THE EFFECT OF TIME-RESTRICTED EATING (TRE) COMBINED WITH ENERGY RESTRICTION ON WEIGHT LOSS AND CARDIOMETABOLIC MARKERS IN OVERWEIGHT/OBESE SUBJECTS: A SYSTEMATIC REVIEW

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Abstract: ***Background:****The global prevalence of overweight and obesity has escalated to alarming, epidemic levels, solidifying its role as a primary and significant risk factor for major cardiometabolic diseases. Time-Restricted Eating (TRE), which operates by simply confining food intake to a limited daily window, has recently emerged as a popular and flexible dietary strategy. However, a crucial question remains: we must systematically examine the true efficacy of TRE when deliberately combined with Energy Restriction (ER), particularly when directly compared against the established Conventional Energy Restriction (CER) diet.* ***Purpose:****The primary objective of this systematic review is to determine the efficacy and compare the outcomes of two dietary strategies, namely TRE combined with ER versus CER, in an adult population with overweight and obesity. The primary outcome assessed is weight loss, while secondary outcomes focus on improvements in cardiometabolic markers.* ***Methods:****This systematic review was conducted on randomized controlled trials (RCTs) comparing TRE+ER interventions with CERs that had similar calorie deficits. The main inclusion criteria involved adult subjects who were overweight or obese. The primary outcome analyzed was Weight Loss, while secondary outcomes included cardiometabolic markers such as HOMA-IR, fasting glucose, and lipid profile.* ***Results:****In general, TRE+ER has been shown to produce weight loss (such as BMI and fat mass) comparable to CER. However, when analyzing meal timing, Early TRE (eTRE) showed significant advantages in improving insulin sensitivity (HOMA-IR), indicating additional metabolic benefits of synchronizing meal timing with the body's biological clock.* ***Conclusions:*** *TRE combined with energy restriction is an effective dietary alternative comparable to CER for weight management. We recommend prioritizing Early TRE because it provides superior benefits in improving insulin resistance, making it an ideal strategy for the prevention and management of cardiometabolic risk.*

INTRODUCTION

The prevalence of overweight and obesity has reached alarming levels worldwide (1), making it a global epidemic. This significant upward trend is predicted to continue until 2050, including in Indonesia (2,3). Obesity is defined as abnormal or excessive body fat accumulation that can be harmful to health (4). This phenomenon is no longer an issue exclusive to developed countries, but has become an urgent public health issue in developing countries. Therefore, this condition requires effective interventions and policies, supported by strong scientific evidence (5).

Obesity, particularly abdominal obesity characterized by visceral and ectopic fat accumulation, is a major independent cause of many cardiovascular risks and increased mortality (6). This pathological condition is closely associated with health problem such as dyslipidemia, hypertension, Type 2 Diabetes Mellitus (T2DM), and Metabolic Syndrome (7). Metabolic Syndrome itself is a cluster or combination of risk factors such as low HDL, high triglycerides, and high fasting glucose that can multiply the risk of Cardiovascular Disease (CVD). Therefore, its is very important target for effective weight management interventions (8).

Effective weight management, often centered on Continuous Energy Restriction (CER) or traditional Calorie Restriction (CR), has been shown to improve metabolic syndrome and reduce systemic inflammation (7). However, many recent studies and meta-analyses show that, in terms of weight loss and body composition, the Intermittent Energy Restriction (IER) dietary approach often yields results comparable to CER when the total calorie deficit is similar (9,10). This limitation has prompted exploration of new dietary modalities.

Among the various forms of Intermittent Fasting (IF), Time-Restricted Eating (TRE) has attracted significant attention. This protocol restricts daily food intake to a specific time window, generally using a 16-hour fasting and 8-hour eating ratio (e.g., 16:8), and has become popular due to its potential for better compliance (11,12). The uniqueness of TRE lies in its focus not only on 'what is eaten,' but also 'when' the food is consumed. Therefore, the main difference currently being investigated is the comparison of efficacy between TRE combined with Energy Restriction (TRE+ER/CR) versus Energy Restriction (ER/CR) alone.

Physiologically, TRE is supported by the concept of Circadian Rhythm, in which meal times are aligned with the body's biological clock, which regulates glucose, lipid, and energy metabolism (13). Disruption of the circadian rhythm has been linked to the risk of metabolic syndrome. Therefore, TRE, particularly the Early TRE (eTRE) approach, which restricts eating to the morning and afternoon hours (in line with chronotype) (14), is hypothesized to provide additional benefits beyond simple calorie deficit.

