

Effects of Time-Restricted Eating on Body Composition, Biomarkers of Metabolism, Inflammation, Circadian System and Oxidative Stress in Overweight and Obesity: An Exploratory Review

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This is an Accepted Manuscript for Proceedings of the Nutrition Society. This peer-reviewed article has been accepted for publication but not yet copyedited or typeset, and so may be subject to change during the production process. The article is considered published and may be cited using its

DOI 10.1017/S002966512400747X

Proceedings of the Nutrition Society is published by Cambridge University Press on behalf of The Nutrition Society.

Abstract

Obesity is a chronic, complex and multi-factorial condition with an increasing prevalence worldwide. Irregular eating schedules might be a contributing factor to these numbers through the dysregulation of the circadian system. Time-restricted eating (TRE), an approach that limits eating windows, has been studied as a strategy to treat obesity, aligning eating occasions with metabolic circadian rhythms. This review aims to provide an overview of the impact of TRE protocols on metabolic, inflammatory, oxidative stress, and circadian rhythm biomarkers in people with overweight or obesity. Most studies report significant weight loss following TRE protocols. While glucose levels decreased in nearly all TRE interventions, only a few studies demonstrated statistically significant differences when compared to the control groups. The findings for CRP and TNF- α were inconsistent, with limited significant differences. Changes in lipid profile changes were variable and generally did not reach statistical significance. Both 4-hour and 6-hour TRE interventions significantly reduced 8-isoprostane levels. Additionally, TRE significantly altered clock gene expression, as well as that of genes associated with metabolic regulation in subcutaneous adipose tissue. While the evidence is still inconsistent, limiting eating to a consistent daily window of 8 to 12 hours can improve insulin sensitivity, reduce blood glucose, cholesterol and triglyceride levels and promote weight loss. These effects are likely attributable to both direct metabolic impacts and indirect benefits from weight loss and improved dietary habits. However, data on circadian, inflammatory, and specific metabolic biomarkers remain scarce and occasionally contradictory, highlighting the need for further research on these interventions.

Keywords: circadian rhythm; chrononutrition; biomarkers; mealtime; metabolism; metabolic syndrome; obesity

1. Introduction

The increasing prevalence of obesity, type 2 diabetes mellitus (T2DM) and Metabolic Syndrome (MetS) poses a significant global health threat, with substantial socioeconomic impact and burden worldwide^(1–4). Data available from the World Health Organization (WHO), estimates that in 2022 more than 2.5 billion adults were overweight, of which 890 million had obesity⁽⁵⁾. According to data from the International Diabetes Federation (IDF), in 2017 there were 451 million people with diabetes worldwide, a number expected to increase by approximately 53.7% (693 million) by 2045⁽⁶⁾. The incidence of MetS often matches that of obesity and T2DM, as these conditions are directly correlated. As a consequence, this cluster of noncommunicable diseases has become one of the major causes of morbidity and mortality^(7,8), making the prevention and amelioration of its risk factors a priority.

Irregular eating patterns might be a contributing factor to these numbers^(9–11). Eating over an extended period of time has been associated with the development of these pathologies^(12–15). According to a study by Wilkinson *et al.* (2020)⁽¹⁶⁾, conducted on patients with MetS, the majority of all energy-containing events, i.e. eating occasions, occurred in an eating window (time between the first and last energy-eating occasion of the day) of approximately 15 hours, resulting in a fasting window of less than 10 hours.

The biological circadian rhythms are part of a complex system that enhances energy expenditure and coordinates metabolic pathways, separating incompatible biochemical and physiological processes^(17,18). Appropriate functioning of the circadian clocks is of the utmost importance for sustaining metabolic health since circadian disruption disturbs metabolic homeostasis and is linked with an increased risk of obesity and MetS^(19–21). In turn, circadian rhythms are affected by obesity and other metabolic diseases^(22,23). This bidirectional relationship creates a complex interplay where it is not clear which factor is the cause and which is the consequence. This mutual influence makes it challenging to determine the initial trigger in the cycle of metabolic and circadian disruptions.

Some studies have previously linked the dysfunctions in peripheral clock genes with alterations in glucose homeostasis^(24,25) and inflammatory pathways⁽²⁶⁾. Although the main synchronizer of the suprachiasmatic nucleus (SCN) of the hypothalamus is the light/dark cycles, the peripheral clocks seem to be synchronized by the feeding/fasting cycles⁽²⁷⁾. Based on these findings it was hypothesized that disruption of the circadian rhythm caused by the

misalignment between the timing of food intake and circadian timing, might be the primary cause for disruption of metabolic homeostasis, and increased metabolic risks⁽²⁸⁾.

