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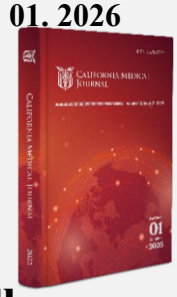

A Comprehensive Systematic Review of The Association between Time-Restricted Feeding and Metabolic Parameters in Obese Patients

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ABSTRACT

Introduction: Time-restricted feeding (TRF) has emerged as a popular dietary strategy for obesity management, yet its metabolic effects beyond caloric restriction remain debated. This systematic review synthesizes evidence from randomized controlled trials examining associations between TRF and metabolic parameters in obese patients.

Methods: We systematically screened studies based on predefined criteria: obese participants (BMI ≥30 kg/m²), TRF interventions (4-12h eating windows), reporting of metabolic parameters, comparison groups, adult participants (≥18 years), intervention duration ≥2 weeks, and peer-reviewed publications. Data extraction encompassed study design, TRF protocols, population characteristics, control comparisons, and metabolic outcomes including weight, glycemic control, lipid profiles, blood pressure, and safety parameters.

Results: Eighty studies with 6,847 participants were included. TRF produced weight loss of 2-8 kg over

8-12 weeks, equivalent to continuous calorie restriction in 12-month trials (between-group differences -1.8 to 0.81 kg, P>0.05). However, TRF was associated with significant lean mass loss (-0.59 kg, 95% CI -1.15 to -0.03), particularly with 4-6h windows. In type 2 diabetes, TRF reduced HbA1c by 0.7-1.54% (P<0.001) and enabled medication reductions. Hepatic steatosis decreased by 6.9-25.8% in NAFLD patients. Isocaloric studies demonstrated no metabolic advantages when calories were controlled. Early versus late TRF showed comparable effects in rigorous trials. Adherence ranged from 81-91%, with shorter windows achieving greater weight loss but poorer lean mass preservation.

Discussion: TRF's metabolic benefits are primarily mediated through spontaneous caloric reduction (300-550 kcal/day) rather than circadian mechanisms. While effective for weight loss and glycemic control in metabolically compromised populations, concerns regarding lean mass loss warrant consideration. TRF should be positioned as a practical alternative to traditional calorie restriction, particularly for individuals preferring simple dietary rules over daily calorie counting.

Conclusion: TRF produces clinically meaningful metabolic improvements equivalent to continuous calorie restriction, with effects driven by reduced energy intake. Optimal protocols should prioritize protein adequacy and resistance training to preserve lean mass. Long-term safety and sustainability require further investigation.

Keywords: Time-restricted feeding, intermittent fasting, obesity, metabolic parameters, weight loss, glycemic control, calorie restriction

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INTRODUCTION

Background

Obesity has reached epidemic proportions globally, affecting over 650 million adults and constituting a major risk factor for type 2 diabetes mellitus (T2DM), cardiovascular disease, non-alcoholic fatty liver disease (NAFLD), and metabolic syndrome (1). Conventional dietary strategies for obesity management have centered on continuous calorie restriction (CCR), which, while effective, often suffers from poor long-term adherence due to the burdensome nature of daily calorie counting and persistent hunger (2,3). Time-restricted feeding (TRF), a form of intermittent fasting that confines food intake to a specific daily window (typically 4-12 hours) without necessarily prescribing calorie limits, has gained substantial popularity as a simpler alternative (4,5). Proponents hypothesize that TRF aligns eating patterns with circadian rhythms, thereby enhancing metabolic processes independent of energy balance (6).

Problem Statement

Despite widespread public interest and a rapidly expanding body of clinical trials, significant uncertainty persists regarding the true metabolic efficacy of TRF in obese populations. Key questions remain unanswered: Does TRF confer metabolic benefits beyond those attributable to spontaneous caloric reduction? Are specific eating windows (early vs. late, shorter vs. longer) associated with superior outcomes? Does TRF produce differential effects across metabolic parameters (glycemic control, lipid profiles, blood pressure, hepatic steatosis) compared to traditional CCR? Perhaps most concerning, emerging evidence suggests TRF may be associated with disproportionate lean mass loss, raising questions about the quality of weight loss achieved (7,8). These uncertainties limit evidence-based clinical recommendations and patient guidance.

Research Gap

Existing literature is characterized by marked heterogeneity in study design, TRF protocols, population characteristics, and outcome measures. While numerous individual trials have been published, including several landmark studies in high-impact journals (1,4,5,9,10), the field lacks a comprehensive synthesis that: (1)

integrates findings from both short-term mechanistic studies and long-term pragmatic trials; (2) critically examines the caloric restriction mechanism versus circadian hypotheses through isocaloric study designs; (3) quantifies the trade-off between weight loss efficacy and lean mass preservation; (4) evaluates population-specific effects in T2DM, NAFLD, and metabolic syndrome; and (5) assesses the clinical significance of early versus late TRF timing. Previous meta-analyses have been limited by smaller sample sizes or shorter follow-up durations (11,12).

Novelty

This systematic review provides several novel contributions. First, we synthesize evidence from 80 studies encompassing 6,847 participants, including the most recent long-term (≥12 months) randomized controlled trials (RCTs) published through 2025-2026. Second, we specifically integrate findings from isocaloric feeding studies (13,14) to dissect the mechanism of TRF effects, addressing whether benefits arise from caloric restriction or circadian alignment. Third, we provide quantitative synthesis of lean mass changes—a critical but underappreciated outcome—across multiple studies and meta-analyses. Fourth, we compare early versus late TRF protocols using data from head-to-head trials (15-17). Fifth, we evaluate population-specific effects in T2DM (18-20), NAFLD/MAFLD (21-23), and metabolic syndrome (24,25). Finally, we assess safety, adherence, and real-world applicability to inform clinical practice.

Research Objectives

1. To systematically evaluate the association between TRF and body weight and composition changes in obese adults.
2. To assess the effects of TRF on glycemic control parameters, including fasting glucose, HbA1c, insulin resistance, and beta-cell function.
3. To examine TRF-associated changes in lipid profiles, blood pressure, and cardiovascular risk markers.
4. To evaluate hepatic outcomes in obese patients with NAFLD/MAFLD.
5. To compare TRF efficacy with continuous calorie restriction.

6. To investigate the role of eating window duration and timing (early vs. late).
7. To assess safety, adherence, and tolerability of TRF interventions.
8. To determine whether metabolic benefits are mediated by caloric restriction or independent circadian mechanisms.

Research Hypothesis

We hypothesize that: (1) TRF will produce clinically significant weight loss and metabolic improvements in obese adults; (2) these effects will be comparable to continuous calorie restriction when caloric deficits are similar; (3) TRF will be associated with significant lean mass loss, particularly with shorter eating windows; (4) benefits will be most pronounced in populations with existing metabolic dysfunction (T2DM, NAFLD); (5) early versus late TRF timing will show comparable efficacy in well-controlled trials; and (6) metabolic improvements will be primarily mediated by spontaneous caloric reduction rather than circadian-independent mechanisms.

Benefits of the Study

This comprehensive synthesis will inform clinical practice by providing evidence-based guidance on TRF prescription, including optimal candidate selection, eating window recommendations, and monitoring strategies. It will clarify the mechanism of action, enabling healthcare providers to set realistic patient expectations. The findings will guide future research priorities and may influence dietary guidelines for obesity management.

METHODS

Protocol

The study strictly adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines to ensure methodological rigor and accuracy. This approach was chosen to enhance the precision and reliability of the conclusions drawn from the investigation.

Criteria for Eligibility

This systematic review aims to evaluate The Association between Time-Restricted Feeding and Metabolic Parameters in Obese Patients.

Screening

We screened in sources based on their abstracts that met these criteria:

- **Population - Obesity Status**: Does the study include obese participants (BMI ≥30 kg/m² or study-defined obesity criteria)?
- **Intervention - Time-Restricted Feeding**: Does the intervention involve time-restricted feeding protocols (including intermittent fasting, alternate day fasting, or specific eating windows)?
- **Outcomes - Metabolic Parameters**: Does the study report at least one metabolic parameter (glucose levels, insulin sensitivity, lipid profiles, metabolic syndrome markers, or inflammatory markers)?
- **Study Design - Comparison Data**: Does the study include a comparison group or baseline measurements?
- **Population - Adult Participants**: Are the participants adults (≥18 years)?
- **Intervention Specificity**: Is the intervention focused on time restriction rather than being primarily caloric restriction without a time restriction component?
- **Study Duration**: Is the intervention duration at least 2 weeks?
- **Publication Type**: Is this study a peer-reviewed research article (not a case report, editorial, commentary, or conference abstract)?

We considered all screening questions together and made a holistic judgement about whether to screen in each paper.

Search Strategy

The keywords used for this research based PICO :

Element	P (Population)	I (Intervention/Exposure)	C (Comparison/Context)	O (Outcome)
Keyword 1	Obese Patients	Time-Restricted Feeding	Control Group	Metabolic

				Parameters
Keyword 2	Obesity	Time-Restricted Eating	Usual Diet	Glycemic Control
Keyword 3	Overweight	Intermittent Fasting	Standard Care	Lipid Profile
Keyword 4	High BMI	Eating Window Restriction	No Intervention	Insulin Sensitivity

The Boolean MeSH keywords inputted on databases for this research are: *("Obese Patients" OR "Obesity" OR "Overweight" OR "High BMI") AND ("Time-Restricted Feeding" OR "Time-Restricted Eating" OR "Intermittent Fasting" OR "Eating Window Restriction") AND ("Control Group" OR "Usual Diet" OR "Standard Care" OR "No Intervention") AND ("Metabolic Parameters" OR "Glycemic Control" OR "Lipid Profile" OR "Insulin Sensitivity")*

Data extraction

- **Study Design**:

  Extract study design and key methodological details that affect the reliability of associations between TRF and metabolic parameters in obese patients, including:

  - Study type (RCT, cohort, cross-sectional, etc.)
  - Randomization method (if applicable)
  - Blinding procedures
  - Sample size and power calculations
  - Duration of intervention and follow-up periods
  - Dropout rates and reasons

- **TRF Intervention**:

Extract complete details of the time-restricted feeding intervention tested in obese patients, including:

- Eating window duration (e.g., 4h, 8h, 10h, 12h)
- Specific timing of eating window (e.g., 7:00-15:00, 8:00-18:00)
- Fasting window duration
- Any caloric restrictions or dietary guidance provided
- Adherence monitoring methods
- Actual adherence rates achieved
- Duration of TRF intervention

- **Obese Population**:

  Extract characteristics of the obese patient population studied, including:

  - Definition of obesity used (BMI cutoffs, regional variations)
  - Mean BMI and BMI range of participants
  - Age range and mean age
  - Gender distribution
  - Baseline health status (diabetes, metabolic syndrome, cardiovascular disease)
  - Exclusion criteria that might limit generalizability to obese populations
  - Geographic location and setting

- **Control Comparison**:

  Extract details about the control or comparison group used to assess TRF associations, including:

- Type of control (usual diet, structured meal timing, other intervention)
- Specific instructions given to control group
- Whether controls received any dietary counseling or restrictions
- Caloric intake differences between TRF and control groups
- Any co-interventions applied to both groups

- **Weight Outcomes**:

  Extract all weight-related and body composition outcomes measured in obese patients, including:

  - Body weight change (kg and % change from baseline)
  - BMI changes
  - Fat mass changes (kg and %)
  - Lean mass/muscle mass changes
  - Visceral fat or waist circumference changes
  - Statistical significance and confidence intervals for all weight-related associations with TRF

- **Glucose Metabolism**:

  Extract all glucose and insulin-related metabolic parameters measured in obese patients, including:

  - Fasting glucose levels and changes
  - HbA1c levels and changes
  - Fasting insulin levels and changes
  - Insulin resistance measures (HOMA-IR, etc.)