Research shows that although TRE without Calorie Restriction (CR) is often not effective enough for weight loss (11), the combination of TRE with CR (TRE+CR) has been proven effective, even significantly reducing fat mass and waist circumference compared to baseline (15) However, this effectiveness raises an important question: If the total calorie deficit of both groups is equalized, does adding the TRE component to an Energy Restriction (ER) diet truly provide an additional statistical advantage compared to Energy Restriction (ER) alone?

Currently, the main debate in the literature has shifted focus to finding the time-specific metabolic benefits of TRE, regardless of its weight loss effects. Recent studies have begun to compare the efficacy of early TRE (eTRE), late TRE (lTRE), and conventional Energy

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Restriction (ER), targeting important outcomes such as fasting glucose, blood pressure, and liver markers (14,16).

Some preliminary results suggest a potential advantage of eTRE+ER over lTRE+ER and ER alone for certain markers, such as fat mass, diastolic blood pressure, and fasting glucose (14). However, it should be noted that benefits on other metabolic markers, including HOMA-IR and lipid profile, are often reported to be equivalent between TRE+ER and ER/CR alone (17).

Contradictions in the existing literature regarding the superiority of TRE+ER over pure ER/CR require a focused systematic review. Some studies show equivalent results, while others find TRE superiority in specific markers. These differences may be due to heterogeneity in intervention protocols, such as TRE duration, placement of the eTRE vs. lTRE eating window, and actual compliance levels, making it difficult to draw firm clinical conclusions (18). Therefore, there is a clear evidence gap in directly comparing cardiometabolic and weight outcomes between TRE+ER and ER/CR with strict calorie control.

The objective of this systematic review is to comprehensively evaluate and compare the efficacy of Time-Restricted Eating (TRE) combined with Energy Restriction (ER/CR) versus Continuous Energy Restriction (CER/CR) alone in an adult population with overweight/obesity. This review will focus on primary outcomes: Weight Loss (such as BMI, fat mass), and secondary outcomes: Cardiometabolic Markers (including insulin sensitivity, fasting glucose, lipid profile, and blood pressure), to provide a synthesis of the latest evidence for future clinical practice and research.

METHODS

Ethical Considerations

This systematic review is a secondary study that analyzes and synthesizes published and publicly available data, so it does not require approval from an ethics committee.

Search Strategy

This systematic review was conducted carefully and thoroughly, following the PRISMA 2020 (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (19). Compliance with these guidelines is essential to ensure three things: accuracy in methodology, openness (transparency) in the entire research process, and replicability by other researchers in the future.

A comprehensive literature search was conducted across all major electronic databases, namely Semantic Scholar, MDPI, PubMed, Elsevier, Springer Nature, and Web of Science. The search aimed to identify relevant Randomized Controlled Trials (RCT) studies published up to 2025. The article selection process was carried out independently by two reviewers based on pre-determined inclusion and exclusion criteria as a form of selection bias mitigation.

The core search string utilized Boolean operators, combining key concepts for population, condition, intervention, and study design:

("Time-restricted eating" OR "Time-restricted feeding" OR TRE) AND ("Energy restriction" OR "Caloric restriction" OR ER OR CR) AND ("Weight loss" OR "Body mass" OR "Cardiometabolic markers" OR "Insulin resistance" OR HOMA-IR OR "Lipid profile") AND (overweight OR obesity)

Eligibility Criteria

Inclusion Criteria

To ensure relevance and quality, studies must meet the following methodological inclusion criteria:

1. Desain Studi: Eksklusif Randomized Controlled Trials (RCT) yang membandingkan efikasi intervensi Puasa Intermiten. Durasi intervensi minimal ≥4 minggu.
2. Populasi: Subjek manusia dewasa (usia 18–65 tahun) dengan status Kelebihan Berat Badan (Overweight) (BMI ≥ 25 kg/m^2) atau Obesitas.
3. Publikasi: Artikel teks lengkap tersedia dalam Bahasa Indonesia atau Bahasa Inggris.
4. Intervensi & Pembanding: Perbandingan langsung antara intervensi Time-Restricted Eating (TRE) yang dikombinasikan dengan Pembatasan Energi/Kalori (ER/CR) dan kelompok kontrol Pembatasan Energi Kontinu (CER) atau Pembatasan Kalori Harian (CR) konvensional yang memiliki defisit kalori serupa.
5. Luaran: Harus melaporkan setidaknya satu hasil tentang Penurunan Berat Badan (misalnya, BMI, berat badan) DAN satu hasil tentang Penanda Kardiometabolik (misalnya, glukosa puasa, HOMA-IR, profil lipid, tekanan darah).

