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Time restricted eating and effects on metabolic syndrome and health markers for metabolic syndrome – a systematic review of human clinical trials

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Abstract

Metabolic syndrome (MetS) is a cluster of risk factors that significantly increase the likelihood of developing chronic health conditions such as cardiovascular disease, type 2 diabetes mellitus, and non-alcoholic fatty liver disease. Time-restricted eating (TRE) is a dietary intervention that shortens the eating window, without limiting energy intake, and has the potential to improve metabolic health by leveraging circadian rhythms.

This thesis aimed to explore the relationship between TRE and MetS, focusing on the potential benefits and drawbacks of implementing TRE interventions in individuals with or at risk of MetS. A systematic search of PubMed identified 27 studies for inclusion, which were then reviewed and compared based on similarities in their interventions or patient populations.

The review of time-restricted eating (TRE) studies revealed that early time-restricted eating (eTRE) is more effective in reducing body weight and improving glucose parameters than late time-restricted eating (lTRE). Both healthy adults and those with overweight or obesity experienced improvements in body composition and cardiometabolic health. Improvements in glycemic control improvements were particularly pronounced in overweight/obese individuals with type 2 diabetes. However, studies on individuals with underlying health conditions presented mixed results due to variations in study design, intervention duration, and eating windows.

In conclusion, the current evidence suggests that TRE, especially eTRE, has the potential to improve weight management and cardiometabolic health in different populations, but further research is required to confirm these findings and to better understand the underlying mechanisms and practical implications of TRE for weight management and cardiometabolic health.

Sammendrag

Metabolsk syndrom (MetS) er en samling av risikofaktorer som betydelig øker sannsynligheten for å utvikle kroniske helseproblemer som hjerte- og karsykdommer, type 2-diabetes og ikke-alkoholisk fettsykdom i leveren. Tidsbegrenset spising (TRE) er en diettintervensjon som forkorter spisevinduet, uten å begrense energiinntaket, og har potensial til å forbedre metabolsk helse ved å utnytte de cirkadiske rytmer.

Denne avhandlingen hadde som mål å utforske forholdet mellom TRE og MetS, og sette søkelys på de mulige fordelene og ulempene ved å gjennomføre TRE-intervensjoner hos personer med eller i risiko for MetS. Et systematisk søk i PubMed identifiserte 27 studier som ble inkludert, og disse ble deretter vurdert og sammenlignet basert på likheter i deres intervensjoner eller pasientpopulasjoner.

Gjennomgangen av tidsbegrenset spising (TRE) studier viste at tidlig tidsbegrenset spising (eTRE) er mer effektivt for å redusere kroppsvekt og forbedre glukoseparametere enn sen tidsbegrenset spising (lTRE). Både friske voksne og de med overvekt eller fedme opplevde forbedringer i kroppssammensetning og kardiometabolsk helse. Forbedringer i glykemisk kontroll var spesielt uttalt hos overvektige personer med type 2 diabetes. Imidlertid presenterte studier på personer med underliggende helsetilstander blandede resultater på grunn av variasjoner i studieoppsett, intervensjonsvarighet og spisevinduer.

For å konkludere tyder den nåværende forskningen på at TRE, spesielt eTRE, har potensiale til å forbedre vektkontroll og kardiometabolsk helse i forskjellige populasjoner, men ytterligere forskning er nødvendig for å bekrefte disse funnene og for å bedre forstå de underliggende mekanismene og praktiske konsekvensene av TRE for vektkontroll og kardiometabolsk helse.

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Abbreviations

ADF = Alternate day fasting

DIO = diet-induced obesity

eTRE = early Time restricted eating

eTRF = early Time restricted feeding

FFA = free fatty acids

HDL = High-density lipoprotein

IBD = Inflammatory bowel disease

IBS = irritable bowel syndrome

lTRE = late Time restricted eating

MetS = Metabolic Syndrome

mTRF = midday Time restricted feeding

MMC = Migrating Motor Complex

SIBO = Small intestinal bacterial overgrowth

TG = Triglycerides

TRE = Time restricted eating

TRF = Time restricted feeding

Introduction

1.1 Metabolic syndrome

1.1.1 Introduction to metabolic syndrome

Metabolic syndrome (MetS), also known as Syndrome X or insulin resistance syndrome, is a cluster of risk factors, including abdominal obesity, insulin resistance, hypertension, and hyperlipidemia, that significantly increases the likelihood of developing chronic health conditions such as cardiovascular disease, type 2 diabetes mellitus, and non-alcoholic fatty liver disease (Grundy et al., 2005; Saklayen, 2018). This complex condition affects millions of people worldwide, and its prevalence continues to rise in parallel with increasing rates of obesity and sedentary lifestyles.