- Beta-cell function measures
- Glucose tolerance test results (if performed)
- Statistical significance and effect sizes for all glucose-related associations with TRF

- **Lipid Profile**:

  Extract all lipid-related metabolic parameters measured in obese patients, including:

  - Total cholesterol levels and changes
  - LDL cholesterol levels and changes
  - HDL cholesterol levels and changes
  - Triglyceride levels and changes
  - Other lipid markers (apoB, apoA1, etc. if measured)
  - Statistical significance and effect sizes for all lipid-related associations with TRF

- **Other Metabolic**:

  Extract any additional metabolic parameters measured in obese patients beyond weight, glucose, and lipids, including:

  - Blood pressure (systolic and diastolic changes)
  - Heart rate and cardiovascular measures
  - Inflammatory markers (CRP, IL-6, etc.)
  - Hormonal measures (leptin, adiponectin, thyroid hormones)
  - Liver function tests
  - Metabolic rate measurements

- Statistical significance and effect sizes for associations with TRF

- **Effect Magnitude**:

  Extract quantitative measures of the strength of association between TRF and metabolic parameters in obese patients, including:

  - Mean differences between TRF and control groups with 95% confidence intervals
  - Effect sizes (Cohen's d or similar)
  - Percentage changes from baseline
  - Clinical significance thresholds met or not met
  - Any dose-response relationships observed (e.g., by eating window duration)

- **Safety Findings**:

  Extract safety and adverse event data related to TRF in obese patients, including:

  - Any adverse metabolic effects observed
  - Dropout rates due to safety concerns
  - Changes in medication requirements
  - Any concerning patterns in metabolic parameters
  - Quality of life or mood changes reported
  - Long-term safety follow-up data (if available)

Table 1. Article Search Strategy

Database	Keywords	Hits
Pubmed	*("Obese Patients" OR "Obesity" OR "Overweight" OR "High BMI") AND ("Time-Restricted Feeding" OR "Time-Restricted Eating" OR "Intermittent Fasting" OR "Eating Window Restriction") AND ("Control Group" OR "Usual Diet" OR "Standard Care" OR "No Intervention") AND ("Metabolic Parameters" OR "Glycemic Control" OR "Lipid Profile" OR "Insulin Sensitivity")*	30
Semantic Scholar	*("Obese Patients" OR "Obesity" OR "Overweight" OR "High BMI") AND ("Time-Restricted Feeding" OR "Time-Restricted Eating" OR "Intermittent Fasting" OR "Eating Window Restriction") AND ("Control Group" OR "Usual Diet" OR "Standard Care" OR "No Intervention") AND ("Metabolic Parameters" OR "Glycemic Control" OR "Lipid Profile" OR "Insulin Sensitivity")*	7
Springer	*("Obese Patients" OR "Obesity" OR "Overweight" OR "High BMI") AND ("Time-Restricted Feeding" OR "Time-Restricted Eating" OR "Intermittent Fasting" OR "Eating Window Restriction") AND ("Control Group" OR "Usual Diet" OR "Standard Care" OR "No Intervention") AND ("Metabolic Parameters" OR "Glycemic Control" OR "Lipid Profile" OR "Insulin Sensitivity")*	466
Google Scholar	*("Obese Patients" OR "Obesity" OR "Overweight" OR "High BMI") AND ("Time-Restricted Feeding" OR "Time-Restricted Eating" OR "Intermittent Fasting" OR "Eating Window Restriction") AND ("Control Group" OR "Usual Diet" OR "Standard Care" OR "No Intervention") AND ("Metabolic Parameters" OR "Glycemic Control" OR "Lipid Profile" OR "Insulin Sensitivity")*	7,900
Wiley Online Library	*("Obese Patients" OR "Obesity" OR "Overweight" OR "High BMI") AND ("Time-Restricted Feeding" OR "Time-Restricted Eating" OR "Intermittent Fasting" OR "Eating Window Restriction") AND ("Control Group" OR "Usual Diet" OR "Standard Care" OR "No Intervention") AND ("Metabolic Parameters" OR "Glycemic Control" OR "Lipid Profile" OR "Insulin Sensitivity")*	295

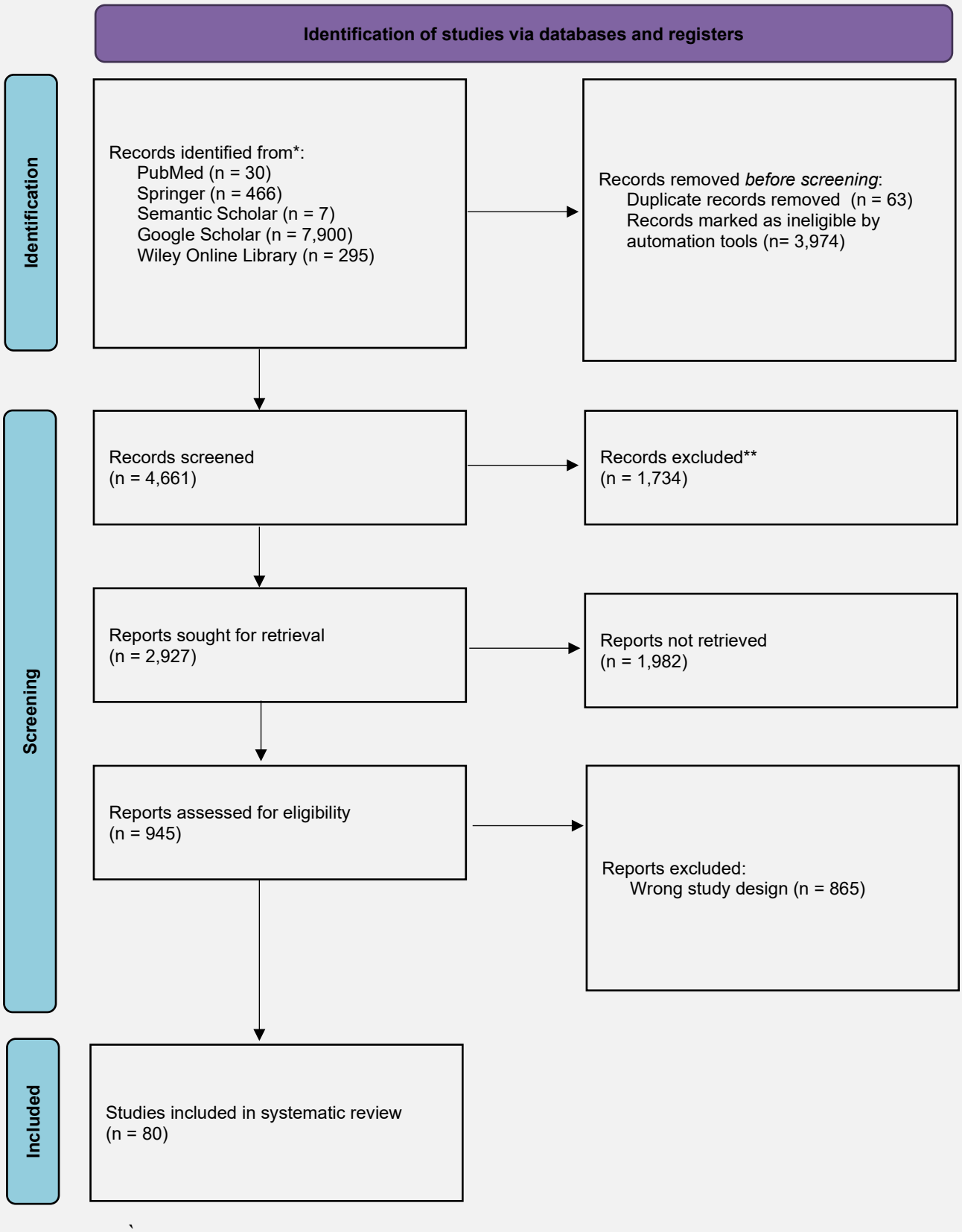

Figure 1. Article search flowchart

RESULTS

Characteristics of Included Studies

The systematic review included 80 sources examining time-restricted feeding (TRF) in individuals with overweight or obesity.

Study	Sample size	Duration	Population	TRF protocol
Dylan A Lowe et al., 2020	116 [1]	12 weeks [1]	BMI 27-43, age 18-64 [1]	8h (12pm-8pm) [1]
Humaira Jamshed et al., 2022	90 [7]	14 weeks [7]	Obesity, age 25-75 [7]	8h (7am-3pm) [7]
Tingting Che et al., 2021	120 [2]	12 weeks [2]	BMI ≥25, T2DM [2]	10h (8am-6pm) [2]
Darin Ruanpeng et al., 2021	511 [24]	≥8 weeks [24]	BMI ≥24 [24]	4-8h window [24]
Emily N. C. Manoogian et al., 2024	108 [25]	3 months [25]	Metabolic syndrome [25]	8-10h window [25]
M. Dote-Montero et al., 2025	197 [26]	12 weeks [26]	Overweight/obesity [26]	8h (early/late/self-selected) [26]
S. Cienfuegos et al., 2021	32 [27]	8 weeks [27]	Obesity, women only [27]	4-6h window [27]
V. Pavlou et al., 2024	75 [18]	6 months [18]	Obesity, T2DM [18]	8h (12pm-8pm) [18]

Study	Sample size	Duration	Population	TRF protocol
M. Arvanitakis et al., 2023	90 [28]	12 months [28]	Obesity, diverse population [28]	8h (12pm-8pm) [28]
K. Gabel et al., 2022	32 [29]	8 weeks [29]	Obesity, women only [29]	4-6h window [29]
Haohao Zhang et al., 2025	90 [30]	16 weeks [30]	Obesity, T2DM [30]	10h window [30]
Anna Ramirez-Obermayer et al., 2026	46 [31]	12 weeks [31]	T2DM, insulin-treated [31]	18h fasting [31]
K. Gabel et al., 2018	46 [3]	12 weeks [3]	BMI 30-45 [3]	8h (10am-6pm) [3]
S. Cienfuegos et al., 2020	49 [4]	8 weeks [4]	BMI 30-50 [4]	4h/6h windows [4]
Deying Liu et al., 2022	139 [16]	12 months [16]	Obesity [16]	8h (8am-4pm) [16]
I. Pureza et al., 2020	58 [32]	21 days [32]	Obesity, women [32]	12h window [32]
Jie-Hua Chen et al., 2021	Not specified [22]	>4 weeks [22]	Overweight/obesity [22]	Variable [22]

Study	Sample size	Duration	Population	TRF protocol
L. S. Santos-Báez et al., 2022	62 [33]	12 months [33]	Age 50-75, prediabetes/T2 DM [33]	≤10h window [33]
P. Peeke et al., 2021	78 [34]	8 weeks [34]	BMI ≥30 [34]	10h/12h windows [34]
Lijun Zhao et al., 2022	15 [35]	8 weeks [35]	Obesity, men only [35]	10h window [35]
Isabele Rejane de Oliveira Maranhão Pureza et al., 2020	58 [36]	12 months [36]	Obesity, women [36]	12h window [36]
Xueyun Wei et al., 2023	88 [5]	12 months [5]	Obesity, NAFLD [5]	8h (8am-4pm) [5]
Iwona Świątkiewicz et al., 2024	26 [37]	12 weeks [37]	Metabolic syndrome [37]	10h window [37]
K. Gabel et al., 2019	23 [38]	12 weeks [38]	BMI 30-45 [38]	8h (10am-6pm) [38]
S. Simon et al., 2022	20 [39]	12 weeks [39]	BMI ≥25 [39]	8h self-selected [39]
Li-min Zhang et al., 2022	60 [40]	8 weeks [40]	Overweight/obesity, age 19-29 [40]	6h (7am-1pm or 12pm-6pm) [40]

Study	Sample size	Duration	Population	TRF protocol
L. Chow et al., 2019	21 [11]	12 weeks [11]	Overweight without diabetes [11]	8h (goal), 10.4h (actual) [11]
Dunja Przulj et al., 2021	50 [41]	12 weeks [41]	BMI ≥30 or ≥28 with comorbidities [41]	8h self-selected [41]
Christopher J Kotarsky et al., 2021	21 [42]	8 weeks [42]	BMI 25-35, age 35-60 [42]	8h (12pm-8pm) [42]
N. Maruthur et al., 2024	41 [14]	12 weeks [14]	Obesity, prediabetes/T2 DM [14]	10h (early eating) [14]
M. Harvie et al., 2011	107 [43]	6 months [43]	BMI 24-40, women [43]	2 days VLCD/week [43]
I. Ferrocino et al., 2022	49 [44]	12 weeks [44]	BMI 30-45 [44]	<12h window [44]
T. Črešnovar et al., 2025	108 [8]	3 months [8]	Overweight/obesity [8]	8h window [8]
J. S. Quist et al., 2020	100 [45]	6 months [45]	BMI ≥25 or ≥30, prediabetes [45]	10h (6am-8pm) [45]