Exclusion Criteria

Studies will be considered ineligible or excluded from the analysis if they meet the following criteria:

1. Desain studi non-RCT (misalnya, studi observasional, review naratif, meta-analyses lain, case reports, in vitro, atau studi pada hewan).
2. Populasi dengan penyakit kronis yang tidak terkontrol (misalnya, Diabetes Melitus tipe 1) atau wanita hamil/menyusui.
3. Intervensi berupa puasa air murni dalam jangka waktu lama, atau diet sangat rendah kalori (Very Low-Calorie Diet/VLCD) yang tidak berfokus pada jadwal makan.
4. Studi yang hanya melaporkan luaran antropometri (berat badan, BMI) tanpa indikator kardiometabolik.

Study Selection

The study selection process was conducted sequentially and carefully, in accordance with the principles of PRISMA 2020 (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) (19). This selection flow is summarized in Figure 1. After initial identification and removal of duplicates, two reviewers independently performed an initial screening of all remaining studies, based solely on their titles and abstracts. Studies that passed were then proceeded to the full-text review stage to assess their eligibility. Finally, eight studies that successfully met all inclusion criteria were selected for comprehensive data extraction and synthesis.

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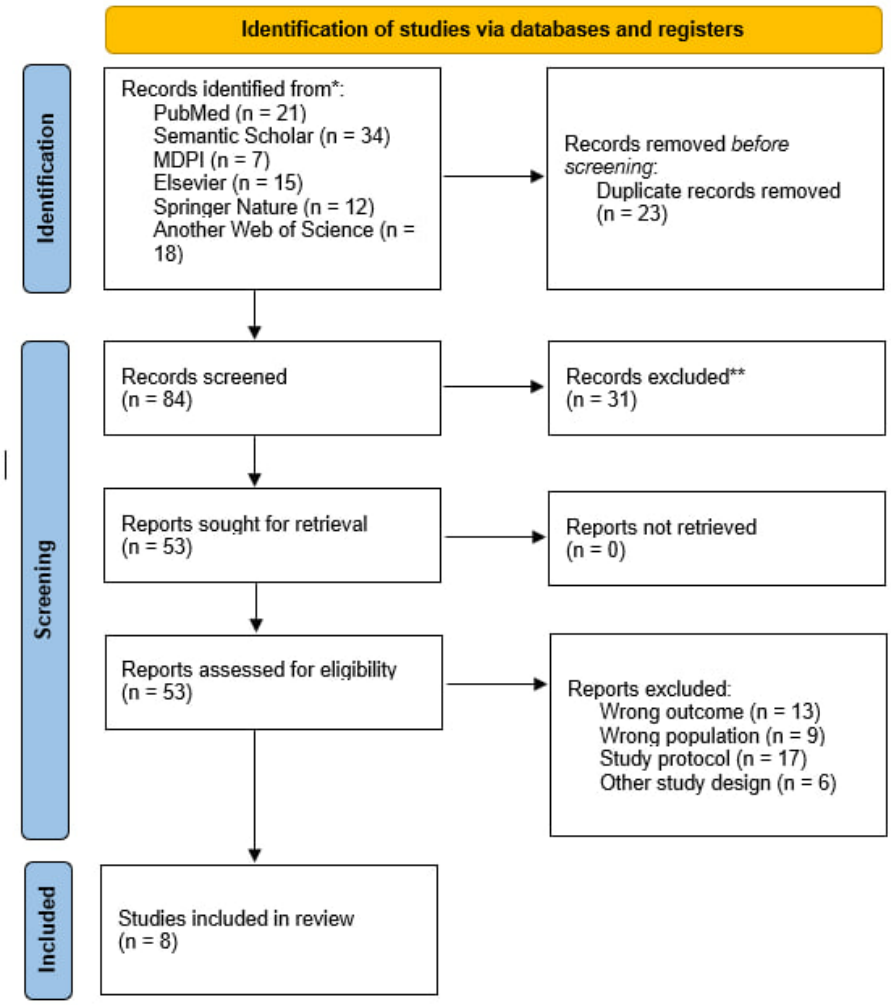

Figure 1. PRISMA Flow Diagram

Data Extraction

Data extraction was performed independently by two trained reviewers (BH and DN) using a standardized data extraction form developed beforehand and created in Microsoft Excel (Microsoft Corp., Redmond, USA). Any inter-reviewer differences were resolved through collective discussion until consensus was reached. Extracted data covered: (1) study characteristics; (2) involved subject profiles; (3) intervention and comparator details; and (4) reported efficacy and safety outcomes.

