day) using CMNT kits following the regular meal schedule.	Three-month intervention: Participants followed ad libitum diets and adhered to the Dietary Guidelines for Diabetes in China.	1, 2, 4
Umphon-sathienet M et al. [1][30] 2022	Thailand	26 (14, 12) 30-60 years	20 weeks intervention: A very-low-calorie diet (VLCD) for 2 days per week (600–800 kcal/day) and consumed a normal diet on the remaining 5 days.	20 weeks intervention: 1,500–2,000 kcal/day diet with ongoing standard diabetes care.	1, 2
Umphon-sathienet M et al. [2][30] 2022	Thailand	26 (14, 12) 30-60 years	20 weeks intervention: A VLCD for 4 days per week (600–800 kcal/day) and consumed a normal diet on the remaining 3 days, with at least 2 VLCD days performed consecutively.	20 weeks intervention:1,500–2,000 kcal/day diet with ongoing standard diabetes care.	1, 2
Che T et al.[31] 2021	China	104 (54, 50) 18-70 years	14-week intervention: Participants followed a 10-hour TRF schedule, eating ad libitum between 8:00 and 18:00 hours, and fasting from 18:00 to 8:00 hours.	14-week intervention:Participants were instructed to maintain their usual eating habits without any restrictions on meal timing.	1, 2, 4
Elske L et al 2024[32]	Netherlands	100 (51, 49) 18-75 years	12 months intervention:The FMD group received 12 cycles of an FMD on five consecutive days monthly as an adjunct to usual care. Day 1 provided ~4600 kJ (~1100 kcal; 10% protein, 56% fat, 34% complex carbohydrate), and days 2–5 each provided ~3150 kJ (~750 kcal; 9% protein, 44% fat, 47% complex carbohydrate).	12 months intervention:usual care only.usual care entailed 3-monthly clinical and biochemical evaluation, lifestyle advice with the option to consult a dietitian, and adaptation of medication use if necessary.	1, 2, 4
Gray KL et al.[33] 2021	Australia	62 (32, 30) ≥18 years	12-month intervention: followed a 500 kcal/day on 2 non-consecutive days/week; habitual diet on remaining days with no prescribed energy restriction.	12-month intervention: followed 1500 kcal/day diets for 7 days/week.	1
McDiarmid S et al.[34] 2021	UK	79 (39, 40) 18-75 years	28-week active phase: 2 days/week of 820 kcal (Optifast®) + 5 days Mediterranean diet; followed by 28-week maintenance: 1-2 days/week of 800 kcal LED + Mediterranean diet; 1 relapse allowed: return to 3-4 weeks of active phase.	12-week active phase comprised 8 weeks of an 820-kcal/day (Optifast®) regimen followed by 4 weeks of a Mediterranean diet (1,000–1,500 kcal/day). 40-week maintenance phase continued the Mediterranean diet with one allowed 820-kcal/day (Optifast®) relapse week.	1
Kender Z et al.[35] 2023	Germany	31 (14, 17) 50-75 years	Participants followed a plant-based fasting-mimicking diet for 5 consecutive days each month, with day 1 providing 4600 kJ and days 2-5 providing 3000 kJ per day.	Participants followed the Mediterranean diet, adapted based on the Mediterranean Diet Score (MDS), and continued their normal diet outside the intervention period.	3
Ash S et al.[36] 2003	Australia	31 (14, 17) 54 years	12-week intervention: 4 days/week of Modifast® (4,180 kJ/day) plus 3 days/week of ad libitum eating; weekly average intake: 6,000–7,000 kJ/day.	12-week interventions：Meals provided on average 6900 kJ/day (1650 kcal/day; 51% of energy from carbohydrate, 20% from protein and 29% from fat).	1, 4, 5

VLCD, very-low-calorie diet; FMD, fasting-mimicking diet; CLED, continuous low-energy diet; ILED, intermittent low-energy diet; TRF, time-restricted feeding.
Main outcome: 1: HbA1c, glycated hemoglobin; 2: FBG, fasting blood glucose; 3: ACR, albumin-to-creatinine ratio; 4: BW, body weight; 5: IER, intermittent energy restriction.

Table 1. The study procedure (cont.)