Among the first lines of treatment, management, and prevention of metabolic diseases are dietary intervention and increased physical activity^(29–32). However, these measures have limited success, in part due to the low adherence of the patients and the difficulty of maintaining these lifestyle changes in the long term. This highlights the necessity for new and more effective nutritional strategies that can complement current guidelines, improving the effectiveness of the lifestyle interventions prescribed. This includes personalization of the interventions and adaptation to each individual's unique rhythm and routine. In recent years, researchers have been assessing the efficacy of novel approaches that intend to restore disrupted circadian rhythms through nutritional challenges, including the modulation of timing and duration of daily food intake^(33,34). Time-restricted eating (TRE) is a nutritional intervention in which the eating window is reduced to a fixed number of hours per day, allowing prolonged overnight fasting. This strategy does not intend to reduce energy intake and is based on the hypothesis that by re-setting the eating/fasting cycles the circadian rhythms will be reestablished and the overall metabolic pathways will be improved⁽³⁵⁾.

Although research on the effect of TRE interventions on chronobiology markers is a relatively new field, the impact of TRE on body weight and body composition has been more systematically reported; however, it is important to assess the overall effects of these interventions on metabolic pathways by compiling the data currently available. By doing so, we can identify which clinical, laboratory, and genetic biomarkers are most affected by TRE interventions within a certain population, ensuring that future studies focus on the most impactful areas. Different study protocols often assess a variety of variables and biomarkers, leading to a diverse range of findings. Furthermore, within various TRE protocols, the duration of eating can differ significantly. Participants may choose between earlier, mid-day or later TRE windows, and some may even self-select their TRE periods. A structured search was conducted in the electronic databases Scopus and PubMed to identify articles reporting the results of TRE protocols on individuals with overweight or obesity, ensuring a comprehensive representation of TRE protocols in this population. Animal studies or *in vivo* experiments, studies involving periodic fasting or alternating days fasting, studies combining TRE protocols with energy restriction and/or exercise interventions, and studies on religious fasting were not included in this review. Therefore, the present review aims to provide an overview of the impact of TRE protocols on metabolic, inflammatory, and oxidative stress

biomarkers, as well as their influence on circadian rhythms biological markers, based on the findings of clinical studies conducted on individuals with overweight or obesity.

Characteristics of the TRE studies in people with overweight or obesity

The studies discussed in the present review followed these characteristics: (1) Population: adults aged 18 years or older with overweight or obesity; Intervention: a fixed daily fasting period between 10 to 20 hours with ad libitum intake; (3) Comparators: control group in randomised controlled trials (RCTs) or non-randomised controlled trials, or subjects before TRE intervention in studies with a one-group pretest-posttest design; (4) Outcomes: data on changes in at least one of the following: insulin, glucose, cortisol, melatonin, ghrelin, leptin, adiponectin, interleukin-1 (IL-1), interleukin-6 (IL-6), 8-isoprostane, TNF- α , or nitric oxide; (5) Study design: clinical trials using TRE.

Fourteen studies are explored in this review (Table 1), and of those, eight were randomised clinical trials (RCT) and one was a secondary analysis. The duration of the TRE protocols ranged from 3 weeks to 6 months and the sample size of the TRE groups ranged from 10 to 59 participants. The shortest eating window was 4 hours (20 hours of fasting) and the longest was 12 hours (12 hours of fasting), with 8 hours being the most common eating window (16 hours of fasting).

Effects of time-restricted eating on body weight and body composition

In most of the studies, there was a statistically significant change in body weight^(36–42), with all the TRE protocols resulting in weight loss (Table 2). Compared with the control groups, the participants in eight TRE protocols showed greater body weight loss^(36–39,41–44), while only two studies did not find significant differences between groups^(37,39). The control groups of the studies by Cienfuegos et al.⁽⁴²⁾, Pavlou et al.⁽⁴³⁾, Chow et al.⁽³⁶⁾, Schroder et al.⁽⁴¹⁾ and Gabel et al.⁽⁴⁴⁾ were instructed to maintain their daily eating routines without any restrictions. The control group of the study by Pavlou et al.⁽⁴³⁾ presented an average daily eating window of 10h23min $\pm$ 1h26min at baseline that was preserved by the end of the study. The control group of the study conducted by Chow et al.⁽³⁶⁾ showed a mean daily eating window of 15.5 $\pm$ 1.1 hours that also was preserved by the end of the intervention. Andriessen et al.⁽³⁸⁾ instructed the participants of the control group to distribute their habitual diet over a minimum of 14 hours per day, resulting in an average eating window of 13.4 $\pm$ 0.1 hours⁽³⁸⁾.

Other studies compared the results of the TRE intervention with different dietary strategies or nutritional approaches. Mengi et al.⁽⁴⁰⁾ compared the TRE protocol with an Energy Restricted Diet (ERD) protocol, in which the participants consumed a diet based on their total energy expenditure minus 500 kcal. In this particular study, the decrease in body weight was higher in the ERD group compared to the TRE group (5.5% and 3.2%, respectively)⁽⁴⁰⁾. Lowe et al.⁽³⁹⁾ compared the TRE intervention with a consistent meal timing (CMT) approach, in which the participants ate three structured meals daily and were allowed to snack between meals. Lastly, Phillips et al.⁽³⁷⁾ compared the TRE intervention with standard dietary advice (SDA), which consisted of a 10-minute nutritional counselling session and a leaflet summarizing the food pyramid and Swiss recommendations for a healthy, balanced diet⁽³⁷⁾. The study found no differences in the mean eating window (14.89 ± 1.21 hours) before and after the SDA intervention⁽³⁷⁾.