Quality Assessment (Risk of Bias)

The methodological quality of the eight RCT studies included was rigorously assessed using the Cochrane Risk of Bias 2 (RoB-2) instrument (20). This assessment focused on five key domains, ranging from potential bias in the randomization process to bias in outcome measurement and reporting. The RoB-2 assessment was conducted independently by two reviewers (BH and DN). To reach consensus, discussions were held; if differences of opinion were difficult to resolve, a third reviewer who was an expert in clinical methodology was involved as a mediator.

Data Synthesis (Narrative Approach)

Data synthesis will focus on two key aspects. First, we will evaluate the direction and magnitude of effects to determine the significance and degree of difference in outcomes (weight loss and cardiometabolic markers) between the TRE+ER and CER/CR groups. Second, interpretation of findings will be linked to the methodological quality of studies (based on RoB-2). Studies with low risk of bias will be given higher priority in interpretation to ensure the internal validity of the conclusions drawn.

RESULTS

Search Results and Study Characteristics

The systematic literature search successfully identified eight studies that met the strict inclusion criteria for analysis. The study selection process is summarized in detail in Figure 1: PRISMA Flow Diagram. All included studies were Randomized Controlled Trials (RCTs) involving adult human subjects with a clinical diagnosis of overweight or obesity (BMI ≥ 25 kg/m^2).

The main intervention evaluated was Time-Restricted Eating (TRE) combined with Energy/Calorie Restriction (ER/CR), which was directly compared with Continuous Energy Restriction (CER) or a conventional daily calorie diet with a comparable energy deficit. Outcomes were measured using validated parameters, with a primary focus on Weight Loss (e.g., body mass and BMI) and a secondary focus on various cardiometabolic markers (e.g., HOMA-IR, fasting glucose, lipid profile, and blood pressure). Detailed characteristics and primary outcomes of the included studies are presented in Table 1.

Table 1. Study Inclusion Summary

No.	Author (Year)	Country	Study Design & Duration	Population (N & Main Criteria)	Intervention & Eating Window	Comparator & Eating Window	Cardiometabolic Outcomes Measured	Conclusion
1.	Habe et al. (2025)	Slovenia (Europe)	Randomized Clinical Trial (RCT), 3 months	90 adults with overweight or obesity	I1: Early TRE + ER (8 hour window) I2: Late TRE + ER (8 hour window)	Only Energy Restriction (12 hour window)	The cardiometabolic outcomes measured included various glycemic markers and insulin resistance, lipid profile (cholesterol and triglycerides), liver function markers (AST and ALT enzymes), and visceral fat	The combination of early time-restricted eating with calorie restriction (eTRE+ER) appears to be more effective at reducing fat mass, Body Mass Index (BMI), and fasting blood sugar, as well as lowering leptin levels and

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							accumulation index.	improving feelings of fullness (appetite control), when compared to late time-restricted eating or calorie restriction alone. However, when looking at most other heart and metabolism markers (cardiometabolic markers)—such as insulin resistance, lipid profile, liver function, and other metabolic hormones—all three interventions showed similar effects (comparable). This suggests that eTRE offers a specific benefit, but not a universal one, across all markers.
2.	Črešnovar et al. (2025)	Slovenia (Europe)	RCT, 3 months	108 adults with overweight or obesity	I1: Early TRE + ER (8 hour window) I2: Late TRE +	Only ER (12 hour window)	The cardiometabolic results looked at in this study included systolic and	Although all groups achieved similar amounts of weight loss, the eTRE +

					ER (8 hour window)		diastolic blood pressure, fasting blood sugar (glucose), and the lipid profile, which consists of triglycerides, total cholesterol, LDL cholesterol, and HDL cholesterol. Additionally, C-reactive protein (CRP) was also measured because it serves as an important marker for cardiometabolic risk	ER approach offered significant extra benefits in terms of reducing fat mass, improving metabolic age, lowering fasting blood sugar, and decreasing diastolic blood pressure, compared to lTRE + ER or ER alone. However, there were no differences observed between the groups concerning lipid profiles or systolic blood pressure.
3.	Zaman et al. (2023)	USA (Colorado/South Carolina)	RCT, 3 months	38 adults with overweight or obesity	eTRE + DCR	Only Daily Calorie Restriction (DCR)	The cardiometabolic results measured in this study were extensive, covering the continuous blood sugar profile (mean level, how much it varies, and the size of daily swings/MAGE), insulin sensitivity (measured by HOMA-IR),	The e-TRE + DCR approach and DCR (Dietary Calorie Restriction) alone resulted in comparable weight loss. However, adding the early time-restricted eating component did not provide significant extra