Study	Country	Participants	Intervention	Control	Main outcome
Carter S et al.[37] 2018	Australia	137 (70, 67) ≥18 years	12-month intermittent energy restriction: 500–600 kcal/day on 2 nonconsecutive days/week; usual diet on other days.	12-month continuous energy restriction: 1,200–1,500 kcal/day, 7 days/week.	1, 4
Williams KV et al. [1][38] 1998	United States	36 (18, 18) 30-70 years	Participants completed 5 consecutive days of VLCD (400–600 kcal/day) in week 2, then one VLCD day weekly during weeks 3–17, with 1,500–1,800 kcal/day on non-VLCD days.	1,500–1,800 kcal/day diet throughout the 20 weeks of the treatment program.	1, 2, 5
Williams KV et al. [2][38] 1998	United States	36 (18, 18) 30-70 years	Participants completed 5 consecutive days of VLCD (400–600 kcal/day) during weeks 2, 7, 12, and 17, with 1,500–1,800 kcal/day on non-VLCD days.	1,500-1,800 kcal/day diet throughout the 20 weeks of the treatment program.	1, 2, 5
Corley BT et al.[39] 2018	New Zealand	37 (18, 19) >18 years	a very-low-calorie diet (2092 kJ for men; 2510 kJ for women) on 2 days per week for 12 weeks, with ad libitum intake on the remaining 5 days; fasting days could be consecutive or not.	continuous day energy restriction for 12 weeks. 2092 kJ in women and 2510 kJ in men.	1
Carter S et al.[40] 2016	Australia	63 (31, 32) ≥18 years	week intervention: 2 days/week of severe energy restriction (1,670–2,500 kJ/day) and 5 days of habitual eating for 12 weeks	12-week energy restriction: 5000–6500 kJ/day.	1, 4
Sulaj A et al.[41] 2022	Germany	40 (21, 19) 50-75years	6-month intervention: monthly 5-day FMD (Day 1: 4,600 kJ — 11% protein, 46% fat, 43% carbs; Days 2–5: 3,000 kJ/day — 9% protein, 44% fat, 47% carbs), followed by 25 days of habitual diet.	6-month intervention: monthly 5-day Mediterranean diet, followed by 25 days of habitual diet.	4
Yahya Pasdar et al.[42] 2025	Iran	49 (24, 25) 18–55 years	12 weeks intervention: Participants maintained their usual calorie intake on 5 days per week and consumed 25% of daily needs (500–600 kcal) on 2 non-consecutive fasting days.	12 weeks intervention: 75% of daily energy requirements and a standard macronutrient ratio (50% carbohydrate, 20% protein, 30% fat).	1, 2, 4

VLCD, very-low-calorie diet; FMD, fasting-mimicking diet; CLED, continuous low-energy diet; ILED, intermittent low-energy diet; TRF, time-restricted feeding.
Main outcome: 1: HbA1c, glycated hemoglobin; 2: FBG, fasting blood glucose; 3: ACR, albumin-to-creatinine ratio; 4: BW, body weight; 5: IER, intermittent energy restriction.

articles were further screened, with 28091 being excluded based on the following criteria: 5909 articles involved animal subjects, 3,781 were related to fasting blood glucose or fasting serum lipids but not intermittent fasting, 3361 were meta-analyses, 5341 were review articles, 6195 were trial registry records, and 3504 involved pregnancy. Following title and abstract screening, 76458 articles did not meet the inclusion criteria. The remaining 98 articles were evaluated according to the inclusion criteria, leading to the inclusion of 14 articles,29-42 while 84 articles were excluded after full-text review for reasons of non-target population, intervention measures not meeting inclusion/exclusion criteria, relevant outcome indicators not reported, duplicate publications, and non-randomized controlled trials. Therefor, 14 articles (16 arms) were included in this review (Figure 1). Among them, 4 RCTs (5arms)29-32 compared IF with ad libitum diet, and 10 RCTs (5 arms)33-42 compared IF with CERD. Details regarding the inclusion are further presented in Table 1.

Main effects: Outcome measures

HbA1c

Ten studies (eleven arms)[33-42] assessed the impact on HbA1c levels between IF and CERD. The forest plot indicates no statistically significant difference between the groups (Figure 2A, [SMD (Hedges's g)] -0.12, 95% CI-0.28, 0.04; p = 0.13, I^2 = 0.00%). The funnel plot demonstrates a pattern that is nearly symmetric (Supplementary Figure 1A), Egger's test indicating no statistically detectable publication bias (Supplementary Table 7).

Four studies (five arms)[29-32] evaluated the effects of intermittent fasting compared with ad libitum diets on HbA1c levels. The pooled analysis demonstrated a statistically significant reduction in HbA1c in the IF group (Figure 2B, [SMD (Hedges's g)] -0.64, 95% CI -1.04, -0.24; *p* = 0.00, I^2 = 65.56%). Visual inspection of the funnel plot suggested asymmetry (Supplementary Figure 1B); however, Egger's test did not indicate statistically significant publication bias (Supplementary Table 8). Sensitivity analyses indicated that the pooled effect