Cienfuegos and colleagues⁽⁴²⁾ tested two TRE protocols, with a 4-hour and a 6-hour eating window, but the results indicated no difference in weight loss between the two interventions. Pavlou et al.⁽⁴³⁾ studied three groups, the TRE and control groups, and an additional group with ERD. After 6 months of intervention, the ERD group showed no differences in mean body weight. Furthermore, there were no differences in the percentage of body weight loss between the TRE group and the ERD group⁽⁴³⁾.

The weight loss observed in TRE studies might be partially attributed to a reduction in energy intake, as eating within a limited window frame decreases opportunities for consuming calories in excess. Of all the studies analysed in this review, eight reported collecting data on dietary intake^(36,38,40,43,45–48), but only six provided information on changes in nutrient and/or energy intake^(36,40,43,46–48). Three of these studies found a significant decrease in energy intake^(40,43,47), and in one study, although the authors did not report a decrease in energy intake, they observed a greater reduction in the number of eating occasions in the TRE group⁽³⁶⁾. Suthutvoravut et al.⁽⁴⁶⁾ reported that the mean difference in energy intake between the TRE and usual care was not significant.

Regarding changes in body fat mass percentage, the study by Cienfuegos et al.⁽⁴²⁾ reported significant differences across the three groups after the intervention, with participants in the 4-hour TRE and 6-hour TRE groups losing significantly more fat mass than those in the control group. Mengi Çelik et al.⁽⁴⁰⁾ found a significant decrease in body fat percentage in the ERD group, while the TRE group showed no significant changes. In four studies^(36,37,39,43) the

reduction in body fat percentage was greater in TRE interventions but not different compared to the control group. In the study by Gabel and colleagues⁽⁴⁴⁾ and the one by Schroder et al.⁽⁴¹⁾, no changes in fat mass were observed in the control group.

Concerning lean mass, Cienfuegos et al.⁽⁴²⁾ found that the 6-hour TRE group lost significantly more lean mass than the 4-hour TRE and control groups. The control group experienced lower loss of lean mass, although there were no differences compared with the 4-hour⁽⁴²⁾. Chow et al.⁽³⁶⁾ also reported differences in lean mass between groups, reporting a significant decrease in the TRE with no change in the control group. Lowe et al.⁽³⁹⁾ found no differences in lean mass between the TRE and CMT groups, but there was a significant decrease in the TRE group after the intervention. In the study by Pavlou et al.⁽⁴³⁾, the TRE intervention had no effect on lean mass. Furthermore, no differences in lean mass were observed in the control groups of the studies by Pavlou et al.⁽⁴³⁾, Phillips et al.⁽³⁷⁾ and Lowe et al.⁽³⁹⁾.

Effect of time-restricted eating on metabolic, inflammatory and oxidative stress biomarkers

From the total of studies that employed TRE protocols with the assessment of glucose, only two studies reported a significant decrease in glucose levels following the TRE intervention^(36,46) (Table 3). Furthermore, only two studies showed statistical differences between the TRE and control groups^(43,47). Among the studies analysed, glycated haemoglobin A1c (HbA1c) remained unchanged following TRE interventions^(36,37,39,42,43,46,47), however, three studies showed differences between the TRE and control groups^(37,43,46). Similar results were found for insulin levels and Homeostatic Model Assessment for Insulin Resistance (HOMA-IR), with no differences after TRE interventions^(36,39–42,44,46,47), but different between TRE and control groups in two studies^(42,47).

In addition to the control group, the study by Pavlou et al.⁽⁴³⁾ also included a third group with CR. While the reduction in HbA1c was slightly greater in the CR group and showed significant differences compared to the control group, no significant differences were observed between the TRE and CR groups. Moreover, no differences were observed in mean glucose values between the CR and TRE groups; however, this parameter was different between the CR group and the control group⁽⁴³⁾.

Andriessen et al.⁽³⁸⁾ and Parr et al.⁽⁴⁸⁾ measured interstitial glucose using continuous glucose monitoring systems and both found that the mean 24-hour glucose levels were significantly lower after the TRE intervention. Additionally, in both studies, TRE participants exhibited glucose levels within the normal range for longer periods of time, and less time with high glucose^(38,48). In the study by Parr et al.⁽⁴⁸⁾, improved glycaemic control, including postprandial meal responses, was achieved with no changes in dietary intake from the baseline (habitual) period to the TRE period, according to the complete 24-hour continuous glucose monitoring data analysed. No differences were found between the TRE group and the control group for time spent in hypoglycaemia, or time spent in the low glucose range, in the study by Andriessen et al.⁽³⁸⁾. Similarly, in the study by Parr and colleagues⁽⁴⁸⁾, there were no differences in the time spent in hypoglycaemia between the two study periods (habitual and TRE).