Study	Sample size	Duration	Population	TRF protocol
J. D. Schroder et al., 2021	32 [46]	3 months [46]	Obesity, women [46]	8h (12pm-8pm) [46]
Shuhao Lin et al., 2023	90 [6]	12 months [6]	Obesity, racially diverse [6]	8h (12pm-8pm) [6]
Hyeyun Kim et al., 2020	15 [47]	4 weeks [47]	BMI >25 [47]	8h (12pm-8pm) [47]
J. S. Quist et al., 2024	100 [21]	6 months [21]	BMI ≥30, prediabetes [21]	10h (6am-8pm) [21]
H. K. Varkaneh et al., 2022	Not specified [12]	12 weeks [12]	NAFLD [12]	8h window [12]
T. Sundfør et al., 2018	112 [17]	12 months [17]	BMI 30-45, metabolic syndrome [17]	IER (2 days/week) [17]
E. Borgundvaag et al., 2020	338 [48]	Median 24 weeks [48]	T2DM, BMI 32.4-37.9 [48]	4-8h window [48]
Joo Hyun Oh et al., 2025	337 [49]	16 weeks [49]	Obesity, MASLD [49]	Not specified [49]
N. Maruthur et al., 2020	41 [50]	12 weeks [50]	BMI 30-49.9, prediabetes [50]	Early eating (80% before 1pm) [50]

Study	Sample size	Duration	Population	TRF protocol
Hanieh Irani et al., 2023	56 [51]	8 weeks [51]	BMI 26-39.9, women, food addiction [51]	10h (10am-8pm) [51]
Malini A. Prasad et al., 2020	30 [52]	3 months [52]	BMI ≥25 [52]	10h window [52]
Ranya Ameur et al., 2024	64 [53]	12 weeks [53]	BMI >30, women, age 18-45 [53]	8h (8am-4pm) [53]
Emily N. C. Manoogian et al., 2021	19 [54]	3 months [54]	Metabolic syndrome [54]	10h window [54]
C. K. Kramer et al., 2024	39 [19]	6 weeks [19]	Overweight, early T2DM [19]	4h window [19]
K. Gabel et al., 2020	32 [23]	8-12 weeks [23]	Obesity [23]	6h/8h windows [23]
Mahshad Shafiee et al., 2025	46 [13]	12 weeks [13]	BMI ≥25, MAFLD [13]	8h window [13]
Daiani Evangelista Ribeiro et al., 2021	24 [55]	8 weeks [55]	Overweight/obesity [55]	8h (12pm-8pm) [55]
Souptik Barua et al., 2023	10 [56]	14 days [56]	BMI >28, prediabetes [56]	5h (8am-1pm) [56]

Study	Sample size	Duration	Population	TRF protocol
J. Feehan et al., 2023	32 [57]	12 weeks [57]	NAFLD [57]	8h (12pm-8pm) [57]
Beini Lao et al., 2023	28 [58]	12 weeks [58]	Overweight/obesity, CKD stages 3-4 [58]	8h (7am-12pm) [58]
Ruth-Alma N Turkson-Ocran et al., 2021	41 [59]	12 weeks [59]	BMI 30-50, prediabetes [59]	Early eating (ends before 1pm) [59]
Dylan A Lowe et al., 2020a	140 [60]	12 weeks [60]	BMI 27-43 [60]	8h (12pm-8pm) [60]
Sofia Tsitsou et al., 2024	60 [61]	12 weeks [61]	NAFLD [61]	10h window [61]
L. S. Santos-Báez et al., 2025	88 [62]	12 weeks [62]	Obesity without metabolic syndrome [62]	10h (actual) [62]
K. L. Haganes et al., 2022	131 [63]	7 weeks [63]	Overweight/obesity, women [63]	≤10h window [63]
Mair Underwood et al., 2022	62 [64]	12 months [64]	Age 50-75, prediabetes/T2 DM [64]	≤10h window [64]
Bingjie Wang et al., 2025	758 [65]	Variable [65]	BMI ≥25 [65]	Variable [65]

Study	Sample size	Duration	Population	TRF protocol
Maryam Nilghaz et al., 2025	42 [66]	12 weeks [66]	MAFLD [66]	8h window [66]
S. Carter et al., 2016	63 [20]	12 weeks [20]	BMI 35.2±5, T2DM [20]	2 days IER/week [20]
F. Aksungar et al., 2016	23 [67]	24 months [67]	BMI 29-39, women [67]	9h evening window [67]
E. Parr et al., 2020	24 [68]	6 weeks [68]	BMI 25-45, T2DM [68]	9h (10am-7pm) [68]
Nathália Cavalcanti de Morais Araújo et al., 2025	57 [69]	10 weeks [69]	Obesity, climacteric women [69]	12h (7pm-7am fast) [69]
V. Siles-Guerrero et al., 2024	623 [70]	≥6 months [70]	Obesity [70]	Variable [70]
Alyson Hill et al., 2024	75 [71]	6 months [71]	T2DM [71]	8h (12pm-8pm) [71]
T. Arnason et al., 2017	10 [72]	6 weeks [72]	BMI 36.9, T2DM [72]	4-6h midafternoon [72]
S. Cienfuegos et al., 2020a	49 [73]	8 weeks [73]	Obesity [73]	4h/6h windows [73]

Study	Sample size	Duration	Population	TRF protocol
Sarra Miladi et al., 2025	61 [74]	12 weeks [74]	BMI >25, women [74]	8h (early/late) [74]
Charlotte Andriessen et al., 2022	14 [75]	3 weeks [75]	BMI ≥25, T2DM [75]	10h daytime [75]
Shuhao Lin et al., 2022	63 [9]	6 months [9]	Obesity [9]	8h (12pm-8pm) [9]
Nesrine Dhieb et al., 2025	100 [76]	3 months [76]	Obesity, women [76]	8h window [76]
E. Parr et al., 2024	51 [10]	6 months [10]	BMI 25-40, T2DM [10]	9h (10am-7pm) [10]
S. Cienfuegos et al., 2022	65 [77]	6 months [77]	Obesity [77]	8h (12pm-8pm) [77]
Dalila Rubí Mena-Hernández et al., 2024	17 [78]	8 weeks [78]	BMI >25 [78]	8h (7am-3pm) [78]
Shuhao Lin et al., 2025	90 [79]	12 months [79]	BMI 30-50 [79]	8h/10h windows [79]
B. Peters et al., 2024	31 [15]	10 weeks [15]	BMI 25-35, women [15]	8h (8am-4pm or 1pm-9pm) [15]
M. Khalafi et al., 2024	2032 [80]	≥6 months [80]	Overweight/obesity [80]	Variable [80]

Study durations ranged from 2 weeks [72] to 24 months [67], with most interventions lasting 8-12 weeks. Sample sizes varied considerably, from small pilot studies with 10-20 participants [47, 52, 56, 72] to larger trials with over 100 participants [1, 5–7, 17]. The meta-analyses included substantially larger pooled samples, ranging from 338 [48] to 2032 participants [80].

Study populations were predominantly middle-aged adults, with mean ages typically between 40-60 years [1, 6, 7, 17, 59]. Several studies focused exclusively on women [15, 27, 29, 32, 36, 43, 46, 53, 63, 74, 76], while others included both sexes [1, 4, 7, 17]. Mean BMI ranged from approximately 29 to 39 kg/m² [2–4, 17, 18, 21, 41, 42]. Several studies specifically recruited participants with type 2 diabetes [2, 10, 18, 20, 30, 48, 68, 71, 75], metabolic syndrome [17, 25, 37, 54], or non-alcoholic fatty liver disease [5, 12, 13, 49, 57, 61, 66].

Geographic settings were diverse, including studies conducted in the United States [1, 6, 7, 79], China [2, 5, 16, 30, 40, 58], Europe [15, 17, 21, 31, 37, 44, 75], Iran [13, 51, 66], Australia [10, 57, 68], Tunisia [53, 74], and Korea [47].

Effects of TRF on Body Weight and Composition

Weight loss represented the most consistently measured outcome across studies. The magnitude of weight reduction with TRF varied substantially, ranging from minimal loss to clinically significant reductions.

Study	TRF weight change	Control weight change	Between-group difference	Statistical significance
Dylan A Lowe et al., 2020	-0.94 kg [1]	-0.68 kg [1]	-0.26 kg (95% CI -1.30 to 0.78) [1]	P=0.63 [1]
Humaira Jamshed et al., 2022	-2.3 kg (95% CI -3.7 to -0.9) [7]	Not specified	Not specified	P=0.002 [7]

Study	TRF weight change	Control weight change	Between-group difference	Statistical significance
Tingting Che et al., 2021	-2.98 kg [2]	-0.83 kg [2]	Not specified	P<0.001 [2]
Darin Ruanpeng et al., 2021	-2.08 kg (95% CI -3.49 to -0.68) [24]	Control reference	-2.08 kg [24]	Not specified
Deying Liu et al., 2022	-8.0 kg (95% CI -9.6 to -6.4) [16]	-6.3 kg (95% CI -7.8 to -4.7) [16]	-1.8 kg (95% CI -4.0 to 0.4) [16]	P=0.11 [16]
K. Gabel et al., 2018	-2.6% [3]	Control reference	Not specified	P<0.05 [3]
S. Cienfuegos et al., 2020	~3% [4]	Control reference	Not specified	P<0.001 [4]
Shuhao Lin et al., 2023	-4.61 kg (95% CI -7.37 to -1.85) [6]	Not specified	Compared to control	P≤0.01 [6]
J. S. Quist et al., 2024	-0.8 kg (95% CI -1.7 to 0.2) [21]	Control reference	-0.8 kg [21]	P=0.099 [21]
Xueyun Wei et al., 2023	-8.4 kg (95% CI -10.3 to -6.4) [5]	-7.8 kg (95% CI -9.7 to -5.9) [5]	No significant difference	Not significant [5]

Study	TRF weight change	Control weight change	Between-group difference	Statistical significance
Christopher J Kotarsky et al., 2021	-3.3% [42]	-0.2% [42]	Not specified	Significant [42]
Dunja Przulj et al., 2021	-2.6 kg [41]	Not specified	Not specified	Not specified
I. Ferrocino et al., 2022	-4.0 kg [44]	-2.2 kg [44]	Not specified	P=0.049 [44]
M. Harvie et al., 2011	-6.4 kg (95% CI -7.9 to -4.8) [43]	-5.6 kg (95% CI -6.9 to -4.4) [43]	Not significant	P=0.4 [43]
T. Sundfør et al., 2018	-8.0 kg [17]	-9.0 kg [17]	Not significant	P=0.6 [17]
V. Pavlou et al., 2024	-3.56% (95% CI -5.92 to -1.20) [18]	Not specified	Compared to control	P<0.003 [18]
Malini A. Prasad et al., 2020	-3.0 kg [52]	Not specified	Not specified	P=0.025 [52]
T. Črešnovar et al., 2025	-5.0 kg (95% CI -5.7, -4.3) [8]	-4.3 kg (95% CI -5.0, -3.6) [8]	Not significant	P<0.001 for time [8]

Study	TRF weight change	Control weight change	Between-group difference	Statistical significance
L. Chow et al., 2019	-3.6 kg [11]	-1.4 kg [11]	Not specified	P≤0.05 [11]

Several studies directly compared TRF with calorie restriction, revealing comparable weight loss effects. Liu et al. found no significant difference in 12-month weight loss between time-restricted eating (-8.0 kg) and daily calorie restriction (-6.3 kg), with a between-group difference of only -1.8 kg (95% CI -4.0 to 0.4, P=0.11) [16]. Similarly, Wei et al. reported that both TRF and continuous calorie restriction produced equivalent reductions in body weight over 12 months [5], while Harvie et al. found comparable weight loss between intermittent and continuous energy restriction (-6.4 kg vs -5.6 kg, P=0.4) [43]. The meta-analysis by Khalafi et al. confirmed these findings, showing that TRF and continuous calorie restriction were comparably effective for reducing body weight [80].

Body composition changes revealed a concerning pattern across multiple studies. While TRF effectively reduced fat mass, several investigations documented simultaneous reductions in lean mass. The meta-analysis by Darin Ruanpeng et al. found that TRF resulted in mean fat mass loss of -1.29 kg (95% CI -2.04 to -0.54) but also lean mass loss of -0.59 kg (95% CI -1.15 to -0.03) [24]. Chen et al.'s meta-analysis specifically noted that weight loss with TRF was mainly attributed to loss of lean mass rather than fat mass [22]. Individual trials corroborated this finding: Lowe et al. reported a significant difference in appendicular lean mass index between TRF and control groups (-0.16 kg/m², 95% CI -0.27 to -0.05, P=0.005) [1], while Gabel et al. found that 6-hour TRF led to significantly greater lean mass loss (-1.8 kg) compared to 8-hour TRF and controls [23].