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							fasting blood sugar and insulin levels, and long-term blood sugar control via hemoglobin A1c (A1c).	benefits in terms of sustained blood sugar profile or insulin sensitivity, compared to using calorie restriction alone. Notably, the DCR-only group actually showed internal improvements in blood sugar variability and insulin sensitivity, which may have been influenced by differences in baseline health measurements and the generally healthy profiles of the participants.
4.	Weiss et al. (2020)	USA (San Francisco subset)	RCT, 3 months	105 adults (men+women) with BMI 27-43	TRE (8 hour window)	Consistent Meal Timing (CMT)	The cardiometabolic results calculated in this study included levels of fasting insulin, fasting blood sugar (glucose), and long-term blood sugar control via hemoglobin	Time-restricted eating (TRE) alone, without making any other changes to calorie intake, is no more effective for losing weight than simply eating throughout

							A1c (HbA1c). Additionally, researchers measured insulin resistance (using HOMA-IR), and the lipid profile (triglycerides, total cholesterol, LDL/bad cholesterol, and HDL/good cholesterol). Blood pressure was also assessed, including both systolic and diastolic readings.	the day (the control group). Although weight loss was seen in the TRE group, the difference compared to the control group was not significant. Furthermore, there were no significant changes in important cardiometabolic markers such as fat mass, fasting insulin, blood sugar, HbA1c, or blood lipids between the two groups. A point of concern is the significant drop in lean muscle mass in the TRE group compared to the control group, which indicates a potential side effect that requires careful consideration
5.	Lin et al. (2021)	Taiwan (Asia)	RCT, 2 months	63 middle aged women in Taiwan	Time Restricted Feeding (TRF) + Low	Only LCD	The cardiometabolic results assessed included	Time-Restricted Feeding (TRF) was found to be

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	with BMI ≥24	Calorie Diet (LCD). TRF 8 hour window	blood pressure readings specifically systolic blood pressure (SBP) and diastolic blood pressure (DBP). In addition, key blood tests were also analyzed, including fasting blood sugar (glucose), fasting insulin, total cholesterol, triglycerides, HDL , and LDL. The status of insulin resistance was also evaluated using the HOMA-IR tool.	more effective than traditional diet methods in reducing both weight and diastolic blood pressure among middle-aged women. Although both groups successfully lost weight, the TRF group showed a greater reduction. However, TRF also caused a significant increase in fasting blood sugar levels and worsened insulin resistance (HOMA-IR). Meanwhile, there were no significant differences in lipid profiles or other fasting insulin levels between the groups. This suggests that while TRF is beneficial for weight loss and blood pressure, the

								potential negative effects on blood sugar control and insulin sensitivity must be carefully considered.
6.	Kundur aci et al. (2020)	Turkey (Istanbul)	RCT, 3 months	65 adults with BMI ≥27	Intermitte nt Energy Restrictio n (IER)	Continuo us Energy Restrictio n (CER)	The cardiometabo lic results that were evaluated included blood pressure (both systolic and diastolic readings), the lipid profile (total cholesterol, triglycerides, LDL/bad cholesterol, and HDL/good cholesterol), and blood sugar markers (fasting glucose, fasting insulin, HbA1c, and HOMA-IR). In addition, components related to Metabolic Syndrome, such as Body Mass Index (BMI) and waist-to-hip ratio, were also measured.	Both intermittent energy restriction (IER) diets and continuous energy restriction (CER) diets are highly effective in achieving substantial weight loss and improving cardiometab olic markers in individuals suffering from metabolic syndrome. Although the IER group showed a slightly greater reduction in weight and fat mass, the two groups were ultimately found to have no significant differences in the improvemen ts seen across blood