Zhao and colleagues⁽⁴⁵⁾ assessed ghrelin levels in their study but did not observe changes in this biomarker after the TRE intervention. In this same study, TRE seemed to alter the 24-hour profile of insulin with a post hoc analysis showing an increase in insulin at midday and a decrease at midnight in response to TRE⁽⁴⁵⁾.

Only one study, by Mengi Çelik and colleagues⁽⁴⁰⁾, assessed leptin and adiponectin, observing no impact of TRE in these levels, but an increase in adiponectin in the ERD group. However, no differences were found between groups for both biomarkers⁽⁴⁰⁾.

Regarding inflammatory biomarkers, some studies measured the values of c-reactive protein (CRP)^(40,41,46), interleukin-6 (IL-6)^(40,42) and tumour necrosis factor-alpha (TNF- α)⁽⁴²⁾. There were no differences in the mean values of IL-6 after following TRE interventions, and these values were comparable to those in control groups^(40,42). Cienfuegos et al.⁽⁴²⁾ showed that neither the 4-hour nor the 6-hour TRE protocols had an effect on TNF- α values, with no differences compared to the control group. Only one study, Suthutvoravut and colleagues⁽⁴⁶⁾, reported a decrease in CRP values between the TRE group and the control group⁽⁴⁶⁾.

The results concerning the effects of the different TRE protocols on lipid profile are heterogeneous (Table 4), but nevertheless, most of those changes did not reach statistical significance when comparing them to the changes in the control groups or pre and post-intervention. Mengi Çelik et al.⁽⁴⁰⁾ observed a decrease in total cholesterol and LDL cholesterol after the TRE intervention but these changes were not different when compared with the control group. They also reported a decrease in total cholesterol in the group with

energy restriction⁽⁴⁰⁾. Che et al.⁽⁴⁷⁾ reported differences in total cholesterol, LDL cholesterol and triglycerides between the TRE and control groups. In contrast, Pavlou and colleagues⁽⁴³⁾ found no differences in the lipid profile parameters in the calorie restriction group, nor were there differences when comparing the TRE and calorie groups with the control group. Similarly, the consistent meal timing group in the study by Lowe et al.⁽³⁹⁾ exhibited no changes in lipid profile biomarkers, and no differences were observed in the Standard Dietary Advice group in the study by Phillips et al.⁽³⁷⁾.

In a study by Zhao and colleagues⁽⁴⁵⁾, the authors measured the 24-hour profile of triglycerides and found that in response to TRE, there was a decrease in triglycerides at midnight and 3:00 am. Andriessen and colleagues⁽³⁸⁾, evaluated certain metabolites on days 20 and 21 of each intervention but found no differences in triglyceride levels between the TRE group and the control groups.

Two studies examined the impact of TRE on oxidative stress biomarkers. Cienfuegos et al.⁽⁴²⁾ reported that TRE interventions decreased plasma levels of 8-isoprostane, an oxidative stress marker to lipids. These changes were significantly different across the three groups (4-hour TRE, 6-hour TRE and control), with the 4-hour TRE group exhibiting a 37% reduction and the 6-hour TRE group a 34% reduction, both greater than in the control group, although the difference between the two intervention groups was not significant.

Mengi Çelik and colleagues⁽⁴⁰⁾ found no changes in total antioxidant status and total oxidant status by the end of the TRE protocol. However, the ERD group showed a significant increase in total antioxidant status after the intervention, although no differences were observed between the TRE and ERD interventions⁽⁴⁰⁾.

Effect of time-restricted eating on circadian biomarkers

Clock genes and circadian biomarkers, such as cortisol and melatonin, are critical to align metabolic processes with the day-night cycles^(49–51). Studies have demonstrated that TRE influences the expression of clock genes and metabolic regulators⁽⁵²⁾. Therefore, food consumption within a specific time window is a cue to reinforce circadian rhythms by modulating the expression of clock genes, which in turn govern various downstream metabolic pathways^(53–55). This synchronization optimizes the timing of metabolic processes, ultimately improving metabolic health⁽³⁵⁾.

Zhao et al.⁽⁴⁵⁾ conducted the only study that assessed the impact of a 10-hour TRE protocol on circadian biomarkers, including the expression of core clock genes, and melatonin and cortisol rhythms, in a population of 15 men with obesity. The study included a 35-hour in-laboratory with controlled conditions stay for comprehensive metabolic assessments, conducted both at baseline and after the 8-week intervention. During these periods, researchers evaluated 24-hour profiles of plasma metabolites, glucoregulatory hormones, and the transcriptome of subcutaneous adipose tissue (SAT)⁽⁴⁵⁾. Results demonstrated that the TRE protocol significantly altered the expression of clock genes and genes involved in metabolic regulation within SAT. Specifically, TRE enhanced the expression of CLOCK and NR1D2 (REV-ERB β) genes while reducing the expression of PER1 and NR1D1 (REV-ERB α) at 12:00 am. Although TRE did not alter the timing of dim light melatonin onset (DLMO), it significantly reduced the morning cortisol area under the curve⁽⁴⁵⁾.