According to the National Cholesterol Education Program's Adult Treatment Panel III (NCEP ATP III), MetS is diagnosed when an individual meets at least three of the following five criteria (Grundy et al., 2005):

1. Abdominal obesity, defined as a waist circumference of greater than 102 cm (40 inches) in men or greater than 88 cm (35 inches) in women.
2. Elevated fasting glucose levels of 5.6 mmol/L (100 mg/dL) or higher.
3. High levels of serum triglycerides, with concentrations of 1.7 mmol/L (150 mg/dL) or higher.
4. Low levels of high-density lipoprotein cholesterol (HDL), with concentrations below 1.0 mmol/L (40 mg/dL) in men and below 1.3 mmol/L (50 mg/dL) in women.
5. Hypertension, with readings of 130/85 mmHg or higher.

The development of MetS is believed to be influenced by a combination of genetic and environmental factors, with lifestyle choices such as poor diet, physical inactivity, and smoking playing significant roles (Grundy et al., 2005). Early identification and management of MetS are crucial for preventing the progression of associated health complications and improving overall health outcomes.

1.1.2 Epidemiology

Prevalence of MetS has been on the rise globally, primarily due to factors such as increasing rates of obesity, sedentary lifestyles, and unhealthy dietary habits (Saklayen, 2018). In the United States, approximately one third of adults have MetS, while in China the numbers are about 15%. While the obesity rate worldwide is high, with 604 million adults and 108 million children being obese (BMI ≥ 30), this is not always synonymous with MetS. Individuals can be so called metabolically healthy obese, and these people account for a significant percentage of the obese population. Global prevalence of diabetes was 8,8% in 2015, and while we do not have similar global data on MetS, it is estimated that since MetS is three times more common than diabetes, the prevalence is about one quarter of the world population. In other words, over a billion people in the world (Saklayen, 2018).

Risk factors for metabolic syndrome include age, family history of type 2 diabetes, ethnicity, and lifestyle choices such as physical inactivity, smoking, and poor diet (Grundy et al., 2005). Metabolic syndrome contributes significantly to the global burden of non-communicable diseases, as it increases the risk of developing type 2 diabetes by five-fold and doubles the risk of cardiovascular disease (Alberti et al., 2009).

1.1.3 Diagnosis and management

Current guidelines for diagnosing and managing metabolic syndrome are based on the National Cholesterol Education Program's Adult Treatment Panel III (NCEP ATP III) criteria, as previously mentioned. Early detection and intervention are critical to preventing the progression of the associated complications and improving overall health outcomes (Grundy et al., 2005).

Management of metabolic syndrome involves addressing the individual risk factors through a combination of lifestyle modifications and, if necessary, pharmacological interventions (Grundy et al., 2005). Lifestyle changes that can help mitigate the risk factors of metabolic syndrome include adopting a balanced diet, engaging in regular physical activity, losing weight, and quitting smoking. In some cases, medications may be prescribed to control blood pressure, blood glucose levels, and cholesterol levels.

With the increasing prevalence of metabolic syndrome worldwide, posing a significant public health challenge, there is a growing interest in identifying dietary interventions that can help prevent or manage the condition. Time restricted eating (TRE) has emerged as a promising approach in this regard.