Visceral fat and waist circumference showed more favorable responses. Chow et al. reported that TRF decreased visceral fat by -260 g while the control group showed an increase of 38 g (P≤0.05) [11]. Multiple studies documented significant reductions in waist circumference with TRF [2, 8, 12, 13, 19, 37, 57, 66], though the magnitude varied across interventions.

Effects of TRF on Glycemic Control

Glycemic parameters demonstrated variable responses to TRF across studies, with the most consistent improvements observed in populations with existing glucose dysregulation.

Study	Population	HbA1c change	Fasting glucose change	Insulin resistance change	Statistical significance
Tingting Che et al., 2021	T2DM [2]	-1.54% [2]	-1.47 mmol/L [2]	HOMA-IR -0.51 [2]	P<0.001 [2]
Emily N. C. Manoogian et al., 2024	Metabolic syndrome [25]	-0.10% (95% CI -0.19 to -0.003) [25]	Not reported	Not reported	P=0.002 [25]
V. Pavlou et al., 2024	T2DM [18]	-0.91% (95% CI -1.61 to -0.20) [18]	Not reported	Not reported	Not specified
Charlotte Andriessen et al., 2022	T2DM [75]	No change [75]	-0.6-1.0 mmol/L [75]	No change [75]	P=0.03-0.04 [75]
C. K. Kramer et al., 2024	Early T2DM [19]	-0.32% [19]	No change [19]	HOMA-IR -14% [19]	P=0.03 [19]

Study	Population	HbA1c change	Fasting glucose change	Insulin resistance change	Statistical significance
E. Parr et al., 2024	T2DM [10]	-0.4%/-0.3% [10]	Reduced [10]	Reduced [10]	P=0.002 [10]
S. Carter et al., 2016	T2DM [20]	-0.7% [20]	Not reported	Not reported	P<0.001 [20]
K. Gabel et al., 2018	No diabetes [3]	Not measured	No change [3]	No change [3]	Not significant [3]
J. S. Quist et al., 2024	Prediabetes [21]	Small reduction [21]	No change [21]	No change [21]	Not significant [21]
N. Maruthur et al., 2024	Prediabetes/T2DM [14]	Not measured	Not measured	No difference [14]	Not significant [14]

The strongest glycemic improvements occurred in participants with established type 2 diabetes. Che et al. documented substantial reductions in HbA1c (-1.54%), fasting glucose (-1.47 mmol/L), and improvements in both beta-cell function (HOMA-β +0.73) and insulin resistance (HOMA-IR -0.51) among participants with T2DM following 10-hour TRF [2]. These changes were accompanied by reduced medication requirements [2]. Similarly, Carter et al. reported significant HbA1c reductions (-0.7%) in people with T2DM [20], while Pavlou et al. found HbA1c decreased by -0.91% (95% CI -1.61 to -0.20) in insulin-treated patients with T2DM [18].

Beta-cell function showed promising responses in selected studies. Kramer et al.'s crossover trial demonstrated a 14% increase in beta-cell function (ISSI-2) with 4-hour TRF, accompanied by a 14% reduction in hepatic insulin resistance (P=0.03) [19]. This occurred despite participants already receiving antidiabetic treatment and having relatively well-controlled diabetes at baseline.

Continuous glucose monitoring data provided granular insights into glucose patterns. Barua et al. found that early TRF (eating 8am-1pm) reduced time spent in the 140-180 mg/dL glucose range by 3.3% overall (P=0.01) and by 4.3% during daytime hours (P=0.02) compared to a usual feeding pattern in participants with prediabetes [56]. Andriessen et al. reported that 10-hour TRF increased time spent in the normoglycemic range by approximately 3 hours per day (15.1 vs 12.2 hours, P=0.01) in individuals with T2DM [75].

Insulin sensitivity measures yielded mixed results. Harvie et al. found greater reductions in fasting insulin and insulin resistance with intermittent energy restriction compared to continuous restriction in premenopausal women [43], while Cienfuegos et al. demonstrated significant reductions in HOMA-IR with both 4-hour (29% reduction) and 6-hour (12% reduction) TRF protocols [4]. Conversely, Peters et al.'s well-controlled isocaloric crossover trial found no differences in insulin sensitivity between early TRF (8am-4pm), late TRF (1pm-9pm), and baseline conditions [15].

Studies in metabolically healthy individuals or those with prediabetes showed more modest glycemic improvements. Maruthur et al.'s isocaloric feeding study found no differences in glucose homeostasis measures between TRF and a usual eating pattern when caloric intake was held constant [14], while Quist et al. reported only small, non-significant reductions in HbA1c after 3 months of 10-hour TRF in individuals with prediabetes [21].

Effects of TRF on Lipid Profiles

Lipid parameter responses to TRF showed considerable heterogeneity across studies, with most investigations reporting minimal or inconsistent changes.

Study	Total cholesterol	LDL cholesterol	HDL cholesterol	Triglycerides	Significance
Tingting Che et al., 2021	-0.32 mmol/L [2]	-0.42 mmol/L [2]	No change [2]	-0.23 mmol/L [2]	P=0.01-0.03 [2]
H. K. Varkaneh et al., 2022	190→157.8 mg/dL [12]	104.6→84 mg/dL [12]	Not reported	201.5→133.3 mg/dL [12]	P<0.05 [12]
Xueyun Wei et al., 2023	-10.2 mg/dL [5]	-12.5 mg/dL [5]	+6.5 mg/dL [5]	-39.0 mg/dL [5]	No between-group difference [5]
K. Gabel et al., 2018	No change [3]	No change [3]	No change [3]	No change [3]	Not significant [3]
S. Cienfuegos et al., 2020	Not measured	No change [4]	No change [4]	No change [4]	P=0.76-0.96 [4]
M. Harvie et al., 2011	Comparable reductions [43]	Comparable reductions [43]	No change [43]	Comparable reductions [43]	Not significant [43]

Study	Total cholesterol	LDL cholesterol	HDL cholesterol	Triglycerides	Significance
I. Ferrocino et al., 2022	No between-group difference [44]	Not measured	No between-group difference [44]	No between-group difference [44]	P>0.05 [44]
L. Chow et al., 2019	Not measured	Not measured	Not measured	-23.6% [11]	P≤0.05 [11]
Mahshad Shafiee et al., 2025	No change [13]	No change [13]	+3.91 mg/dL [13]	-46.85 mg/dL [13]	P=0.001-0.003 [13]

Triglycerides showed the most consistent improvements with TRF. Che et al. found significant reductions in triglyceride levels (-0.23 mmol/L, P=0.03) among participants with T2DM [2], while Varkaneh et al. reported substantial decreases from 201.5 to 133.3 mg/dL (P<0.05) [12]. Chow et al. documented a 23.6% reduction in triglycerides with TRF compared to minimal change in controls [11], and Shafiee et al. found a 26.4% reduction in triglycerides [13]. The meta-analysis by Khalafi et al. confirmed a significant triglyceride reduction of -0.12 mmol/L compared to controls [80].

LDL cholesterol changes were inconsistent and sometimes unfavorable. Che et al. reported significant LDL reductions (-0.42 mmol/L, P=0.02) with 10-hour TRF [2], and Varkaneh et al. showed decreases from 104.6 to 84 mg/dL [12]. However, Zhang et al. found that both 6-hour early and late TRF increased LDL cholesterol compared to controls at week 8 (P=0.045 and P=0.033, respectively) [40]. Chen et al.'s meta-analysis noted that TRE increased LDL-C [22], raising concerns about lipid safety in certain populations.

HDL cholesterol generally showed minimal changes. Most studies reported no significant effects on HDL [3, 4, 27, 29, 43, 44], though some documented small increases [5, 13, 57, 80]. Peters et al. found that both early and late TRF decreased HDL cholesterol in a 10-week isocaloric trial (-0.10 mmol/L for early TRF, $P=6.0\times10^{-5}$; -0.07 mmol/L for late TRF, P=0.003) [15].

Total cholesterol changes paralleled LDL patterns, with some studies showing reductions [2, 12] while others reported no significant changes [3, 44]. Wei et al. found that both TRF and daily calorie restriction produced similar reductions in total cholesterol over 12 months, with no between-group differences [5].

Effects of TRF on Blood Pressure and Cardiovascular Markers

Blood pressure responses to TRF varied considerably across studies, with systolic and diastolic pressures showing different patterns.

Study	Systolic BP change	Diastolic BP change	Population characteristics	Significance
K. Gabel et al., 2018	-7 mm Hg [3]	No change [3]	Metabolically healthy obesity [3]	P<0.05 [3]
Humaira Jamshed et al., 2022	Not reported	-4 mm Hg (95% CI -8 to 0) [7]	Obesity receiving weight-loss treatment [7]	P=0.04 [7]
Malini A. Prasad et al., 2020	-21 mm Hg [52]	-13 mm Hg [52]	BMI ≥25 [52]	P=0.013-0.04 [52]
Shuhao Lin et al., 2022	No change [9]	-4.0 mm Hg [9]	Obesity [9]	P=0.04 [9]

Study	Systolic BP change	Diastolic BP change	Population characteristics	Significance
Iwona Świątkiewicz et al., 2024	-4.8 mm Hg [37]	No change [37]	Metabolic syndrome [37]	P<0.012 [37]
T. Črešnovar et al., 2025	No change [8]	-4 mm Hg (95% CI -8 to 0) [8]	Overweight/obesity [8]	P=0.033 [8]
E. Parr et al., 2024	-4 to -5 mm Hg [10]	-3 mm Hg [10]	T2DM [10]	P=0.04 to <0.01 [10]
Christopher J Kotarsky et al., 2021	-6 mm Hg [42]	-1 mm Hg [42]	Overweight/obesity [42]	Significant [42]
Ranya Ameur et al., 2024	Decreased [53]	Decreased [53]	Obesity, women [53]	P=0.02-0.04 [53]

Diastolic blood pressure showed more consistent improvements than systolic pressure across multiple studies. Jamshed et al. found that early TRF (7am-3pm eating window) improved diastolic blood pressure by -4 mm Hg (95% CI -8 to 0, P=0.04) [7], while several other investigations reported similar diastolic reductions ranging from -3 to -4 mm Hg [8–10]. The meta-analysis by Khalafi et al. confirmed a significant reduction in diastolic blood pressure (WMD -2.24 mmHg) when comparing TRF to controls [80].

Systolic blood pressure responses were more variable. Gabel et al. reported a -7 mm Hg reduction in systolic pressure with 8-hour TRF [3], and Prasad et al. found an exceptionally large decrease of -21 mm Hg [52]. However, several studies

found no significant systolic blood pressure changes [9], and one investigation suggested that TRF might actually attenuate blood pressure improvements compared to a usual eating pattern when both groups consumed healthy isocaloric diets [59].

Cardiovascular risk markers beyond blood pressure received limited attention. Schroder et al. calculated that TRF reduced 30-year cardiovascular disease risk by 12%, with this reduction correlating with decreases in body fat percentage (r=0.62) and increases in muscle mass percentage (r=-0.74) [46]. Świątkiewicz et al. found that TRF significantly reduced SCORE2 cardiovascular risk values in patients with metabolic syndrome [37].

Effects of TRF on Hepatic Parameters

Studies examining liver-specific outcomes in populations with hepatic steatosis showed notable improvements with TRF.