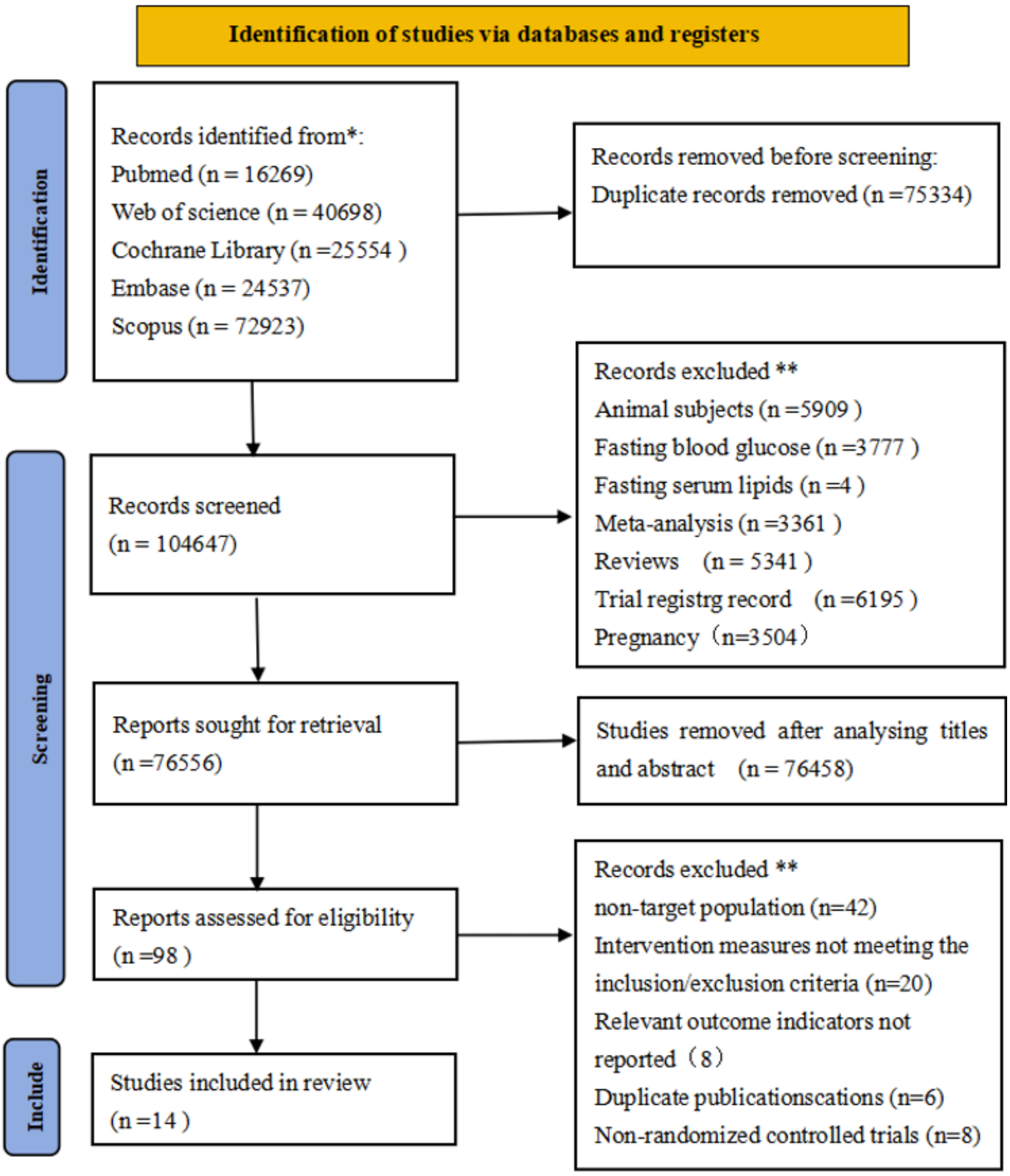

Figure 1. PRISMA flow diagram for the investigated studies.