1.2 Fasting and Time restricted eating

TRE is a set of meal timing strategies where individuals shorten their eating window, without limiting energy intake, thus fasting outside the eating window, and extending the overnight fast. TRE is partly based on the understanding of circadian rhythms, a ~24h clock that governs a number of metabolic functions in all cells, that is both regulated by light/dark cycles and meal patterns (Panda, 2016). Most experimental data regarding the impact of circadian rhythms in relation to nutrition and timing of eating has come from studies in rodents (Manoogian et al., 2021). The circadian rhythm promotes preparatory changes in metabolic functions, when anticipating predictable changes in temperature, light and availability of nutrients. Experiments done by Manoogian, and coworkers showed that the rodents would wake up a few hours before they would get food and start moving as if they were anticipating food, even when the food were given during the daytime, when they normally would not anticipate it. This daytime access to food changed the circadian clock components in the liver of the rodents, and that timing of access to food is what drives all the rhythmic transcripts of the liver. Other experiments have also seen this outcome for other organs (Mukherji, Kobiita, & Chambon, 2015; Mukherji, Kobiita, Damara, et al., 2015). The conclusion was that timing of food intake is a powerful tool to determine the circadian transcriptional programs in many peripheral organs, and parts of the brain, giving a new method to alleviate circadian rhythm disruptions.

The potential of TRE to positively affect the components of metabolic syndrome has been demonstrated in various studies. The metabolic benefits of time-restricted feeding (TRF) were first shown in diet-induced obesity (DIO) mouse models, with access to ad libitum high-fat diet (Manoogian et al., 2021). Mice fed a normal diet consumed around 85% of their energy during the night, while the high-fat fed mice consumed more than 30% of their energy during the day. Intriguingly, when the high-

fat diet was given only during the dark period (night) consuming the same energy as those fed high-fat diet *ad libitum*, these mice showed improved molecular rhythms in the circadian clock components and these mice were largely protected from high-fat induced obesity and related metabolic illness (Hatori et al., 2012). The initial experiments were used with an 8h window, thus giving life to the 16:8 diet, with an eating window for 8-hours and fasting for 16-hour.

There is currently no consensus on an optimal length of the eating window for humans. In human studies it typically lies between an 8- to 10-h interval, although some studies have chosen interval as short as 4- and 6-h, while others as long as 12-h (Manoogian et al., 2021).

TRE/TRF are grouped under intermittent fasting, which includes all types of fasting from hours to days, without necessarily considering the circadian rhythms of the body (Manoogian et al., 2021).

1.2.1 Introduction to fasting

Fasting refers to a period with voluntary abstinence from eating and drinking and often with a calorie restriction, for spiritual, therapeutic, political or health reasons (Attinà et al., 2021).

Historically, fasting has been used both as spiritual development, promotion of health and as a religious practice worldwide (Kerndt et al., 1982). It was used in ancient Greece, mentioned in the Old Testament In ancient Greece, and is used in both Islam and Christianity (Fazel, 1998). Fasting for health has been advocated since the time of ancient China, Greece, and Rome (Anton et al., 2018). Fasting as a therapy for obesity has long been recommended (Kerndt et al., 1982).

1.2.2 Biological Mechanisms induced by fasting

Migrating Motor Complex

The Migrating Motor Complex (MMC) is a system of recurring peristaltic motility waves that migrate through the small intestine, starting in the stomach (Deloose et

al., 2012). It occurs in between meals and during the fasting stage in four distinct phases and will stop immediately after ingestion of food.

The role of the MMC is to move residues of undigested food, bacteria, and dead enterocytes from the stomach and the small intestine and finally empty these residues into the colon (Deloose et al., 2012). In humans, the absence or reduced function of MMC has been associated with bacterial overgrowth in the small intestines, indicating that removal of surplus bacteria is of major importance for MMC function. Small intestinal bacterial overgrowth (SIBO) can cause gastrointestinal symptoms, and has been linked to diseases such as irritable bowel syndrome (IBS), inflammatory bowel disease (IBD), systemic sclerosis, motility disorders, cirrhosis, fatty liver and various other conditions (Pimentel et al., 2020).

MMC usually last between 90-120 minutes and consists of four phases. Phase I is the dormant phase with no contractions; phase II has random contractions; phase III has a sudden beginning with a burst of contractions, this is the most active phase; phase IV has a rapid decrease of contractions. Phase III is regulated by the hormone motilin. Expansion of the stomach stops the MMC activity in the stomach and upper part of small bowel, while the entire small bowels MMC is stopped when fluid or nutrients are present. The gastrointestinal rumbling noticed during fasting is associated with the MMC (Deloose et al., 2012).