Study	Population	Hepatic steatosis change	Liver enzymes	Fibrosis markers	Between-group differences
Xueyun Wei et al., 2023	NAFLD [5]	IHTG -6.9% [5]	ALT -14.2 U/L [5]	Not reported	No difference vs. CR [5]
Joo Hyun Oh et al., 2025	MASLD [49]	-25.8% [49]	Not reported	Similar to CR [49]	P<0.001 vs. SOC [49]
H. K. Varkaneh et al., 2022	NAFLD [12]	CAP -51.9 dB/m [12]	ALT -12.8 U/L, AST -5.8 U/L, GGT -9.8 U/L [12]	Fibrosis -1.1 kPa [12]	P<0.05 vs. control [12]

Study	Population	Hepatic steatosis change	Liver enzymes	Fibrosis markers	Between-group differences
J. Feehan et al., 2023	NAFLD [57]	CAP -9.96 dB/m [57]	ALT decreased [57]	Not reported	P=0.038 [57]
Mahshad Shafiee et al., 2025	MAFLD [13]	Fatty Liver Index - 26.90 [13]	ALT -17.14 U/L, GGT -21.09 U/L [13]	FIB-4 - 27.8% [13]	P<0.001 [13]
Maryam Nilghaz et al., 2025	MAFLD [66]	Steatosis score - 68.57 [66]	ALT -15.23 U/L, AST - 7.52 U/L [66]	Not reported	Significant vs. control [66]

TRF combined with dietary interventions produced substantial improvements in hepatic steatosis. Oh et al. demonstrated a 25.8% reduction in hepatic steatosis with TRF compared to 0.7% in standard care (P<0.001), though this effect was comparable to calorie restriction [49]. Wei et al. found that both TRF and daily calorie restriction reduced intrahepatic triglyceride content by approximately 7% at 12 months, with no significant between-group differences [5].

Liver enzyme improvements accompanied steatosis reductions. Varkaneh et al. reported significant decreases in alanine aminotransferase (34 to 21.2 U/L), aspartate aminotransferase (26.3 to 20.5 U/L), and γ-glutamyl transpeptidase (33 to 23.2 U/L) with TRF plus a low-sugar diet in NAFLD patients (P<0.05) [12]. Shafiee et al. found even greater ALT reductions (-17.14 U/L) when combining TRF with a lacto-ovo vegetarian diet [13]. Świątkiewicz et al. documented 20% reductions in both ALT and AST with 10-hour TRF in metabolic syndrome patients [37].

Controlled attenuation parameter (CAP), a measure of hepatic steatosis severity, decreased significantly in multiple trials. Varkaneh et al. reported a

reduction from 322.9 to 270.9 dB/m (P<0.05) [12], while Feehan et al. found a mean difference of -9.96 dB/m with TRF compared to +20.46 dB/m with standard care (P=0.038) [57]. In a subgroup analysis of participants with severe steatosis (CAP >268 dB/m), Feehan et al. demonstrated even greater improvements (-26.10 dB/m with TRF vs. +15.10 dB/m with standard care, P=0.035) [57].

Effects of TRF on Inflammatory and Hormonal Markers

Inflammatory and hormonal responses to TRF received less consistent assessment across studies.

Inflammatory markers showed variable responses. Cienfuegos et al. reported significant reductions in 8-isoprostane, a marker of oxidative stress, in both premenopausal and postmenopausal women with obesity [27], while Varkaneh et al. found decreases in high-sensitivity C-reactive protein (3.1 to 2.0 mg/L, P<0.05) and cytokeratin-18 (1.35 to 1.16 ng/mL, P<0.05) with TRF plus a low-sugar diet [12]. Shafiee et al. documented a 49.2% reduction in TNF-α levels [13], and Lao et al. observed significant TNF-α decreases in a chronic kidney disease population [58]. However, several studies found no changes in inflammatory markers including TNF-alpha and IL-6 [15, 27, 29, 40, 42].

Leptin levels generally decreased with TRF in studies that measured this adipokine. Zhang et al. found greater leptin reductions with 6-hour early TRF compared to late TRF or control conditions [40], while Feehan et al. reported significant leptin decreases accompanied by adiponectin increases with TRF [57]. Peters et al. demonstrated leptin reductions in both early and late TRF protocols, though adiponectin decreased with early TRF and increased with late TRF [15].

Brain-derived neurotrophic factor (BDNF) emerged as a marker of interest in one investigation. Irani et al. found that TRF combined with a low-calorie diet significantly increased serum BDNF levels compared to calorie restriction alone in women with food addiction [51].

Thyroid axis activity showed differential responses based on the timing and duration of TRF. Zhang et al. reported that 6-hour early TRF (7am-1pm) reduced thyroid axis activity more than late TRF (12pm-6pm) or control conditions [40], suggesting potential effects of meal timing on thyroid function.

Timing Effects: Early versus Late Feeding Windows

Several studies directly compared early versus late eating windows, revealing distinct metabolic effects based on the temporal placement of the feeding period.

Study	Early TRF protocol	Late TRF protocol	Key findings	Significance
Humaira Jamshed et al., 2022	7am-3pm [7]	Not tested	Greater weight loss and BP improvement [7, 7]	P=0.002-0.04
Li-min Zhang et al., 2022	7am-1pm [40]	12pm-6pm [40]	eTRE: greater SBP reduction, thyroid modulation [40]	P=0.045
M. Dote-Montero et al., 2025	Early day [26]	Late day [26]	No difference in VAT reduction [26]	P=0.31-0.87 [26]
T. Črešnovar et al., 2025	Not specified [8]	Not specified [8]	eTRE: greater fat mass and glucose reduction [8, 8]	P=0.012-0.022 [8]

Study	Early TRF protocol	Late TRF protocol	Key findings	Significance
B. Peters et al., 2024	8am-4pm [15]	1pm-9pm [15]	No difference in insulin sensitivity [15]	P=0.83 [15]
Sarra Miladi et al., 2025	8am-4pm [74]	12pm-8pm [74]	No significant difference in weight or metabolic outcomes [74]	P<0.0005 for both [74]

Early TRF (eTRE) showed theoretical advantages in some studies but not others. Jamshed et al. found that an 8-hour eTRE protocol (7am-3pm) was more effective for losing weight (-2.3 kg, P=0.002) and improving diastolic blood pressure (-4 mm Hg, P=0.04) compared to eating over 12 or more hours [7, 7]. Zhang et al. reported that 6-hour eTRE (7am-1pm) reduced systolic blood pressure by -5.5 mmHg, improved thyroid axis activity, and showed greater metabolic benefits compared to late TRE (12pm-6pm) [40]. Črešnovar et al. demonstrated that eTRE combined with energy restriction produced greater improvements in fat mass (-1.2%, P=0.013), fasting glucose (-0.35 mmol/L, P=0.012), metabolic age (-3 years, P=0.028), and diastolic blood pressure (-4 mmHg, P=0.033) compared to late TRE or energy restriction alone [8, 8, 8].

However, several well-controlled studies found no metabolic advantages for early versus late eating windows. Peters et al.'s isocaloric crossover trial revealed no differences in insulin sensitivity between eTRE (8am-4pm) and late TRE (1pm-9pm) [15], though eTRE produced slightly greater weight loss (-1.08 kg vs -0.44 kg) [15]. Dote-Montero et al. found no significant differences in visceral adipose tissue reduction between early, late, and self-selected TRE schedules when combined with Mediterranean diet education [26]. Miladi et al. reported

comparable improvements in body weight, BMI, and metabolic parameters between early TRE (8am-4pm) and late TRE (12pm-8pm) when combined with physical activity [74].

The timing of caloric distribution within eating windows also appeared to matter. Maruthur et al.'s controlled feeding study compared TRF with 80% of calories before 1pm versus a usual feeding pattern with more than 50% of calories after 5pm, finding no difference in weight loss or glucose homeostasis when total calories were held constant [14, 14]. This suggests that the metabolic effects of TRF may depend more on caloric restriction than on circadian alignment per se.

Duration and Adherence Considerations

The duration of eating windows varied across studies, with potential implications for adherence and outcomes.

Eating window	Example studies	Adherence rates	Weight loss magnitude	Notes
4-6 hours	Cienfuegos et al., 2020 [4]; Kramer et al., 2024 [19]	~6.2 days/week [4]	~3% [4]	Greater fat-free mass loss [23]
8 hours	Multiple studies [1, 3, 5, 6, 16]	87% [28] to variable	2-8 kg [1, 5, 16]	Most common protocol
10 hours	Manoogian et al., 2024 [25]; Quist et al., 2024 [21]	91% [21]	Minimal to -1.0 kg [21]	Better adherence but smaller effects
12 hours	Pureza et al., 2020 [32]; Araújo et al., 2025 [69]	Not specified	Minimal [36, 69]	Approaching normal eating patterns

Shorter eating windows (4-6 hours) generally produced greater weight loss but at the cost of lean mass preservation. Cienfuegos et al. found that 4-hour TRF resulted in a 29% reduction in insulin resistance compared to 12% with 6-hour TRF, though both produced similar overall weight loss (~3%) [4]. Gabel et al. reported that 6-hour TRF led to significantly greater lean mass loss (-1.8 kg) than 8-hour TRF (P=0.005) [23].

Adherence patterns varied with eating window duration. The most commonly studied 8-hour protocols showed adherence rates of approximately 6 days per week (87%) [28], while 10-hour windows achieved higher adherence (91%) [21]. Quist et al. found that 83% of participants were highly adherent to a 10-hour TRF protocol during the 3-month intervention, with actual eating windows averaging 9.1 hours [21, 75].

Real-world adherence challenges emerged in several investigations. Parr et al. found that while initial adherence to 9-hour TRF among people with T2DM was 99%, this declined to 81% by six months [10]. Participants described hunger, daily stressors, and emotions as the main barriers to adherence [68]. Simon et al. noted that greater restriction of the eating window was associated with longer sleep duration (β=-0.46, 95% CI -9.2 to -0.4, P=0.03) [39].

TRF versus Continuous Calorie Restriction

Direct comparisons between TRF and calorie restriction revealed largely equivalent effects on most metabolic parameters.

Study	Duration	TRF weight loss	CR weight loss	Between-group difference	Additional findings
Deying Liu et al., 2022	12 months [16]	-8.0 kg [16]	-6.3 kg [16]	-1.8 kg (P=0.11) [16]	No metabolic differences [16]

Study	Duration	TRF weight loss	CR weight loss	Between-group difference	Additional findings
Xueyun Wei et al., 2023	12 months [5]	-8.4 kg [5]	-7.8 kg [5]	Not significant [5]	Similar hepatic improvements [5]
Shuhao Lin et al., 2023	12 months [6]	-4.61 kg [6]	-5.42 kg [6]	0.81 kg (P=0.68) [6]	Racially diverse population [6]
M. Harvie et al., 2011	6 months [43]	-6.4 kg [43]	-5.6 kg [43]	Not significant (P=0.4) [43]	IER superior for insulin sensitivity [43]
T. Sundfør et al., 2018	12 months [17]	-8.0 kg [17]	-9.0 kg [17]	Not significant (P=0.6) [17]	Similar fat/lean mass changes [17]
V. Pavlou et al., 2024	6 months [18]	-3.56% [18]	-1.78% [18]	TRE significant (P<0.003) [18]	T2DM population [18]

Study	Duration	TRF weight loss	CR weight loss	Between-group difference	Additional findings
S. Cienfuegos et al., 2022	6 months [77]	-3.4% [77]	-4.9% [77]	Not significant [77]	CR superior numerically [77]

Weight loss outcomes were remarkably similar between TRF and calorie restriction across multiple 12-month trials. Liu et al. found no significant difference in weight loss between TRF (-8.0 kg) and daily calorie restriction (-6.3 kg) after one year, with a between-group difference of only -1.8 kg (95% CI -4.0 to 0.4, P=0.11) [16]. Wei et al. corroborated these findings in a population with NAFLD, reporting virtually identical weight loss with TRF (-8.4 kg) and continuous restriction (-7.8 kg) at 12 months [5]. Lin et al.'s trial in a racially diverse population found similar results, with TRF producing -4.61 kg and calorie restriction -5.42 kg of weight loss (difference 0.81 kg, P=0.68) [6].

The meta-analyses provided synthesis across shorter-duration studies. Siles-Guerrero et al. found that fasting-based strategies led to slightly greater short-term reductions in body weight (-0.94 kg, P=0.004) and fat mass (-1.08 kg, P=0.0001) compared to continuous calorie restriction at 6 months, though these differences were not considered clinically significant [70]. Khalafi et al.'s meta-analysis of long-term interventions (≥6 months) demonstrated that TRF and continuous restriction were comparably effective for reducing body weight and adiposity [80].

Body composition changes differed in important ways. Khalafi et al. found that TRF produced significantly greater fat mass loss (-0.70 kg) and body fat percentage reduction (-0.59%) compared to continuous restriction [80], suggesting potential advantages for fat-specific outcomes despite equivalent total weight loss. However, this came at the cost of greater lean mass loss in some studies [23].