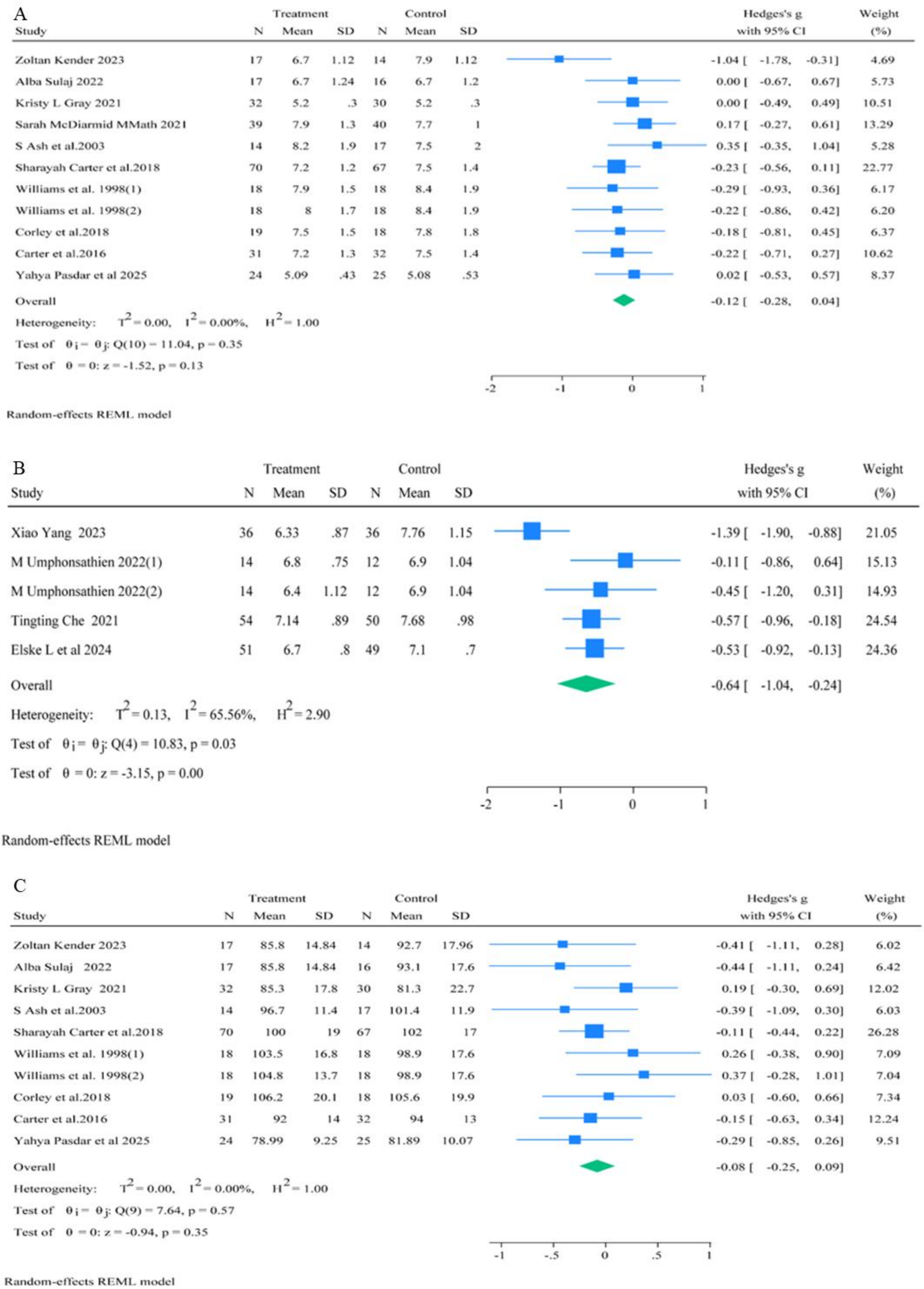

Figure 2. Forest plots comparing IF with CERD and ad libitum diet for glycaemic and anthropometric outcomes: (A-B) HbA1c; (C-D) BW; (E–F) BMI; (G-H) FBG. IF, intermittent fasting; CERD, continuous energy restriction diet.

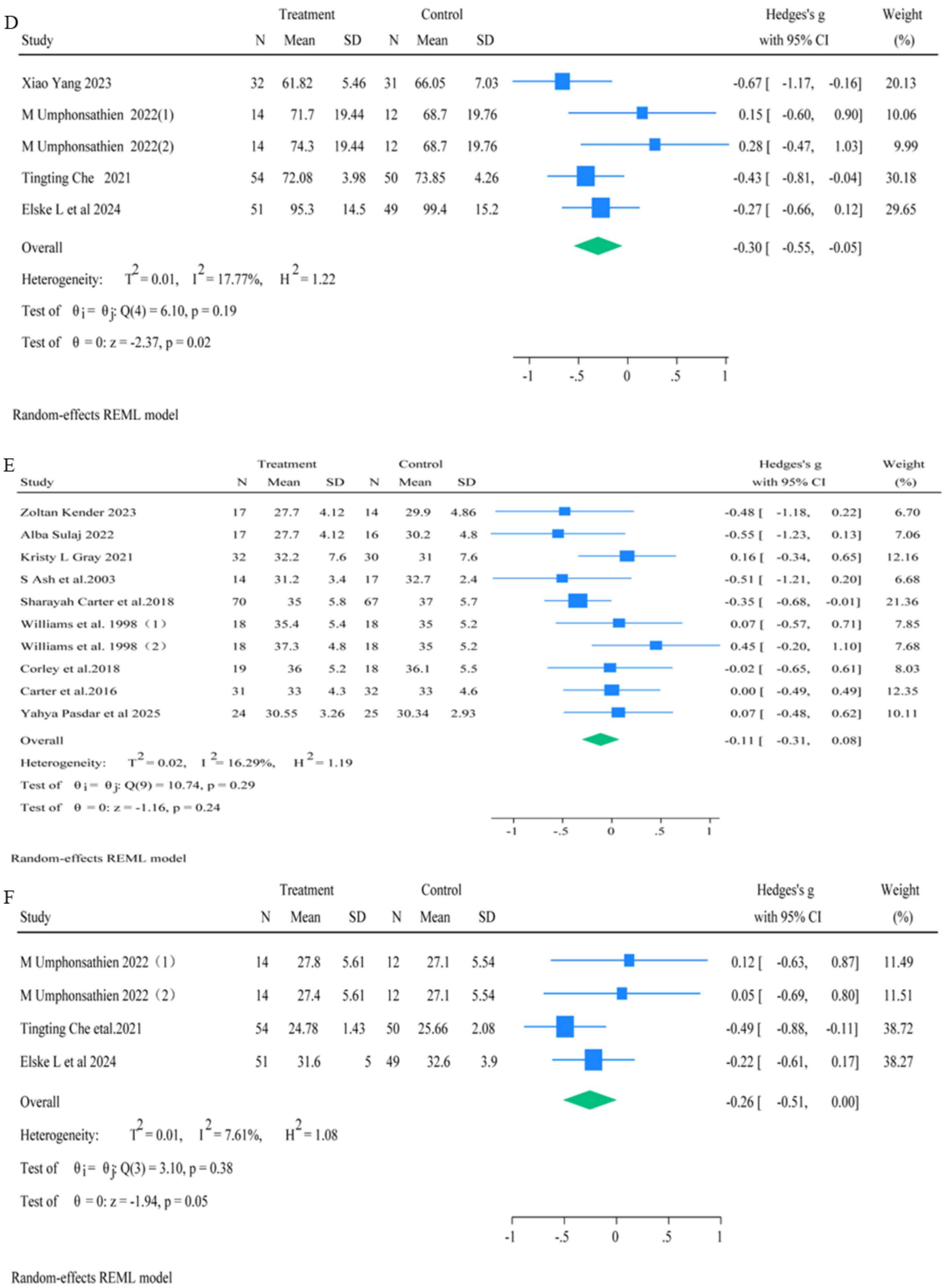

Figure 2. (cont.) Forest plots comparing IF with CERD and ad libitum diet for glycaemic and anthropometric outcomes: (A-B) HbA1c; (C-D) BW; (E–F) BMI; (G-H) FBG. IF, intermittent fasting; CERD, continuous energy restriction diet.