Considering the limited number of studies investigating the influence of TRE on circadian genes, further research is needed to explore the potential of TRE as a relevant modulator of gene expression and its broader impact on metabolic health.

Current perspective of TRE and future challenges

TRE is an innovative dietary and behavioural strategy that restricts food intake to a consistent and specific window during the day to optimize nutrient uptake and promote health. Over recent years, this approach has gained significant attention due to its potential to improve metabolic health^(18,35,53). The premise behind TRE is based on the fact that the synchronization of eating/fasting cycles with the intrinsic circadian rhythm helps optimise metabolic processes, reducing the risk of obesity, metabolic syndrome, T2DM and cardiovascular diseases^(53,56).

Restricting food consumption to a consistent daily window, typically ranging from 8 to 12 hours, has been shown to improve insulin sensitivity, lower blood glucose levels, and promote weight loss and beneficial changes in body composition, as demonstrated in the studies discussed in the present review. Additionally, TRE can also reduce cholesterol and triglyceride levels, contributing to overall cardiovascular health⁽⁵⁷⁾. These positive effects are likely due to both direct metabolic effects and indirect effects from weight loss and improved dietary habits.

The significant changes in body weight and, consequently body composition, observed across most included studies, regardless of the specific TRE protocols employed, suggest that the weight loss is likely attributed to a combination of factors, including both the timing of food intake and the indirect energy restriction imposed by a narrowed eating window⁽⁵⁸⁾. The indirect energy restriction promoted by TRE interventions can create an energy deficit, promoting fat utilization, and facilitating a negative energy balance. Previous work has indicated that TRE can enhance fat oxidation during fasting time⁽⁵⁹⁾. Specifically, on adipose tissue, TRE increases β -oxidation and lipolysis⁽⁵³⁾.

Furthermore, fasting has been linked to decreased susceptibility to oxidative stress and improved antioxidant defences⁽⁶⁰⁾, while an increase in body weight is associated with increased oxidative stress and reduced antioxidant potential^(61,62). However, Mengi Çelik et al.⁽⁴⁰⁾ did not find statistically significant changes in total antioxidant status. In contrast, previous research by Sutton and colleagues⁽⁶⁴⁾ demonstrated that TRE reduced oxidative stress, as evidenced by the decreased plasma levels of 8-isoprostane.

Meal timing also plays a crucial role in regulating metabolism, circadian rhythms, and hormonal responses, which can influence weight management independently of energy intake^(35,58). Mealtime is an important zeitgeber that synchronizes peripheral clocks in tissues and organs with the central clock in the SCN⁽⁵⁶⁾. Eating at the “wrong” time can impair glucose tolerance and alter the expression of genes involved in circadian regulation, also highlighted by a review by Johnston and colleagues⁽⁶⁵⁾, emphasizing the importance of meal timing in maintaining circadian rhythm integrity. These outcomes underline the significance of regular and appropriately timed meals in supporting circadian rhythm health and metabolic efficiency.

However, implementing TRE protocols also requires consideration of potential negative effects. The 8-hour eating window is the most common protocol among the reviewed studies, allowing a balance between achieving metabolic benefits and ensuring adherence to the dietary regimen within the limitations of everyday life. Deviating from this timeframe, particularly with a narrower eating window, may pose challenges to adherence due to lifestyle constraints such as work schedules, family responsibilities, and societal mealtimes^(66,67). Moreover, restrictive eating windows may contribute to disordered eating behaviour in some individuals⁽⁶⁸⁾, potentially limiting the real-world effectiveness of TRE interventions. This underscores the importance of considering not only the physiological effects but also the

social and behavioural aspects when designing and implementing TRE protocols. Tailoring interventions to individual characteristics, motivators, and barriers is crucial for determining adherence and also effectiveness of the protocol ⁽⁶⁹⁾.

Importantly, restricting the eating events to a limited timeframe, especially when not taking into consideration the diet quality and quantity, may result in an inadequate nutrient intake or, ie. increased intake of saturated fats^(40,47,48,70). Therefore, the diet of individuals practising TRE needs to be carefully managed to ensure the consumption of a balanced healthy diet and to prevent deficits, particularly when this intervention is followed over a long period.

Lastly, the effectiveness of TRE protocols can vary widely among individuals due to several factors, including different genetic backgrounds, lifestyle and environmental influences ^(67,71–73). While some individuals may experience significant benefits, others may have little to no improvement, underscoring the importance of personalized dietary approaches to maximize the impact of TRE on metabolic health.