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								pressure, lipid profile, and blood sugar markers. This suggests that both intermittent and continuous calorie restriction methods are equally successful in alleviating the metabolic syndrome biomarkers that result from weight loss.
7.	Queiroz et al. (2023)	Brazil (Rio Grande do Sul)	RCT, 2 months	37 adults with BMI 24-34.9	I1; eTRE+ CR (8 hour window) I2: dTRE+CR (8 hour window)	Only CR	The cardiometabolic outcomes evaluated were comprehensive, focusing on three main areas: blood sugar regulation (including fasting glucose/insulin, insulin resistance markers like HOMA-IR, and the OGTT), lipid profile (total cholesterol, LDL, HDL, and triglycerides), and blood pressure (systolic, diastolic, and mean	This study concluded that early time-restricted eating (eTRE), delayed time-restricted eating (dTRE), and traditional calorie restriction (CR) all produced similar and substantial reductions in both body weight and fat mass. Furthermore, all groups showed comparable improvements across various

							readings). Additionally, the study assessed energy metabolism (resting metabolic rate) and fasting ketone levels.	cardiometabolic markers, including reductions in fasting blood sugar, insulin, and insulin resistance, as well as positive changes in lipid profiles. Overall, the study found no significant difference in the effectiveness of these different dietary methods for weight loss and overall cardiometabolic health.
8.	Pinto et al. (2019)	UK (London)	RCT, 1 month	43 adults with central obesity	Intermittent Energy Restriction (IER) with Calorie Restriction 2 days/week (600 kcal/day)	CER	The primary cardiometabolic measure in this study was the R-QUICKI index (a key marker of insulin sensitivity). Secondary outcomes were extensive, covering multiple aspects: blood sugar control (including HOMA-IR, glucose, insulin, and NEFA), body fat indicators	This study concluded that Intermittent Energy Restriction (IER) and Continuous Energy Restriction (CER) are equally effective in achieving similar short-term weight loss (approximately 2.6–2.9%) and improving most cardiometabolic health markers in

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		(BMI, waist circumference, leptin, adiponectin), lipid profile (total cholesterol, HDL, LDL, TAG), and inflammatory markers (a score plus specific cytokines like TNF-α and IL-6). The study also assessed sympathetic activity and heart rhythm variation (HRV), along with resting metabolism (RMR) and ketone levels (β-OHB).	adults with central obesity. While IER showed adaptive shifts in metabolism —such as greater use of fat for energy and changes in liver glucose output—and CER alone successfully lowered fasting glucose, there were no significant differences between the two groups in the resulting improvements to insulin sensitivity, lipid profile, inflammatory markers, blood pressure, or heart rate variability. These findings strongly suggest that the reduction in fat mass is the main reason for the observed health benefits, positioning IER as a practical and viable alternative to

	CER for short-term weight management .

Methodological Quality Assessment

The quality of the eight included RCTs was assessed strictly using the Cochrane Risk of Bias 2 (RoB-2) tool [20], with the results summarized in Figure 2. Overall, the studies show a low risk of bias, meaning the evidence is strong. Most concerns about bias were low in areas like how people were assigned to groups (D1), missing data (D3), measuring results (D4), and reporting outcomes (D5)—all of which support the reliability of the studies. However, the biggest potential for bias came from the fact that participants knew which diet they were on (D2), which cannot be avoided in diet studies (lack of blinding). Despite this unavoidable limitation, the studies were considered reliable enough to confidently draw conclusions in this systematic review.

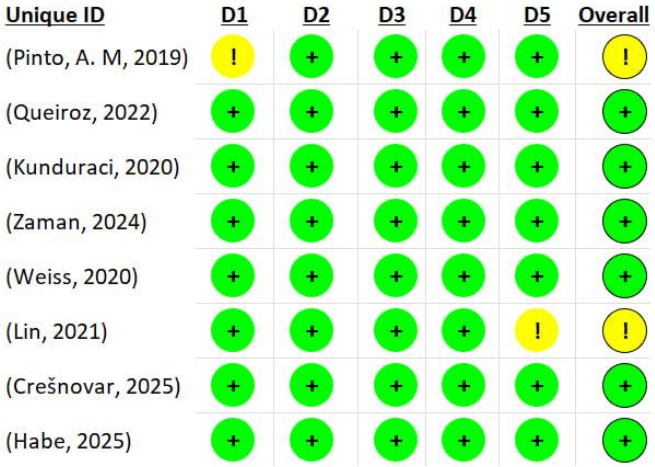

Figure 2. Summary of Methodological Quality Assessment Using the ROB-2 Instrument

Synthesis of Efficacy Findings

A narrative synthesis of eight Randomized Controlled Trials (RCTs) evaluating Time-Restricted Eating combined with Energy Restriction (TRE+ER) compared to Continuous Energy Restriction (CER/CR) shows that the effects on the primary outcome (weight loss) are largely comparable, but potential differentiation is observed in cardiometabolic outcomes. In general, both dietary regimens were effective in inducing significant weight and fat mass loss in overweight/obese subjects. However, this review confirms that, when the actual calorie deficit between groups was isocaloric, TRE+ER did not show a statistically significant advantage over CER/CR in weight loss outcomes. Findings from the studies by Lowe et al. (TREAT Trial) and Lin et al. strongly support the principle that weight loss is primarily driven by the level of energy restriction (ER/CR) achieved, rather than by the restriction of the eating window itself (11,12).