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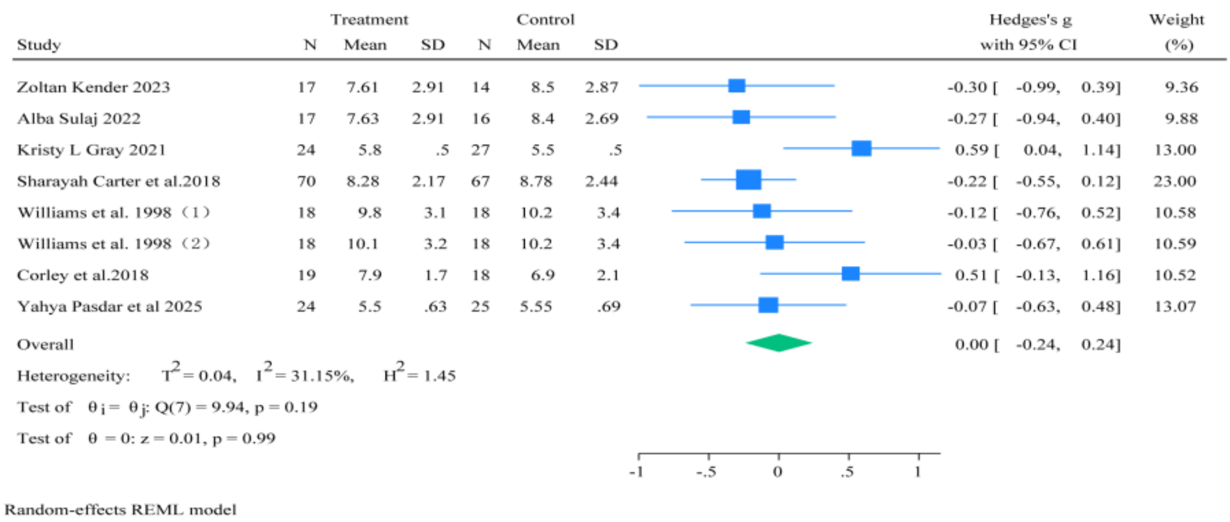

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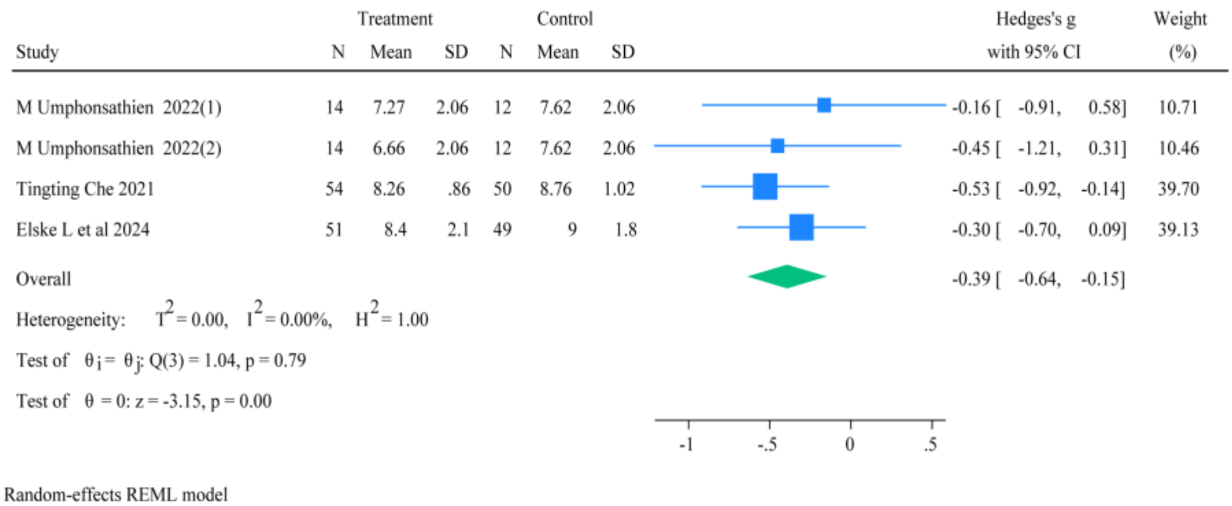

Figure 2. (cont.) Forest plots comparing IF with CERD and ad libitum diet for glycaemic and anthropometric outcomes: (A-B) HbA1c; (C-D) BW; (E–F) BMI; (G-H) FBG. IF, intermittent fasting; CERD, continuous energy restriction diet.

estimate was relatively robust, although the potential influence of between-study heterogeneity or undetected publication bias could not be completely excluded (Supplementary Figure 2).