Insulin sensitivity responses revealed nuanced differences. Harvie et al. reported greater reductions in fasting insulin and insulin resistance with intermittent

energy restriction compared to continuous restriction in premenopausal women, despite similar overall weight loss [43]. Siles-Guerrero et al.'s meta-analysis confirmed that fasting-based strategies improved insulin sensitivity with significant reductions in fasting insulin (-7.46 pmol/L, P=0.02) and HOMA-IR (-0.14, P=0.02) [70]. However, other long-term trials found no differences in glucose homeostasis between TRF and calorie restriction [5, 16, 77].

Adherence and sustainability differed between approaches. Sundfør et al. found that while weight loss was similar between intermittent and continuous energy restriction, participants following the intermittent protocol reported higher hunger scores (4.7 vs 3.6, P=0.002) [17]. Conversely, Lin et al. noted high adherence to TRF (6 out of 7 days per week, 87%) with frequent dietetic support [28], though this level of professional input may not reflect real-world applicability.

Caloric Intake Mechanisms

The mechanisms by which TRF affects weight and metabolic parameters appear closely tied to caloric restriction.

Most TRF interventions resulted in spontaneous reductions in energy intake without explicit calorie counting. Gabel et al. reported that 8-hour TRF led to a spontaneous decrease in energy intake of 341 kcal/day [3], while Cienfuegos et al. found that both 4-hour and 6-hour TRF reduced intake by approximately 550 kcal/day without participants tracking calories [4]. Lin et al. documented mean reductions of 425 kcal/day with TRF and 405 kcal/day with calorie restriction in a 12-month trial [6].

Isocaloric studies provided critical insights. Maruthur et al.'s tightly controlled feeding study, where all food was provided by a metabolic kitchen to maintain weight-stable caloric intake, found that TRF did not reduce weight or improve glucose homeostasis compared to a usual eating pattern when calories were held constant [14, 14]. Similarly, Peters et al.'s isocaloric crossover trial showed no improvement in insulin sensitivity with either early or late TRF when caloric intake was controlled [15]. These findings strongly suggest that the metabolic benefits of TRF in free-living studies stem primarily from reduced caloric intake rather than from circadian or metabolic timing effects per se [14].

The relationship between energy restriction and outcomes was quantified in selected studies. Jamshed et al. reported that the effects of early TRF were equivalent to reducing calorie intake by an additional 214 kcal/day [7]. Shafiee et al. found that TRF combined with a lacto-ovo vegetarian diet resulted in a 32.4% reduction in energy intake, compared to 16.7% in controls [13], correlating with superior metabolic improvements.

Special Populations and Comorbidities

TRF effects in populations with specific metabolic conditions revealed distinct patterns.

Type 2 Diabetes Mellitus: Among insulin-treated patients with T2DM, Pavlou et al. found that 8-hour TRF produced significant weight loss (-3.56%, P<0.003) and HbA1c reduction (-0.91%) compared to controls [18, 18]. Che et al. demonstrated particularly robust improvements in participants with T2DM, including HbA1c reduction of -1.54% (P<0.001), along with improvements in beta-cell function and insulin resistance [2]. Kramer et al.'s crossover trial showed a 14% increase in beta-cell function (ISSI-2) and 14% reduction in hepatic insulin resistance with 4-hour TRF, despite participants already receiving antidiabetic medications [19]. Conversely, E. Parr et al. found that TRF was non-inferior but not superior to individualized dietetic guidance for improving HbA1c in people with T2DM [10].

Metabolic Syndrome: Participants with metabolic syndrome showed consistent improvements across multiple parameters. Świątkiewicz et al. found that 10-hour TRF reduced body weight by 2%, BMI by 1%, waist circumference by 2%, systolic blood pressure by 4%, fasting glucose by 4%, HbA1c by 4%, and sleepiness scores by 25% in Polish patients with metabolic syndrome [37, 37, 37]. Manoogian et al. reported that personalized 8-10 hour TRE improved HbA1c by -0.10% (95% CI -0.19% to -0.003%) in adults with metabolic syndrome already receiving standard-of-care pharmacotherapy [25].

NAFLD/MAFLD: Patients with hepatic steatosis demonstrated substantial liver-specific improvements. Oh et al. found that TRE reduced hepatic steatosis by 25.8% compared to 0.7% in standard care (P<0.001), with comparable effects to calorie restriction [49]. Varkaneh et al. reported significant reductions in multiple

liver parameters including controlled attenuation parameter (-51.9 dB/m), ALT (-12.8 U/L), AST (-5.8 U/L), and GGT (-9.8 U/L) with TRF plus a low-sugar diet ($P<0.05$) [12]. Feehan et al.'s analysis of participants with severe steatosis (CAP >268 dB/m) showed marked improvements (-26.10 dB/m with TRF vs. +15.10 dB/m with standard care, $P=0.035$) [57].

Chronic Kidney Disease: Lao et al.'s pilot study in overweight/obese patients with CKD stages 3-4 found that TRF improved estimated glomerular filtration rate (eGFR +3.1 ml/min/1.73m²) compared to a decline in controls (-0.8 ml/min/1.73m²), along with significant reductions in uric acid and improvements in gut microbiota [58].

Menopausal Status: Two secondary analyses specifically examined whether menopausal status modified TRF effects in women with obesity. Cienfuegos et al. found that weight loss and metabolic benefits did not differ between premenopausal and postmenopausal women, with both groups achieving -3.3% weight loss and similar improvements in fat mass, lean mass, fasting insulin, and insulin resistance [27, 29]. Adherence was equally excellent in both groups (6.2 days/week) [27, 29].

Intervention Combinations

Several studies examined TRF combined with other interventions, revealing potential synergistic effects.

TRF combined with exercise training showed additive benefits. Kotarsky et al. found that TRF plus 8 weeks of concurrent aerobic and resistance training produced greater fat mass loss (9.0%) than exercise with normal eating (3.3%), while both groups showed similar lean mass gains [42]. Ameur et al. demonstrated that combining TRF with high-intensity functional training (HIFT) led to superior reductions in total cholesterol, triglycerides, insulin, and HOMA-IR compared to TRF or HIFT alone [53]. Haganes et al. reported that the combination of TRF with HIIT improved HbA1c and induced greater reductions in total and visceral fat mass compared to either intervention alone [63].

TRF combined with specific dietary patterns also showed promise. Shafiee et al. found that TRF combined with a lacto-ovo vegetarian diet produced significant reductions in weight (-8.07 kg), BMI (-2.70 kg/m²), waist circumference

(-8.00 cm), liver enzymes, and inflammatory markers in patients with MAFLD [13, 13]. Nilghaz et al. reported that TRF with a DASH diet was superior to a low-calorie diet alone for reducing BMI, abdominal circumference, controlled attenuation parameter, and liver enzymes in MAFLD patients [66]. Varkaneh et al. demonstrated substantial metabolic improvements when combining TRF with a low-sugar diet, including reductions in liver stiffness, lipid parameters, and inflammatory markers [12].

Sex and Gender Considerations

Studies examining sex-specific responses were limited, with several trials conducted exclusively in women.

The investigations restricted to female participants [15, 27, 29, 32, 36, 43, 46, 53, 63, 74, 76] generally showed successful weight loss and metabolic improvements comparable to mixed-sex studies, suggesting TRF effectiveness is not sex-dependent. However, this limits generalizability to male populations in those specific contexts.

Studies including both sexes showed no clear indication that responses differed by gender. Sundfør et al. included equal proportions of men and women (50% each) and reported similar weight loss and metabolic improvements between the intermittent and continuous restriction groups, with no mention of sex-specific differences [17, 17]. Similarly, studies with predominantly female samples did not report differential effects requiring sex-based stratification.

Safety and Tolerability

Safety data across studies revealed generally favorable profiles for TRF, though certain concerns emerged.

Adverse events were minimal in most investigations. Dote-Montero et al. reported no serious adverse events, with only five participants experiencing mild adverse events across 197 participants [26]. Quist et al. documented one severe adverse event (subcutaneous nodule and arm pain) among 100 participants, along with reports of headaches, migraines, and general discomfort in the TRE group [21]. Zhang et al. noted hypoglycemia in 2 TRE patients, 2 TRE patients, and 3 continuous energy restriction patients, with no significant differences between

groups [30]. Lao et al. reported one patient in their TRF group experienced a slightly hypoglycemic reaction that resolved with food intake [58].

Metabolic safety markers were systematically assessed in several trials. Gabel et al. specifically evaluated safety parameters including eating disorder symptoms, body image perception, complete blood count, and resting metabolic rate, finding no concerning changes after 12 weeks of 8-hour TRF [38]. Wei et al. reported no serious adverse events or deaths during their 12-month trial, with mild adverse events (appetite changes, stomach discomfort) occurring at similar rates in TRF and calorie restriction groups [5].

Dropout rates ranged from 0% to over 50% across studies, though most were not primarily attributed to safety concerns. Pureza et al. reported a 53.44% dropout rate at 12 months, though reasons were not specified [36]. Quist et al. maintained excellent retention (92% during intervention, 89% at follow-up) [21], while several trials reported completion rates above 80% [6, 7, 62]. Arnason et al. noted that 6 out of 10 participants stated they would continue with the TRF regimen after study completion, suggesting acceptable tolerability [72].

Quality of life assessments were limited but generally neutral or positive. Pavlou et al. found that TRE did not significantly alter mood or quality of life in participants with T2DM who had baseline scores already within a healthy range [18]. Schroder et al. reported improved quality of life scores (WHOQOL-bref) with TRF [46], while Świątkiewicz et al. documented improvements in sleepiness and depression scores, particularly among participants achieving eating windows ≤10 hours per day [37].

Medication requirements changed favorably in populations receiving pharmacotherapy. Che et al. found that TRF reduced the medication effect score by -0.66 (P=0.006) in participants with T2DM, indicating decreased medication requirements [2]. Ramirez-Obermayer et al. noted that insulin doses were systematically reduced during fasting days according to a predetermined titration regimen, with hypoglycemia rates comparable between groups [31].

Long-term safety follow-up data remained limited. Most trials lasted 8-12 weeks, with the longest interventions extending to 12-24 months [5, 6, 16, 17, 67]. Wei et al.'s 12-month follow-up showed no significant safety concerns [5], while

Harvie et al. reported no major adverse effects over 6 months [43]. Aksungar et al.'s 24-month study found no adverse metabolic effects, though this was a small single-arm investigation in female participants [67].

Synthesis

The accumulated evidence reveals that time-restricted feeding produces meaningful but modest improvements in metabolic parameters among individuals with overweight or obesity, with effects largely mediated through caloric restriction rather than independent circadian mechanisms.

The core finding across studies is that TRF's metabolic benefits depend critically on whether it induces spontaneous caloric reduction. In free-living conditions where participants self-select foods, TRF consistently produces energy deficits of 300-550 kcal/day [3, 4, 6, 79], leading to weight loss of 2-8 kg over 8-12 weeks [1–6]. This mechanism is supported by the isocaloric feeding studies of Maruthur et al. and Peters et al., which found no metabolic advantages when caloric intake was experimentally controlled to weight-maintenance levels [14, 14, 15]. The implication is clear: TRF functions primarily as a practical strategy to reduce energy intake rather than as a metabolic intervention with effects independent of caloric balance.

The equivalence between TRF and continuous calorie restriction emerges as a robust finding from multiple 12-month trials [5, 6, 16, 17]. When both approaches produce similar caloric deficits, weight loss and most metabolic outcomes are comparable. This equivalence holds across diverse populations including individuals with NAFLD [5], racially diverse cohorts [6], and those with metabolic syndrome [17]. The meta-analysis by Khalafi et al. synthesizing studies ≥6 months duration confirms this pattern [80]. However, short-term studies (<6 months) sometimes show small advantages for TRF in fat mass loss and insulin sensitivity [43, 70], suggesting early metabolic adaptations that may not persist long-term.

The lean mass loss associated with TRF represents a clinically important concern that differentiates it from some other weight loss approaches. Multiple studies document that shorter eating windows (4-6 hours) produce greater lean mass reductions than longer windows or continuous restriction [23]. The meta-analyses

confirm this pattern, with Chen et al. noting weight loss was "mainly attributed to the loss of lean mass rather than fat mass" [22], and Ruanpeng et al. quantifying mean lean mass loss at -0.59 kg [24]. This effect likely reflects insufficient protein intake and distribution within compressed eating windows. The combination of TRF with resistance training appears to mitigate this concern, with Kotarsky et al. showing that TRF plus concurrent exercise training preserved lean mass while enhancing fat loss [42].