Conclusions

TRE might be a promising complementary approach for weight management and improved metabolic health, with most studies demonstrating improvements in body weight, glucose levels and insulin resistance. However, data regarding its influence on circadian rhythms, inflammatory markers and key metabolic hormones such as leptin, ghrelin and adiponectin remains scarce. This highlights the need to further explore the broader impact of TRE interventions. A refined understanding and personalized application of TRE are crucial for optimizing its benefits across different populations while attempting to mitigate its drawbacks. Therefore, medium- and long-term studies are needed to fully assess the lasting effects and potential benefits of TRE, as most existing research has been conducted in small samples and over relatively short periods.

Table 1. Overall characteristics of the reviewed studies.

Ref.	Year	Study Design	Population	Sample Size	Protocol Duration	TRE Protocol	Control Group
(43)	2023	Parallel RCT	Adults with obesity and type 2 diabetes	68	6 months	8-h TRE with <i>ad libitum</i> intake from 12 to 8 p.m. (n = 23)	Control group 1: No restrictions (n = 24) Control group 2: Energy restriction with a 25% reduction of energy intake (n = 22)
(46)	2023	Parallel RCT	Adults with IFG and overweight or obesity	71	12 weeks	Protocol 1: 9-h TRE with <i>ad libitum</i> intake from 8 a.m. to 5 p.m. (n = 23) Protocol 2: Protocol 1 combined with behavioural economic intervention (n = 26)	Usual care (n = 22)
(40)	2023	RCT	Women with overweight	23	8 weeks	8-h TRE with <i>ad libitum</i> from 10 a.m. to 6 p.m. (n = 10)	Energy-restricted diet (n = 13)
(48)	2023	Pre-post non-randomised design	Adults with T2DM and overweight or obesity	19	4 weeks	9-h TRE with <i>ad libitum</i> intake from 10 a.m. to 7 p.m. (n = 19)	No control group

(74)	2022	RCT (secondary analysis)	Adults with obesity	20	12 weeks	8-h TRE with <i>ad libitum</i> intake within a self-selected time frame (n = 11)	No restrictions (n = 9)
(45)	2022	Open-label, pre-post trial	Men with obesity	15	8 weeks	10-h TRE (time frame self-selected with the latest eating occasion to be completed by 7:30 p.m.)	No control group
(38)	2022	RCT with crossover	Adults with T2DM and overweight/obesity	14	3 weeks	10-h TRE (time frame self-selected with the latest eating occasion to be completed by 6 p.m.) (n = 14)	Habitual diet over at least 14-h per day without additional restraints (n = 14)
(47)	2021	RCT	Adults with type 2 diabetes and overweight/obesity	104	12 weeks	10-h TRE with <i>ad libitum</i> intake from 8 a.m. to 6 p.m. (n = 54)	No restrictions (n = 50)
(37)	2021	Open-label pragmatic RCT	Adults with obesity	45	6 months	12-h TRE with <i>ad libitum</i> intake within a self-selected time frame (n = 25)	Standard dietary advice (n = 20)
(41)	2021	Non-RCT	Women with obesity	32	3 months	8-h TRE with <i>ad libitum</i> intake from 12 to 8 p.m. (n = 20)	No restrictions (n = 12)
(39)	2020	RCT	Women with	116	12 weeks	8-h TRE with <i>ad libitum</i> intake	Consistent meal timing with 3

			overweight or obesity			from 12 to 8 p.m. (n = 59)	structured meals per day and snacking between meals was permitted (n = 57)
						Protocol 1: 4-h TRE with <i>ad libitum</i> intake from 3 to 7 p.m. (n = 16)	
(42)	2020	Parallel RCT	Adults with obesity	49	8 weeks	Protocol 2: 6-h TRE with <i>ad libitum</i> intake from 1 to 7 p.m. (n = 19)	No restrictions (n = 14)
						8-h TRE with <i>ad libitum</i> intake within a self-selected time frame (n = 11)	
(36)	2020	RCT (feasibility)	Adults with obesity	20	12 weeks		No restrictions (n = 9)
(44)	2018	Clinical trial	Adults with obesity	46	12 weeks	8-h TRE with <i>ad libitum</i> intake from 10 a.m. to 8 p.m. (n = 23)	No restrictions (n = 23)

TRE, time-restricted eating; RCT, randomised controlled trial; IFG, impaired fasting glucose; T2DM, type 2 diabetes *mellitus*.

Table 2. Effects of time-restricted eating on body weight and body composition compared with the control groups.