To further explore potential sources of heterogeneity, subgroup analyses stratified by IF modality were performed. A significant reduction in HbA1c was observed in the FMD subgroup (two arms[29, 32]; p = 0.01), whereas no significant difference was detected between MADF and ad libitum diets (two arms[30]). For the TRF subgroup, only one arm was available, which precluded meta-analytic pooling or formal statistical testing; accordingly, no p value or heterogeneity estimate was calculated (Table 2).

Body weight

Nine studies (ten arms)[33, 35-42] assessed the impact on BW between IF and CERD. The forest plot indicates no statistically significant difference between the groups (Figure 2C, [SMD (Hedges's g)] -0.08, 95% CI -0.25, 0.09; p = 0.35, I^2 = 0.00%). The funnel plot demonstrates a pattern that is nearly symmetric (Supplementary Figure 1C), Egger's test indicating no statistically detectable publication bias (Supplementary Table 9).

Four studies (five arms)[29-32] assessed the impact on BW between IF and ad libitum diets. The forest plot indicates a statistically significant difference between the groups (Figure 2D, [SMD (Hedges's g)] -0.30, 95% CI -0.55, -0.05; p = 0.02, I^2 = 17.77%). The funnel plot demonstrates a pattern that is nearly symmetric (Supplementary Figure 1D), Egger's test indicating no statistically detectable publication bias (Supplementary Table 10).

BMI

Nine studies (ten arms)[33, 35-42] assessed the impact on BMI between IF and CERD. The forest plot showed no statistically significant difference (Figure 2E, [SMD (Hedges's g)] -0.11, 95% CI -0.31, 0.08; p = 0.24, I^2 = 16.29%). IF and CERD both led to significant reductions in BMI. The funnel plot demonstrates a pattern that is nearly symmetric (Supplementary Figure 1E), Egger's test indicating no statistically detectable publication bias (Supplementary Table 11).

Three studies (four arms)[30-32] assessed the impact on BW between IF and ad libitum diets. The forest plot indicates a statistically significant difference between the groups (Figure 2F, [SMD (Hedges's g)] -0.26, 95% CI -0.51, 0.00; $p = 0.05$, $I^2 = 7.61\%$). The funnel plot demonstrates a pattern that is nearly symmetric (Supplementary Figure 1F), Egger's test indicating no statistically detectable publication bias (Supplementary Table 12).

Fasting blood glucose

Seven studies (eight arms)[33, 35, 37-39, 41, 42] showed no statistically significant difference between IF and CERD regarding FBG (Figure 2G, [SMD (Hedges's g)] 0.00, 95% CI-0.24, 0.24; $p = 0.99$, $I^2 = 31.15\%$). The funnel plot demonstrates a pattern that is nearly symmetric (Supplementary Figure 1G), Egger's test indicating no statistically detectable publication bias (Supplementary Table 13).

Three studies (four arms)[30-32] assessed the impact FBG between IF and ad libitum diets. The forest plot indicates a statistically significant difference between the groups (Figure 2H, [SMD (Hedges's g)] -0.39, 95% CI -0.64, -0.15; $p = 0.00$, $I^2 = 0.00\%$). The funnel plot demonstrates a pattern that is nearly symmetric (Supplementary Figure 1H), Egger's test indicating no statistically detectable publication bias (Supplementary Table 14).

Dropout rate

Among the 14 included studies, 494 participants were in the IF group with 106 dropouts (21.5%), 336 in the CERD group with 88 dropouts (26.2%), and 157 in the ad libitum group with 25 dropouts (15.9%). Dropout rates differed significantly between the CERD and ad libitum groups ($p < 0.05$), whereas no significant differences were observed between IF and CERD or between IF and ad libitum (Table 3). These findings indicate that CERD may be associated with higher attrition compared with ad libitum eating.

Quality assessment

Each study's risk of bias was independently assessed using the Cochrane Handbook, and statistical evaluations were conducted using Review Manager software (Review Manager 5.3). The assessment included randomization methods, allocation concealment, blinding, completeness of outcome data, selective reporting, and other sources of bias. During the assessment, the reviewers grouped the studies into "low risk," "high risk," or "unclear risk. If a study adequately addresses all elements of selection bias, performance bias, attrition bias, and reporting bias, it is considered to have a low risk of bias. Studies in which the outcomes are not adequately addressed are considered to have a high risk of bias, while studies for which a clear judgment can be made are considered to have an unclear risk of bias. The eligibility assessment process for the included literature is carried out independently by two unobstructed researchers. In the event of any discrepancies, they are resolved through discussion or referred to a third researcher for resolution. Fourteen RCTs were included,[29-42] with ten[29, 30, 32, 34-36, 38, 39, 41, 42] having complete data and four[33, 31, 37, 40] with incomplete data. The risk of bias graph is presented in Figure 3, the risk of bias summary is presented in Figure 4.

Ethics and dissemination

This systematic review is based solely on data retrieved from published literature and does not entail any new clinical trials. Consequently, neither ethical approval nor patient informed consent is necessary.