Energy metabolism during fasting

After a meal, in the postprandial phase, our body, triggered by insulin release, stores energy in the form of glycogen (liver and muscle) and triglycerides (adipose tissue). Also protein translation is stimulated during this phase. During over-night fasting, the flow of energy is switched, with a release of glucose from the liver due to hydrolysis of glycogen into glucose and induction of gluconeogenesis. From adipose tissue, there is a large release of free fatty acids catalyzed by a set of lipases in the adipose tissue. These processes are dependent on the absence of insulin and the presence of glucagon. If the fasting persists beyond an over-night fast, utilization of glucose as energy source is reduced and mobilization of fatty acids become more important. Free fatty acids (FFA) taken up by the liver, will facilitate the production of ketones which happens during fasting when glycogen in the hepatocytes in the liver are

depleted (Anton et al., 2018). This usually occurs 12 to 36 hours after the last meal, all depending on the content of glycogen in the liver at the beginning of the fast, and energy expenditure. The adipose tissue lipolysis accelerates, and the release of fatty acids and glycerol increases. Other cell types begin generating ketones on their own, but FFAs are also metabolized to produce the ketone b-hydroxybutyrate and acetoacetate.

Ketones are transported into cells with high metabolic activity, like muscle cells and neurons, where they are used as an energy source for muscle and brain cells during fasting (Anton et al., 2018). The switch from using glucose to ketones serve to preserve muscle mass (less dependence on gluconeogenesis) and the retention of lean mass is increased, as shown in intermittent fasting regimens for weight loss, compared to caloric restriction regimens.

Autophagy

Autophagy is a process taking place in most or all cells when cells experience a scarcity of macronutrients, foremost amino acids. Autophagy, meaning “eating of self”, is a degradation process which removes and recycle damaged cell components and aggregated and misfolded proteins and is also important for maintaining energy levels to sustain the cell’s basic functions (Bagherniya et al., 2018). It prevents necrosis and has a protective role against genome instability, and therefore it is likely to play a part in the prevention of several diseases like diabetes, liver disease, cancers, autoimmune diseases, and infections. Deregulated autophagy has been associated with disorders like metabolic diseases, neurodegenerative disorders, and cancer.

Fasting has been shown to induce autophagy in various tissues, including the liver, muscles, and brain (Alirezaei et al., 2010; Bagherniya et al., 2018). This induction of autophagy during fasting serves as a cellular response to nutrient deprivation and energy stress, promoting the recycling of cellular components to maintain cellular function and survival. By promoting autophagy, fasting may contribute to the prevention and treatment of various diseases associated with cellular dysfunction.

1.2.3 Types of fasting intervention

There are several different types of fasting interventions. Intermittent fasting is an umbrella term, that includes several types of fasting, and is the practice of alternating between eating and fasting. Some popular fasting interventions include:

1. Time restricted eating (TRE) or Time restricted feeding (TRF): as previously explained, TRE involves restricting the eating window to a certain number of hours per day, like 16:8 with an 8-hour eating window and 16-hour fast and includes the following sub-categories:
    a. Early time restricted eating (eTRE): eTRE restricts food intake to early in the day, with the last meal typically around 15:00.
    b. Midday time restricted eating (mTRE): mTRE limits food intake to the middle of the day, with the first meal starting around 12:00.
    c. Late time restricted eating (lTRE): lTRE restricts food intake to late afternoon or evening, often having the first meal around 16:00.
2. Alternate day fasting (ADF), and Alternate day modified fasting (ADMF): ADF involves alternating between days of unrestricted eating and days of complete or partial fasting, while during ADMF individuals consume 25% of their daily caloric need on the “fasting” days.
3. 5:2 diet: The 5:2 diet consists of eating normally for five days of the week and restricting caloric intake to around 500-600 calories for the other non-consecutive two days.

Other popular fasting interventions also exists, like fasting mimicking diet and prolonged fasting.