Although the primary outcome (weight loss) showed equivalence, the analysis revealed a more detailed and complex picture in the secondary outcomes, especially those related to meal timing. Several studies showed additional benefits associated with Early Time-

Restricted Eating (eTRE), which involves limiting meal times to earlier in the day.

Specifically, studies by Črešnovar et al. and Habe et al. reported that eTRE+ER showed better improvement in fasting glucose and diastolic blood pressure compared to the lTRE and CER groups alone. The potential advantage of eTRE is thought to occur due to the adjustment of meal times to the body's biological clock (circadian rhythm), which can increase insulin sensitivity independently of weight loss (14,16).

However, for other cardiometabolic markers, such as lipid profile and Systolic Blood Pressure, studies by Pinto et al. and Queiroz et al. found that the improvements achieved by TRE+ER and CER/CR remained comparable. This widespread similarity in results is likely due to methodological factors, namely the studies' success in ensuring that the total calorie deficit of both groups was the same, as well as the relatively short duration of the intervention (e.g., 3 months), which may not have been sufficient to demonstrate the long-term metabolic benefits of TRE (17,21).

DISCUSSION

Interpretation of Core Findings

Efficacy Equivalence of Weight Loss

This systematic review clearly shows that Time-Restricted Eating combined with Energy Restriction (TRE+ER) and Continuous Energy Restriction (CER/CR) are equally effective in promoting significant weight and fat mass loss in overweight and obese subjects (9,13,15). These findings consistently conclude that, as long as the actual calorie deficit between groups is maintained at the same level (isocaloric), TRE+ER does not provide any additional statistical advantage in weight loss outcomes compared to CER/CR (11,12,21).

The basic principles of energy thermodynamics confirm that weight loss is essentially driven by cumulative energy deficit (11). The equivalence we observed in primary outcomes, such as reduced body mass and fat percentage, reinforces the idea that Energy Restriction (ER/CR) is the primary determinant. In this context, time-restricted eating (TRE) functions more as a facilitating tool to help achieve this calorie deficit, rather than as a standalone weight loss mechanism (11,15).

Differentiation in Cardiometabolic Markers

Although the results appear to be equivalent in terms of primary outcomes, a thorough examination of secondary outcomes reveals significant differences, particularly those influenced by meal timing. Study data show that Early TRE (eTRE), which is the habit of eating earlier in the day, has the potential to provide better improvements in fasting blood sugar and diastolic blood pressure compared to Late TRE (lTRE) or regular CER/CR (14,16). These improvements are also supported by findings showing more stable glucose control in eTRE+ER (18).

However, for most other markers of cardiovascular and metabolic health, such as lipid profile (cholesterol and triglycerides) and Systolic Blood Pressure, the improvements observed between the TRE+ER and CER/CR groups tend to be balanced. Improvements in these markers are largely considered to be a direct result of the successful weight loss achieved, rather than due to any unique properties of the time-restricted eating itself (21).

Mechanistic Insights

Circadian Alignment and Insulin Sensitivity

The potential advantage of Early TRE (eTRE) lies in its interaction with our body's biological clock, known as the Circadian Rhythm (14). Most metabolic processes, including how the body processes sugar (glucose) and fat (lipids), undergo significant changes throughout the day that are regulated by this internal clock (16).

By consuming food at the most biologically optimal time, namely in morning to midday, when the body's insulin sensitivity is at its peak, the process of clearing sugar from the blood can proceed more efficiently. This helps to improve insulin sensitivity independently, not just as a result of weight loss (18).

The study by Habe et al. clearly highlights this hypothesis, stating that aligning meal times with the Circadian Rhythm through eTRE can improve insulin sensitivity better than CER or lTRE, which are not time-aligned. However, this benefit does not apply to all metabolic markers, suggesting that the effects of Circadian Rhythm adjustment may be most pronounced in parameters that show the most significant daily fluctuations, such as glucose metabolism (17).