DISCUSSION

This study assessed the effects of IF on glycemic and weight control in patients with T2DM and prediabetes, using ad libitum eating and CERD as control groups. IF has been shown to be a simple and effective dietary intervention for improving metabolic diseases and reducing body weight.[43-45] It helps improve blood glucose levels and promote weight loss in T2DM patients by reducing adipose tissue, enhancing β-cell survival, and inducing gut microbiota remodeling, thereby offering both preventive and therapeutic benefits for T2DM.[46, 47] According to an American survey, every kilogram increase in body

Table 2. Subgroup analysis of HbA1c between different IF modalities and ad libitum diet

Subgroup (Treatment duration)	No. of studies	Included studies	Effect size (MD, 95% CI)	*p*-value	I^2 (Heterogeneity)
FMD	2	[29][32]	-0.95 (-1.80, -0.10)	0.01	85.4%
TRF	1	[31]	-0.58 (-0.97, -0.19)	-	-
MADF	2	[30]1[30]2	-0.28 (-0.83, 0.27)	0.53	0%

FMD, fasting-mimicking diet; TRF, time-restricted feeding; MADF, modified alternate-day fasting

Table 3. Dropout rates among IF, CERD, and ad libitum diet

Dietary group	Participants	Dropouts, n (%)
IF	494	106 (21%)
CERN	336	88 (26%)*
ad libitum diet	157	25 (16%)

CERD, Continuous energy restriction diet; IF, Intermittent fasting.
*$p < 0.05$ vs ad libitum diet group

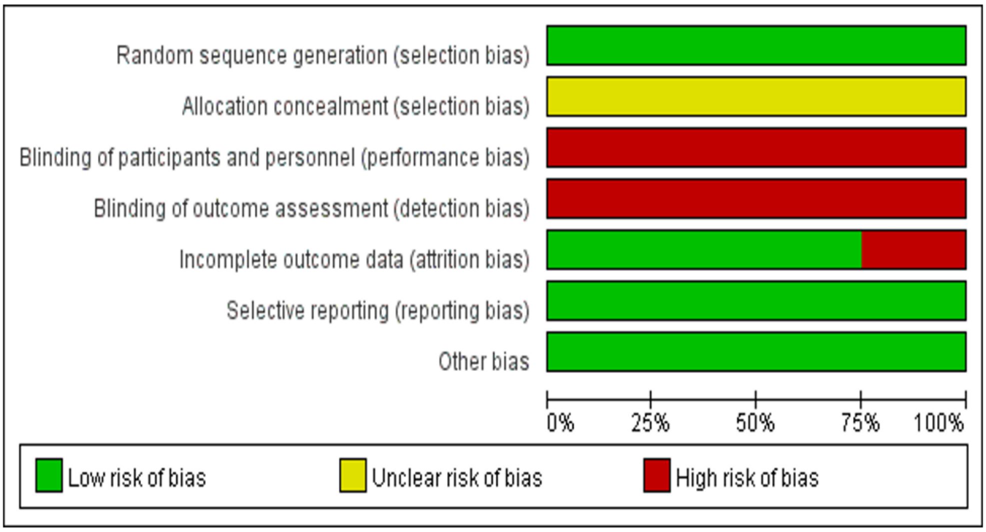

Figure 3. Risk of bias graph

weight increases the risk of developing T2DM by sevenfold.[48] Both IF and CERD not only help patients with T2DM and prediabetes lose weight and reduce BMI but also effectively control blood glucose levels. This may be attributed to the body's metabolic shift toward fatty acid oxidation during fasting, which lowers glucose and insulin levels. Additionally, IF and CERD may promote lean tissue retention, increase norepinephrine levels, and enhance neuropeptide Y expression, leading to faster fat consumption, weight loss, and BMI reduction.[49-51]

To determine whether IF can be as effective as, or even superior to, CERD in terms of weight and glycemic control, we conducted a meta-analysis of 14 RCTs with 14 studies (16 arms).[29-42] Of these, ten studies (eleven arms) compared IF to CERD, and four studies (five arms) compared IF to ad libitum eating. Our meta-analysis revealed that IF was more effective than ad libitum eating in improving HbA1c, BW, BMI, and FBG. However, studies comparing the effects of IF and ad libitum eating on HbA1c showed considerable variability. Funnel plot and sensitivity analyses further revealed significant bias, while stratified analysis suggested that variations in different IF modalities could influence the final outcomes. Compared to CERD, IF demonstrated similar effects in reducing HbA1c, BW, BMI, and FBG. This suggests that both IF and CERD are effective in reducing weight and improving glycemic control in patients with T2DM and prediabetes.

Regarding attrition, the ad libitum group exhibited the lowest dropout rate (15.9%), whereas higher rates were observed in the IF (21.5%) and CERD (26.2%) groups. Formal statistical comparisons demonstrated that attrition was significantly higher in the CERD group than in the ad libitum group, whereas no significant differences were detected between IF and ad libitum or between IF and CERD. These findings suggest that continuous energy restriction may be associated with reduced adherence compared with unrestricted eating, while IF did not differ