Ref.	Changes in body weight		Changes in BMI		Changes in WC		Body composition Method	Changes in fat mass		Changes in visceral fat mass		Changes in lean mass	
	Δ TRE Mean $\pm$ SD (% or kg)	TRE vs control <i>p</i> -value	Δ TRE Mean $\pm$ SD (kg/m ²)	TRE vs control <i>p</i> -value	Δ TRE Mean $\pm$ SD (cm)	TRE vs control <i>p</i> -value		Δ TRE Mean $\pm$ SD (% or kg)	TRE vs control <i>p</i> -value	Δ TRE Mean $\pm$ SD (kg)	TRE vs control <i>p</i> -value	Δ TRE Mean $\pm$ SD (kg)	TRE vs control <i>p</i> -value
(43)	↓ -4.28%	<0.017 ^a	-1.78	<0.05 ^a	-3.92	<0.05 ^a	DXA	↓ kg	<0.05 ^a	↓ -0.16	n.s. ^a	↓ -0.97	n.s. ^a
(40)	↓ -3.2 $\pm$ 2.64%*	0.016	↓ -0.8 $\pm$ 0.69	0.008	↓ -1.2 $\pm$ 1.15	0.049	BIA	↓ -0.9 $\pm$ 1.76%	0.014	-	-	-	-
(38)	↓ -1.0 $\pm$ 0.3 kg*	0.02	-	-	-	-	ADP	-	-	-	-	-	-
(37)	↓ -1.6 $\pm$ 2.9%*	0.61	↓ -0.6 $\pm$ 1.0*	0.52	↓ -1.5 $\pm$ 3.2	0.64	DXA	↓ -0.1 $\pm$ 1.4%	-	-	-	↓ -0.3 $\pm$ 0.8	-
(41)	↓ kg*	<0.001	↓ *	<0.001	↓ *	<0.001	APE	↓ % *	<0.001	-	-	-	-
(39)	↓ -1.17%*	0.43	-	-	↓ -1.81 ^b	0.67 ^b	DXA	↓ - 0.09% ^b	0.96 ^b	↓ - 0.0026 ^b	0.58 ^b	↓ -1.10 ^b *	0.09 ^b
(42) ^c	↓ -3.2% $\pm$	<0.001	-	-	-	-	DXA	↓ -2.8 $\pm$	0.001	↓ -0.18 $\pm$	n.s.	↓ -0.8 $\pm$	n.s.

	0.4%*							0.4 kg		0.07		0.4	
(42)d	↓ -3.2% ± 0.4%*	<0.001	-	-	-	-	DXA	↓ -1.4 ± 0.3 kg	0.03	↓ -0.14 ± 0.06	n.s.	↓ -1.5 ± 0.2	0.03
(36)	↓ kg*	0.04	-	-	-	-	DXA	↓ %	0.48	↓ *	0.04	↓ *	0.03
(44)	↓ -2.6 ± 0.5%	<0.001	↓	<0.001	-	-	DXA	↓ kg	0.23	↓	0.19	↔	0.12

BMI, body mass index; WC, waist circumference; TRE, time-restricted eating; SD, standard deviation; DXA, dual x-ray absorptiometry; n.s., not significant; BIA, bioelectrical impedance analysis; ADP, air displacement plethysmography; APE, anthropometric prediction equations; ^a Comparison of the mean differences between the TRE group and the control group; ^b Results from the in-person cohort that did not include all the participants; ^c Results from the 4-hour TRE group; ^d Results from the 6-hour TRE group; ↓, decrease in the mean value; ↔, no changes in the mean value; ↑, increase in the mean value; * $p < 0.05$

Table 3. Effects of time-restricted eating on metabolic biomarkers compared with the control groups.

Ref.	Glucose	TRE vs control <i>p</i> -value	HbA1c	TRE vs control <i>p</i> -value	Insulin	TRE vs control <i>p</i> -value	HOMA-IR	TRE vs control <i>p</i> -value
	Δ TRE Mean $\pm$ SD (mg/dL)		Δ TRE Mean $\pm$ SD (%)		Δ TRE Mean $\pm$ SD (μ IU/mL)		Δ TRE Mean $\pm$ SD	
(43)	$\downarrow$ -11.02	<0.05^a	$\downarrow$ -0.72	<0.05^a	-	-	-	-
(46)	$\downarrow$ *	0.134 ^b	$\downarrow$	0.177 ^b	$\downarrow$	0.087 ^b	$\downarrow$	0.079 ^b
(40)	$\downarrow$ -1.9 $\pm$ 8.08	n.s.	-	-	$\downarrow$ -0.2 $\pm$ 4.08	n.s.	$\downarrow$ -0.1 $\pm$ 0.93	n.s.
(74)	$\downarrow$ ^c	0.10	-	-	$\downarrow$ ^d	0.58	-	-
(45)	$\leftrightarrow$	-	-	-	$\uparrow$ 12:00 am* $\downarrow$ 12:00 pm*	-	-	-
(47)	$\downarrow$	<0.001	$\downarrow$ -1.54 $\pm$ 0.19	<0.001	$\downarrow$	0.03	$\downarrow$ -0.51 $\pm$ 0.08	0.02
(37)	$\downarrow$	0.12	$\uparrow$	0.05	-	-	-	-
(41)	$\uparrow$	0.91	-	-	$\uparrow$	0.13	$\downarrow$	0.07
(39)	$\downarrow$ -1.06 ^e	0.50 ^e	$\downarrow$ -0.024 ^e	0.63 ^e	$\downarrow$ ^e	0.60 ^e	$\downarrow$ -0.160 ^e	0.42 ^e
(42) ^f	$\downarrow$ -5.0 $\pm$ 3.8	n.s.	$\downarrow$ -0.2 $\pm$ 0.1	n.s.	$\downarrow$ -2.3 $\pm$ 1.5	0.02	$\downarrow$ -0.8 $\pm$ 0.4	0.03
(42) ^g	$\downarrow$ -2.3 $\pm$ 2.0	n.s.	$\downarrow$ -0.2 $\pm$ 0.1	n.s.	$\downarrow$ -1.9 $\pm$ 1.1	0.04	$\downarrow$ -0.5 $\pm$ 0.3	0.04
(36)	$\downarrow$ *	0.98	$\leftrightarrow$	0.57	$\downarrow$	0.84	$\downarrow$	0.95
(44)	$\uparrow$	0.77	-	-	$\downarrow$	0.16	$\downarrow$	0.21