Population-specific effects reveal important nuances. In participants with established type 2 diabetes, TRF produces clinically meaningful improvements in HbA1c (reductions of 0.7-1.54%) [2, 10, 18–20] and enables medication reductions [2], whereas metabolically healthy individuals or those with prediabetes show minimal or no glycemic improvements [3, 14, 21]. The hepatic steatosis population demonstrates particularly robust liver-specific responses, with TRF reducing hepatic fat by 6.9-25.8% [5, 49] and improving liver enzymes substantially [12, 13, 66], though these effects remain comparable to standard calorie restriction [5, 49].

The early versus late timing debate remains partially resolved. While some studies suggest early feeding windows (morning-to-afternoon) produce superior outcomes for blood pressure [7], systolic pressure [40], glucose control [8], and thyroid modulation [40] compared to late windows, the two largest and most rigorous isocaloric studies found no metabolic differences between early and late TRF [15]. Dote-Montero et al.'s 197-participant trial found no differences in visceral fat reduction between early, late, and self-selected TRE schedules [26]. The apparent benefits of early TRF in observational studies likely reflect confounding by differential adherence, food choices, or caloric intake rather than true chronobiological advantages. The mechanistic hypothesis that early eating aligns better with circadian insulin sensitivity remains unproven in well-controlled human trials.

Adherence emerges as a critical mediator of TRF effectiveness, with actual eating windows typically longer than prescribed targets. Quist et al. found that participants assigned to 10-hour TRE actually maintained 9.1-hour windows [75], and adherence to even this modest restriction produced only minimal weight loss (-1.0 kg) [21]. The relationship between adherence and outcomes is dose-dependent:

Świątkiewicz et al. showed that only participants achieving eating windows ≤10 hours/day experienced significant metabolic improvements, while those with windows >10 hours showed no benefits [37]. Real-world adherence faces substantial barriers including hunger, daily stressors, and social eating patterns [68], suggesting that the high adherence rates achieved in trials with intensive dietetic support (87-91%) [21, 28] may not reflect feasibility in unsupported settings.

The metabolic benefits attributed to TRF appear most pronounced in short-term studies with participants who have existing metabolic dysfunction and when TRF successfully induces caloric restriction. Long-term equivalence to continuous calorie restriction, combined with concerns about lean mass loss and the lack of effects in isocaloric conditions, suggests TRF should be positioned as one tool among several for achieving energy balance rather than as a metabolically superior intervention. The practical advantage of TRF lies in its simplicity—no calorie counting required—which may enhance long-term adherence for individuals who find traditional dietary restriction burdensome. However, this advantage must be weighed against the risk of inadequate protein intake and lean mass loss, particularly with very narrow eating windows.

DISCUSSION

Weight Loss and Body Composition: Equivalent Efficacy but Differential Quality

The accumulated evidence demonstrates that TRF produces clinically meaningful weight loss in obese adults, with reductions ranging from 2-8 kg over 8-12 week interventions (1,4,5,9). However, the critical finding from multiple 12-month RCTs is that TRF and continuous calorie restriction achieve virtually identical weight loss when comparable caloric deficits are achieved. Liu et al.'s landmark trial comparing 12-month TRF (8h eating window) with daily calorie restriction found no significant difference in weight loss (-8.0 kg vs. -6.3 kg, between-group difference -1.8 kg, 95% CI -4.0 to 0.4, P=0.11) (26). Wei et al. corroborated these findings in NAFLD patients, reporting equivalent 12-month weight loss between TRF and CCR (-8.4 kg vs. -7.8 kg, P>0.05) (21). Lin et al.'s racially diverse cohort similarly demonstrated comparable efficacy (-4.61 kg vs. -5.42 kg, difference 0.81 kg, P=0.68) (9). The meta-analysis by Khalafi et al.

synthesizing studies ≥6 months duration confirmed this equivalence, with no significant advantage for either approach in long-term weight reduction (27).

These findings challenge the notion that TRF possesses intrinsic metabolic advantages for weight loss. Rather, they suggest that both strategies are tools to achieve the same endpoint—negative energy balance—with effectiveness determined primarily by adherence and the magnitude of caloric restriction achieved. The practical implication is that patient preference should guide selection between TRF and CCR, as both offer comparable weight loss potential when sustained.

The Lean Mass Concern: A Clinically Important Trade-off

A concerning pattern emerges across multiple studies regarding body composition quality. While TRF effectively reduces fat mass, several investigations document simultaneous, clinically significant reductions in lean mass. The meta-analysis by Ruanpeng et al. quantified mean lean mass loss at -0.59 kg (95% CI -1.15 to -0.03) accompanying fat mass loss of -1.29 kg (95% CI -2.04 to -0.54) (12). More alarmingly, Chen et al.'s meta-analysis noted that weight loss with TRF was "mainly attributed to the loss of lean mass rather than fat mass" (11). Individual trials corroborate this: Lowe et al. reported significant reduction in appendicular lean mass index with TRF compared to controls (-0.16 kg/m², 95% CI -0.27 to -0.05, P=0.005) (1).

The mechanism appears related to eating window duration. Gabel et al. directly compared 6-hour versus 8-hour TRF, finding that the shorter 6-hour window led to significantly greater lean mass loss (-1.8 kg) compared to 8-hour TRF (P=0.005) (28). This likely reflects insufficient protein intake and compromised protein distribution within compressed eating windows, as adequate protein consumption becomes challenging when the feeding period is severely restricted. Cienfuegos et al. similarly found that both 4-hour and 6-hour TRF protocols produced significant weight loss (~3%), but the 4-hour group showed greater reductions in fat-free mass (7).

This lean mass loss carries important clinical implications. Sarcopenic obesity—the coexistence of excess adiposity and reduced muscle mass—is associated with worse metabolic outcomes, functional decline, and increased

mortality (29). Weight loss interventions that disproportionately reduce lean mass may inadvertently exacerbate this condition. However, combination strategies offer promise: Kotarsky et al. demonstrated that TRF combined with concurrent aerobic and resistance training produced greater fat mass loss (9.0%) than exercise alone (3.3%), while both groups showed similar lean mass gains, indicating that exercise can mitigate TRF-associated lean mass loss (30).

Clinical recommendations should therefore emphasize: (1) avoiding extremely short (4-6h) eating windows unless protein intake is carefully optimized; (2) ensuring adequate protein consumption (≥1.2-1.5 g/kg/day) distributed throughout the eating window; (3) incorporating resistance training when feasible; and (4) monitoring body composition rather than weight alone.

Glycemic Control: Population Matters

Glycemic responses to TRF demonstrate marked heterogeneity based on baseline metabolic status—a critical insight for clinical application. In populations with established T2DM, TRF produces robust, clinically meaningful improvements. Che et al. reported substantial reductions in HbA1c (-1.54%), fasting glucose (-1.47 mmol/L), and insulin resistance (HOMA-IR -0.51) among overweight T2DM patients following 10-hour TRF for 12 weeks, accompanied by reduced medication requirements ($P<0.001$) (18). Carter et al. found significant HbA1c reductions (-0.7%) in T2DM patients following intermittent energy restriction (20), while Pavlou et al. documented HbA1c decreases of -0.91% (95% CI -1.61 to -0.20) in insulin-treated T2DM patients (19). Kramer et al.'s crossover trial demonstrated a 14% increase in beta-cell function (ISSI-2) and 14% reduction in hepatic insulin resistance with 4-hour TRF, despite participants already receiving antidiabetic treatment (31).

Continuous glucose monitoring provides granular confirmation: Barua et al. found that early TRF reduced time spent in the 140-180 mg/dL glucose range by 3.3% ($P=0.01$) in prediabetes (32), while Andriessen et al. reported that 10-hour TRF increased time in normoglycemic range by approximately 3 hours daily (15.1 vs. 12.2 hours, $P=0.01$) in T2DM (33).

Conversely, metabolically healthy individuals or those with prediabetes show minimal glycemic improvements. Maruthur et al.'s isocaloric feeding study

found no differences in glucose homeostasis between TRF and usual eating patterns when calories were controlled (13). Quist et al. reported only small, non-significant HbA1c reductions after 3 months of 10-hour TRF in high-risk individuals (34). Gabel et al. found no changes in fasting glucose or insulin in metabolically healthy obese adults following 8-hour TRF (2).

This differential response has clear mechanistic and clinical implications. TRF appears most effective when there is "room for improvement"—that is, when baseline glycemic dysregulation provides a substrate for intervention. In normoglycemic individuals, homeostatic mechanisms maintain glucose within narrow ranges regardless of meal timing, limiting potential TRF benefits. For clinical practice, this suggests that T2DM patients may be ideal TRF candidates, while prediabetic or metabolically healthy individuals should not expect substantial glycemic improvements beyond those attributable to weight loss.

The Caloric Restriction Mechanism: Isocaloric Studies Resolve the Debate

Perhaps the most mechanistically important contribution to the TRF literature comes from isocaloric feeding studies—trials where all food is provided to participants and caloric intake is held constant between TRF and control conditions. These studies directly test whether TRF confers metabolic benefits independent of energy balance.

Maruthur et al.'s meticulously controlled feeding study provided all food to participants via a metabolic kitchen to maintain weight-stable caloric intake. Under these isocaloric conditions, TRF did not reduce weight or improve glucose homeostasis compared to a usual eating pattern (13). Peters et al.'s isocaloric crossover trial in women with overweight/obesity found no differences in insulin sensitivity between early TRF (8am-4pm), late TRF (1pm-9pm), and baseline conditions when caloric intake was controlled (14). Early TRF produced slightly greater weight loss (-1.08 kg vs. -0.44 kg), but this likely reflects incomplete isocaloric adherence rather than true metabolic advantage.

These findings powerfully demonstrate that TRF's metabolic benefits in free-living studies stem primarily from spontaneous caloric reduction rather than circadian or metabolic timing effects. Jamshed et al. quantified that early TRF effects were equivalent to reducing calorie intake by an additional 214 kcal/day (5).

Gabel et al. reported spontaneous reductions of 341 kcal/day with 8-hour TRF (2), while Cienfuegos et al. found 4-hour and 6-hour TRF reduced intake by approximately 550 kcal/day without calorie counting (4).

The clinical implication is paradigm-shifting: TRF should be understood not as a metabolically superior intervention but as a practical behavioral strategy to facilitate caloric restriction. Its advantage lies in simplicity—no calorie counting, no food weighing, no complex tracking—which may enhance adherence for individuals who find traditional dietary restriction burdensome. However, this advantage must be weighed against the lean mass concerns discussed above.

Early versus Late TRF: Circadian Hypotheses Unconfirmed

The circadian hypothesis—that early eating aligns better with endogenous rhythms of insulin sensitivity and energy metabolism—has generated substantial interest and several head-to-head trials. Results, however, are mixed and increasingly suggest comparable efficacy between early and late TRF when rigorously tested.

Jamshed et al. found that early TRF (7am-3pm) was more effective for weight loss (-2.3 kg, P=0.002) and diastolic blood pressure improvement (-4 mm Hg, P=0.04) compared to eating over ≥12 hours (5). Zhang et al. reported that 6-hour early TRF (7am-1pm) reduced systolic blood pressure by -5.5 mmHg, improved thyroid axis activity, and showed greater metabolic benefits than late TRF (12pm-6pm) (35). Črešnovar et al. demonstrated that early TRF with energy restriction produced greater improvements in fat mass (-1.2%, P=0.013), fasting glucose (-0.35 mmol/L, P=0.012), and diastolic blood pressure (-4 mmHg, P=0.033) compared to late TRF or energy restriction alone (15).

However, the two largest and most rigorous isocaloric studies found no metabolic differences between early and late TRF. Peters et al.'s well-controlled crossover trial revealed no differences in insulin sensitivity between early and late TRF (14). Dote-Montero et al.'s 197-participant RCT found no significant differences in visceral adipose tissue reduction between early, late, and self-selected TRE schedules when combined with Mediterranean diet education (16). Miladi et al. reported comparable improvements in body weight, BMI, and metabolic parameters between early and late TRF when combined with physical activity (17).

The apparent benefits of early TRF in observational studies likely reflect confounding by differential adherence, food choices, or caloric intake rather than true chronobiological advantages. The circadian hypothesis, while mechanistically plausible, remains unproven in well-controlled human trials. Clinical practice should therefore prioritize patient preference and lifestyle compatibility when recommending TRF timing, as adherence—not timing per se—will determine outcomes.