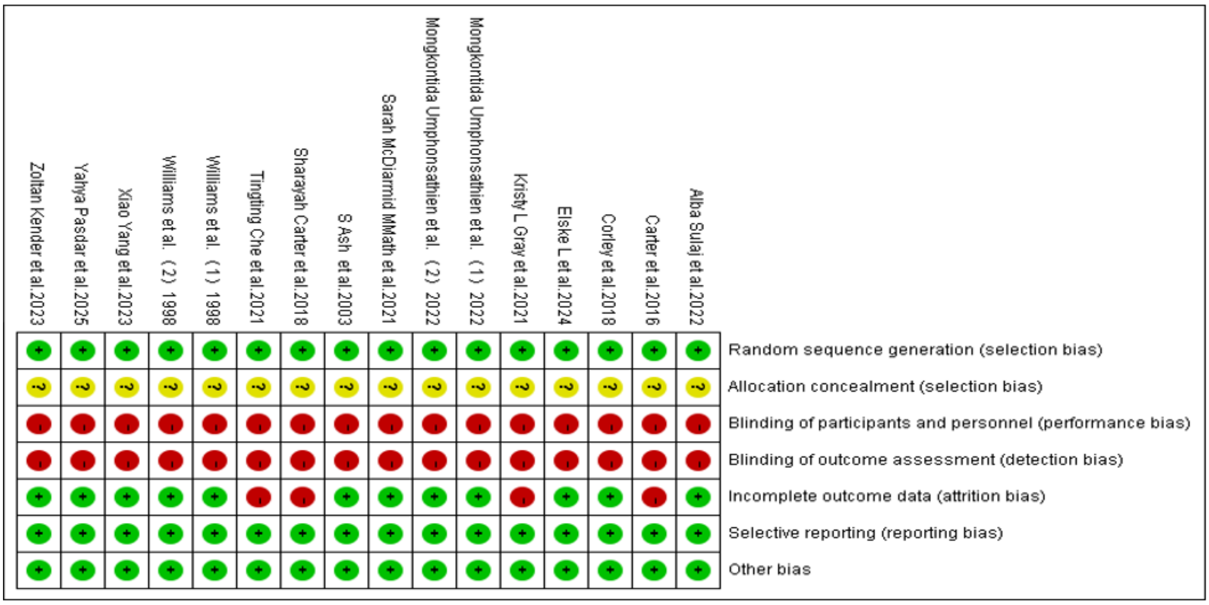

Figure 4. Risk of bias summary

significantly from ad libitum intake in terms of adherence.

Several limitations should be acknowledged. First, although our findings suggest that intermittent fasting may confer potential metabolic benefits, these results should be interpreted with caution given the limited number of trials, substantial heterogeneity, and insufficient safety data. Second, the number of eligible trials and participants was limited for several outcomes, and considerable between-study heterogeneity was observed. Third, safety and adverse-event data were insufficiently reported, precluding a comprehensive evaluation of the long-term safety of intermittent fasting regimens. Fourth, the limited number of eligible studies precluded subgroup analyses based on patient characteristics such as baseline BMI and the severity of diabetes. In addition, due to insufficient data, we were unable to perform subtype-specific analyses for different intermittent fasting regimens (e.g., ADF and TRF), which may exert differential metabolic effects. Finally, the inclusion of Mediterranean diet–based interventions in the CERD comparator group may have introduced potential confounding, as such diets may independently influence metabolic outcomes.

The main challenge now is how to improve patient acceptance of energy-restricted diets to ensure more people can persist with these interventions. Although this meta-analysis indicates that intermittent fasting has a positive effect on improving blood glucose and weight control in patients with T2DM and prediabetes, the controversy regarding meal timing and fasting in diabetes management still requires further exploration. It is important to emphasize that patient selection and individualized monitoring are of great significance. Intermittent fasting is not suitable for all patients with T2DM. For example, it should be used with caution in patients with hypoglycemia unawareness.[52] However, structured IF under clinical monitoring has demonstrated feasibility in patients with good adherence, it should be noted that this study did not specifically evaluate safety outcomes, and future large-scale, long-term randomized trials are needed to confirm both the efficacy and safety of different IF regimens.[53] Such evidence should be incorporated into future guideline revisions, taking into account both the standardization of the regimen and individualized risk assessment.

Conclusion

Current research indicates that IF can reduce blood glucose and body weight in T2DM and prediabetes patients. IF significantly reduced HbA1c, body weight, BMI, and fasting blood glucose compared with ad libitum eating. Notably, the magnitude of HbA1c reduction varied across different IF modalities, warranting further investigation into modality-specific glycemic responses. When compared to CERD, IF shows similar effects on HbA1c, BW, BMI, and FBG, establishing it as an effective strategy for managing T2DM and prediabetes. IF may serve as a viable alternative to CERD for the prevention and management of chronic metabolic diseases. Compared with ad libitum eating, CERD was associated with significantly higher attrition, whereas intermittent fasting did not differ significantly from ad libitum intake in terms of adherence. Potential side effects of both dietary approaches should be carefully considered, and their implementation should be supervised by healthcare professionals.

Limitations

Several limitations of our study warrant discussion. First, adverse outcomes were not included in the meta-analysis, limiting our ability to comprehensively assess the benefits and safety of IF. Second, this analysis included only 14 studies (16 arms) that met the inclusion criteria, lacking larger sample sizes, which hindered a deeper exploration of study heterogeneity, particularly with regard to different intervention durations. Third, our review did not examine whether IF is associated with clinical outcomes such as cancer, cardiovascular events, or mortality. Finally, we did not conduct a classification analysis of different IF protocols, which raises questions about the effectiveness of various IF regimens in glycemic control.

CONFLICT OF INTEREST AND FUNDING DISCLOSURES

The authors declare no conflict of interest.

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