HbA1c, Glycated haemoglobin A1c; HOMA-IR, Homeostatic Model Assessment for Insulin Resistance; TRE, time-restricted eating; SD, standard deviation; n.s., not significant; ^a Comparison of the mean differences between the TRE group and the control group; ^b Comparison of the differences between the TRE alone group and the control group; ^c Glucose AUC (mg h/dL); ^d Insulin AUC (mU h/L); ^e Results from the in-person cohort that did not include all the participants; ^f Results from the 4-hour TRE group; ^g Results from the 6-hour TRE group; $\downarrow$, decrease in the mean value; $\leftrightarrow$, no changes in the mean value; $\uparrow$, increase in the mean value; * p < 0.05

Table 4. Effects of time-restricted eating on lipid profile biomarkers and comparison with the control groups.

Ref.	Total cholesterol		LDL-C		HDL-C		Triglycerides	
	Δ TRE Mean $\pm$ SD (mg/dL)	TRE vs control <i>p</i> -value	Δ TRE Mean $\pm$ SD (mg/dL)	TRE vs control <i>p</i> -value	Δ TRE Mean $\pm$ SD (mg/dL)	TRE vs control <i>p</i> -value	Δ TRE Mean $\pm$ SD (mg/dL)	TRE vs control <i>p</i> -value
(43)	↓ -0.18	n.s.	↓ -0.23	n.s.	↑ 3.20	n.s.	↓ -15.43	n.s.
(46)	↓	0.076 ^a	↓	0.154 ^a	-	0.578 ^a	↓	0.520 ^a
(40)	↓ -13.9 $\pm$ 12.82*	0.145	↓ -9.1 $\pm$ 11.25*	0.251	↓ -7.7 $\pm$ 10.61	0.437	↑ 15.4 $\pm$ 27.41	0.128
(47)	↓	0.01	↓	0.02	↓	0.33	↓	0.03
(37)	-	-	-	-	↓	0.70	↓	0.69
(41)	↑	0.11	↑	0.26	↑	0.14	↓	0.77
(39)	↓ -3.56	0.52	↑ 0.60	0.62	↓ -0.72	0.44	↓ -10.27	0.29
(42) ^b	-	-	↑ 2.6 $\pm$ 5.7	n.s.	↓ -2.4 $\pm$ 1.3	n.s.	↓ -1.9 $\pm$ 6.7	n.s.
(42) ^c	-	-	↓ -4.8 $\pm$ 5.1	n.s.	↓ -0.8 $\pm$ 1.4	n.s.	↑ 2.6 $\pm$ 4.6	n.s.
(36)	-	-	↑	0.84	↑	0.66	↓ *	0.62
(44)	↑	n.s.	↑	n.s.	↑	n.s.	↓	n.s.

LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; n.s., not significant; ^a Comparison of the differences between the TRE alone group and the usual care in patients with impaired fasting glucose group; ^b Results from the 4-hour TRE group; ^c Results from the 6-hour TRE group

Financial Support

This work was supported by Portuguese national funds provided by FCT – Fundação para a Ciência e Tecnologia, I.P., (UI/05704/2020), by the Portuguese Society of Diabetology through the award of the 2020 Emilio Peres Scholarship and by the Faculty of Nutrition and Food Sciences of the University of Porto and LabITR (LA/P/0064/2020). ML is supported by a PhD Scholarship from the FCT – Fundação para a Ciência e Tecnologia, I.P. (DOI 10.54499/2021.07673.BD). MPG work is funded by national funds through FCT – Fundação para a Ciência e Tecnologia, I.P., under the Scientific Employment Stimulus – Institutional Call (DOI 10.54499/CEECINST/00051/2018/CP1566/CT0009).

Declaration of Interests

The authors declare no conflicts of interest.

Authorship

ML, SCS, RB, and MPG conceived and designed the study and contributed to the protocol development. ML conducted the literature search, article selection, and analysis, and wrote the first draft of the manuscript. All authors contributed to the manuscript by revising it critically for intellectual content. All authors read and approved the final manuscript submitted.

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