The Role of Fasting Duration and Fatty Acid Oxidation

The core mechanism of intermittent fasting is to force the body to switch from using glucose to using fatty acids/ketones (10). Longer fasting durations such as 16:8 in TRE theoretically extend the time the body spends in a fat-burning state (free fatty acid oxidation/FFA) compared to conventional CER/CR with distributed calorie deficits (12).

However, findings comparing TRE+ER and CER/CR with isocaloric calorie deficits indicate that metabolic benefits in lipid profiles, such as reduced triglycerides, are largely a function of total fat mass reduction (21). In an isocaloric context, the metabolic shifts resulting from TRE that are separate from weight loss, such as increased fat oxidation, do not appear to be significant enough to produce statistically notable differences in key cardiometabolic markers over relatively short intervention periods, e.g., 3–12 months (11).

CONCLUSION

Time-Restricted Eating combined with Energy Restriction (TRE+ER) is as effective as Continuous Energy Restriction (CER/CR) in terms of weight loss, BMI, and fat mass, provided that the total calorie deficit of both groups is the same. The similarity in these body measurements confirms that cumulative energy deficit is the main determinant of weight change.

However, at the metabolic level, the data suggest a potential advantage of the TRE mechanism that is independent of weight loss. This advantage is closely related to the principles of chrononutrition and blood sugar management. Specifically, the eTRE protocol, which aligns meal timing with the body's active circadian phase, was statistically superior in improving insulin sensitivity, as indicated by reduced HOMA-IR and fasting blood sugar levels, compared to CER or lTRE.

This improvement is thought to stem from more optimal blood sugar management after meals, as well as more efficient regulation of clock genes in the liver and fat. Clinically, TRE+ER is a valid dietary therapy option that is as effective as CER for managing

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overweight/obesity, and offers additional benefits in terms of long-term patient compliance. Therefore, for patients with clear metabolic issues (e.g., insulin resistance), Early TRE should be prioritized to maximize benefits for heart health and metabolism through mechanisms supported by circadian physiology.

IMPLICATION

Clinical and Policy Implications

From a clinical perspective, the results of this review provide a strong basis for doctors to recommend Time-Restricted Eating (TRE) accompanied by energy restriction (ER). TRE+ER has been proven to be an alternative diet that is as effective as a conventional calorie diet (CER) for weight loss. The main advantage of TRE lies in its flexibility, which has great potential to improve patient compliance.

It is recommended to prioritize Early TRE (eTRE), with earlier meal times during the day, as eTRE has been shown to be more effective in improving insulin sensitivity (HOMA-IR). This makes it an ideal strategy for patients at high risk of developing Type 2 Diabetes Mellitus. The important implication is that TRE, particularly eTRE, needs to be formally recognized and integrated into clinical guidelines for obesity management.

Future Research

Given that most of the evidence we found is short-term, future research should focus on interventions with longer durations at least 12 months to ensure successful weight maintenance and evaluate the impact on long-term cardiovascular outcomes. It is also important to further explore specific molecular mechanisms, such as the role of the body's biological clock in the metabolic effects of eTRE. In addition, research should be more balanced in sample composition and prospectively test whether the effectiveness of TRE is influenced by individual chronotypes, for example, differences between morning larks and night owls.

STRENGTHS AND LIMITATION

Strengths

This review has a strong methodological foundation because we only included Randomized Controlled Trials (RCTs). Its main advantage is that it compares the TRE+ER group with a control group that has an equivalent calorie deficit (isocaloric). This allows us to isolate and measure the specific effects of meal timing itself, rather than just the effects of calorie reduction.

Limitations

However, the quality of the conclusions is affected by limitations in the primary studies. We found considerable variation (heterogeneity) in the TRE protocols applied (e.g., different fasting times). The duration of the studies, which were mostly only 1 to 3 months, also limited the long-term conclusions. Finally, a classic issue in nutrition studies is the reliance on patients' self-reported diets, which are prone to reporting bias and need to be interpreted with caution.

CONFLICT OF INTEREST

All authors declare that there are no financial or personal relationships that could

potentially cause bias in this work. This research was not supported by any special funding from any funding agency. The authors also guarantee that they have full access to all data, and that the funding agency (if any) did not intervene in the data analysis process or manuscript preparation.

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DECLARATION OF USING AI

The authors emphasize that Artificial Intelligence (AI) tools are only used as aids in the writing process for the purpose of improving language, including grammar checking, paraphrasing, and improving sentence clarity. No AI tools are used to generate original content, perform data analysis, or interpret research findings. Full responsibility for the content, interpretation, and conclusions in this manuscript rests solely with the authors.

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