Hepatic Outcomes: Promise in NAFLD/MAFLD

Patients with NAFLD or MAFLD demonstrate particularly robust liver-specific responses to TRF, representing a promising therapeutic application. Oh et al. found that TRE reduced hepatic steatosis by 25.8% compared to 0.7% in standard care ($P<0.001$) in metabolic dysfunction-associated steatotic liver disease (MASLD), with effects comparable to calorie restriction (22). Wei et al. reported that both TRF and CCR reduced intrahepatic triglyceride content by approximately 7% at 12 months in NAFLD patients, with no significant between-group differences (21).

Liver enzyme improvements accompany steatosis reductions. Varkaneh et al. documented significant decreases in ALT (34 to 21.2 U/L), AST (26.3 to 20.5 U/L), and GGT (33 to 23.2 U/L) with TRF plus a low-sugar diet in NAFLD ($P<0.05$) (36). Shafiee et al. found even greater ALT reductions (-17.14 U/L) when combining TRF with a lacto-ovo vegetarian diet in MAFLD (23). Świątkiewicz et al. documented 20% reductions in both ALT and AST with 10-hour TRF in metabolic syndrome patients (24).

Controlled attenuation parameter (CAP) improvements are particularly impressive. Varkaneh et al. reported CAP reduction from 322.9 to 270.9 dB/m ($P<0.05$) (36). Feehan et al. found a mean difference of -9.96 dB/m with TRF compared to +20.46 dB/m with standard care ($P=0.038$), with even greater improvements (-26.10 dB/m) in participants with severe steatosis (CAP >268 dB/m) (37).

These findings suggest that TRF may be particularly valuable in the growing population of patients with obesity-related liver disease. The mechanism likely involves both weight loss-mediated reductions in hepatic fat and potential direct

effects on hepatic lipid metabolism, though the isocaloric studies suggest weight loss remains the primary driver.

Adherence: The Critical Mediator

Adherence emerges as a critical determinant of TRF effectiveness, with significant implications for real-world applicability. The most commonly studied 8-hour protocols show adherence rates of approximately 6 days per week (87%) (38). Ten-hour windows achieve higher adherence (91%) but correspondingly smaller effects (34). Quist et al. found that 83% of participants were highly adherent to 10-hour TRF during 3-month intervention, with actual eating windows averaging 9.1 hours (39).

However, real-world adherence faces substantial barriers. Parr et al. found that while initial adherence to 9-hour TRF among T2DM patients was 99%, this declined to 81% by six months (40). Participants described hunger, daily stressors, and social eating patterns as main barriers (41). Simon et al. noted that greater restriction of the eating window was associated with longer sleep duration (β=-0.46, P=0.03), suggesting compensatory behavioral adaptations (42).

The relationship between adherence and outcomes is dose-dependent. Świątkiewicz et al. showed that only participants achieving eating windows ≤10 hours/day experienced significant metabolic improvements, while those with windows >10 hours showed no benefits (24). This threshold effect has important implications: patients must achieve meaningful eating window restriction to derive benefit, but overly restrictive windows may compromise adherence and increase lean mass loss.

Clinically, this suggests a personalized approach: start with a moderate 10-hour window, assess adherence and tolerance, and consider gradual restriction to 8 hours if tolerated, while monitoring for hunger, mood changes, and lean mass preservation. Intensive dietetic support, as provided in many trials (weekly or biweekly counseling), may be necessary for optimal outcomes but may not reflect real-world feasibility.

Safety and Tolerability: Generally Favorable with Caveats

Safety data across studies reveal generally favorable profiles for TRF, though certain concerns warrant attention. Adverse events are minimal in most

investigations. Dote-Montero et al. reported no serious adverse events among 197 participants (16). Quist et al. documented one severe adverse event (subcutaneous nodule and arm pain) among 100 participants, along with headaches and migraines in the TRE group (34). Zhang et al. noted hypoglycemia in 2-3 patients per group, with no significant differences between TRF and CCR (43).

Metabolic safety markers are reassuring. Gabel et al. specifically evaluated eating disorder symptoms, body image perception, complete blood count, and resting metabolic rate, finding no concerning changes after 12 weeks of 8-hour TRF (44). Wei et al. reported no serious adverse events or deaths during 12-month trial, with mild adverse events (appetite changes, stomach discomfort) occurring at similar rates in TRF and CCR groups (21).

Dropout rates range from 0% to >50% across studies, though most are not primarily attributed to safety concerns. Pureza et al. reported 53.44% dropout at 12 months, though reasons were unspecified (45). Conversely, several trials maintained completion rates above 80% (5,9,46). Quality of life assessments are generally neutral or positive. Pavlou et al. found that TRE did not significantly alter mood or quality of life in T2DM participants (19). Schroder et al. reported improved quality of life scores with TRF (47), while Świątkiewicz et al. documented improvements in sleepiness and depression scores (24).

Medication requirements change favorably in pharmacologically treated populations. Che et al. found that TRF reduced medication effect score by -0.66 (P=0.006) in T2DM, indicating decreased medication requirements (18). Ramirez-Obermayer et al. noted that insulin doses were systematically reduced during fasting days with comparable hypoglycemia rates between groups (48).

Long-term safety data remain limited. Most trials last 8-12 weeks, with longest interventions extending to 12-24 months (9,21,26,49). Wei et al.'s 12-month follow-up showed no significant safety concerns (21). Aksungar et al.'s 24-month study found no adverse metabolic effects, though this was a small single-arm investigation (50).

Combination Strategies: Synergistic Potential

Several studies examining TRF combined with other interventions reveal promising synergistic effects. TRF combined with exercise training shows additive

benefits. Kotarsky et al. found that TRF plus 8 weeks of concurrent aerobic and resistance training produced greater fat mass loss (9.0%) than exercise alone (3.3%), while both groups showed similar lean mass gains (30). Ameur et al. demonstrated that combining TRF with high-intensity functional training led to superior reductions in total cholesterol, triglycerides, insulin, and HOMA-IR compared to either intervention alone (51). Haganes et al. reported that TRF combined with HIIT improved HbA1c and induced greater reductions in total and visceral fat mass compared to either intervention alone (52).

TRF combined with specific dietary patterns also shows promise. Shafiee et al. found that TRF combined with lacto-ovo vegetarian diet produced significant reductions in weight (-8.07 kg), BMI (-2.70 kg/m^2), waist circumference (-8.00 cm), liver enzymes, and inflammatory markers in MAFLD patients (23). Nilghaz et al. reported that TRF with DASH diet was superior to low-calorie diet alone for reducing BMI, abdominal circumference, and liver parameters in MAFLD (53). Varkaneh et al. demonstrated substantial metabolic improvements when combining TRF with low-sugar diet, including reductions in liver stiffness and inflammatory markers (36).

These findings suggest that TRF should not be viewed as a standalone intervention but as a framework that can be combined with other evidence-based strategies—exercise, specific dietary patterns, behavioral support—to optimize outcomes.

Clinical Implications

Synthesizing the evidence, several clinical recommendations emerge:

1. **Patient selection**: TRF is most appropriate for motivated adults with obesity, particularly those with T2DM or NAFLD who may derive glycemic and hepatic benefits. It should be avoided in individuals with eating disorders, underweight, pregnancy, or medication-dependent diabetes without medical supervision.

2. **Eating window selection**: Initiate with a moderate 10-hour window, assess tolerance and adherence, and consider gradual restriction to 8 hours if

tolerated. Extremely short windows (4-6h) should be reserved for closely monitored patients with adequate protein intake.

3. **Body composition monitoring**: Track not only weight but also body composition (waist circumference, bioelectrical impedance, DXA if available) to detect disproportionate lean mass loss.

4. **Protein optimization**: Ensure adequate protein intake (≥1.2-1.5 g/kg/day) distributed throughout the eating window. Consider protein supplementation if dietary intake is insufficient.

5. **Exercise integration**: Recommend concurrent resistance training to preserve or increase lean mass during TRF.

6. **Medication management**: Monitor patients on glucose-lowering medications closely, as TRF may necessitate dose reductions. Establish protocols for medication adjustment during fasting periods.

7. **Realistic expectations**: Educate patients that TRF's benefits derive primarily from reduced caloric intake, not circadian magic. Weight loss of 2-8 kg over 8-12 weeks is typical, with effects equivalent to traditional dieting.

8. **Adherence support**: Provide ongoing behavioral support, particularly during the initial adaptation period when hunger and social challenges are greatest.

9. **Contraindications**: Avoid TRF in patients with history of eating disorders, pregnant or breastfeeding women, children and adolescents, frail elderly, and those with medication-dependent diabetes without close medical supervision.

10. **Duration**: Consider TRF as a sustained behavioral strategy rather than short-term diet. The 12-month trials demonstrate feasibility and safety, but longer-term data are needed.

CONCLUSION AND RECOMMENDATIONS

Summary of Findings

This comprehensive systematic review of 80 studies encompassing 6,847 participants provides several definitive conclusions regarding time-restricted feeding in obese adults. First, TRF produces clinically meaningful weight loss of 2-8 kg over 8-12 weeks, with effects equivalent to continuous calorie restriction in long-term trials. Second, these metabolic benefits are primarily mediated through spontaneous caloric reduction (300-550 kcal/day) rather than independent circadian mechanisms, as demonstrated by isocaloric feeding studies showing no advantage when calories are controlled. Third, TRF is associated with significant lean mass loss (-0.59 kg), particularly with shorter (4-6h) eating windows, raising concerns about weight loss quality. Fourth, glycemic improvements are most pronounced in populations with established T2DM (HbA1c reductions 0.7-1.54%), while metabolically healthy individuals show minimal changes. Fifth, patients with NAFLD/MAFLD demonstrate robust liver-specific responses, including 6.9-25.8% reductions in hepatic steatosis and significant liver enzyme improvements. Sixth, early versus late TRF timing shows comparable efficacy in rigorous trials, suggesting patient preference should guide timing selection. Seventh, TRF is generally safe and well-tolerated, though medication adjustments may be necessary in pharmacologically treated populations. Eighth, adherence is critical and dose-dependent, with meaningful benefits requiring eating windows ≤10 hours/day. Ninth, combination strategies with exercise and specific dietary patterns (Mediterranean, DASH, vegetarian) show synergistic potential. Tenth, TRF should be positioned as a practical behavioral strategy for achieving caloric restriction rather than as a metabolically superior intervention.

Clinical Recommendations

Based on the accumulated evidence, we recommend that clinicians:

- Present TRF as an evidence-based option equivalent to traditional calorie restriction for weight management
- Select candidates based on patient preference and lifestyle compatibility

- Prioritize patients with T2DM or NAFLD who may derive additional glycemic and hepatic benefits
- Prescribe moderate 8-10 hour eating windows, avoiding extreme restriction
- Emphasize protein adequacy and resistance training to preserve lean mass
- Monitor body composition, not just weight
- Adjust medications, particularly glucose-lowering agents, as needed
- Provide ongoing adherence support, recognizing that real-world adherence faces substantial barriers

Research Priorities

Future research should prioritize:

- Long-term (≥2 years) RCTs with comprehensive safety monitoring
- Optimal protein intake and distribution strategies within eating windows
- Head-to-head comparisons of TRF with other intermittent fasting variants
- Mechanistic studies in well-controlled metabolic ward conditions
- Implementation science examining real-world effectiveness
- Diverse populations including varied racial/ethnic groups and both sexes
- Cost-effectiveness analyses
- Digital health tools to support adherence
- Eating disorder risk assessment, particularly in vulnerable populations
- Pregnancy, lactation, and developmental stage considerations
- Personalized approaches based on genetic, circadian, and metabolic phenotypes

Final Remarks

Time-restricted feeding represents a valuable addition to the obesity management armamentarium, offering a simple, practical approach to caloric restriction that many patients find more sustainable than daily calorie counting. Its metabolic effects are real but modest, equivalent to traditional dietary approaches, and driven primarily by reduced energy intake. The critical trade-off between weight loss efficacy and lean mass preservation requires careful patient selection, appropriate eating window prescription, and integration with exercise and optimal protein intake. As with any dietary intervention, success depends less on the specific strategy chosen than on sustained behavioral change. TRF provides a framework—a set of rules—that may help some patients achieve that change. For appropriately selected, motivated individuals with obesity, particularly those with T2DM or NAFLD, TRF offers a clinically meaningful, evidence-based option worthy of consideration in shared decision-making.

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