1.2.4 Potential downsides and risks of fasting

While fasting has been shown to provide various health benefits, it is important to consider the potential downsides and risks associated with this practice. Some potential risks and downsides of fasting include:

1. Nutrient deficiencies: Prolonged fasting or improperly planned intermittent fasting regimens can lead to inadequate nutrient intake, increasing the risk of nutrient deficiencies.

2. Loss of lean body mass: Although fasting can help preserve lean body mass, some degree of lean mass loss can still occur, particularly during prolonged fasting periods (Tinsley & La Bounty, 2015)

3. Disordered eating patterns: Fasting may contribute to disordered eating patterns, particularly in individuals with a history of eating disorders or those susceptible to developing them.

4. Medical risks: Fasting may not be suitable for individuals with certain medical conditions, such as diabetes, eating disorders, or during pregnancy and breastfeeding. It is essential to consult with a healthcare professional before starting a fasting regimen, especially for individuals with pre-existing health conditions.

There have been several benefits linked to fasting of different sorts, including several bodily functions that can be activated during fasting. Fasting often leads to calorie restriction due to a shortened eating window, which can aid in weight loss. The question then arises: does fasting have any positive outcomes in the context of metabolic syndrome?

1.3 Thesis Aim

The primary aim of this thesis is to explore the relationship between time-restricted eating (TRE) and metabolic syndrome, focusing on the potential benefits and drawbacks of implementing TRE interventions in individuals with or at risk of metabolic syndrome. Specific objectives include:

1. To provide a comprehensive review of human clinical trials in which time-restricted eating (TRE) and its various forms have been explored.
2. Compare different strategies of TRF in relation to impact on metabolic processes associated with metabolic syndrome in healthy and metabolically dysregulated individuals.

3. To identify potential limitations and gaps in the current literature, as well as pointing towards future research questions to further elucidate the role of time-restricted eating in metabolic health.

By addressing these objectives, this thesis aims to contribute to the growing body of knowledge on the potential of time-restricted eating as a feasible dietary intervention for individuals with metabolic syndrome or at risk of developing the condition.

2. Methods

2.1 Non-Systematic Search

A non-systematic literature search was first carried out from November until December 2022, mainly in PubMed and some in google scholar, to find pertinent literature and create a list of relevant search terms to be used in the systematic search. PubMed was chosen for the systematic search, as it is the biggest database for fields in health and biomedicine. Combinations of the words ``time-restricted eating", "time-restricted feeding" and "metabolic syndrome" in various forms were used, and "metabolic syndrome" as a Medical Subject Heading (MeSH) term was explored to find relevant search terms.

2.2 Systematic Search

The systematic search was performed in PubMed on January 6th, 2023, and again on 24th February 2023. The search on the 24th of February was an updated search, to find newly published studies, resulting in 224 finds. Only the last search was used in this thesis.

In the systematic search, the search terms were divided into two groups. The first group aimed to find studies about time-restricted eating/feeding, while the second group aimed to find studies related to metabolic syndrome and its various symptoms. The search terms within each group were combined using the Boolean operator "OR", and the two groups were combined using the Boolean operator "AND".

The specific search string used was as follows:

("time-restricted eating"[tiab] OR "time-restricted feeding"[tiab] OR "time restricted eating"[tiab] OR "time restricted feeding"[tiab]) AND ("metabolic syndrome"[tiab] OR metabolic syndrome[mesh] OR "hypertension"[tiab] OR "blood pressure"[tiab] OR "glucose intolerance"[tiab] OR "glucose tolerance"[tiab] OR "abdominal obesity"[tiab] OR "triglyceride*"[tiab] OR "high density lipoprotein"[tiab] OR "cardiovascular disease*"[tiab] OR "dyslipidemia"[tiab] OR "hyperglycemia"[tiab] OR "insulin resistance"[tiab] OR "HbA1C"[tiab] OR "fasting insulin"[tiab])

The search terms were identified in the title or abstract using the [tiab] tag, and the Medical Subject Heading (MeSH) terms were identified using the[mesh] tag. An asterisk (*) was used to search for variations of the search terms. Titles and abstracts of all 224 articles were independently screened twice.

The results and search process are shown in the flow chart in figure 1.

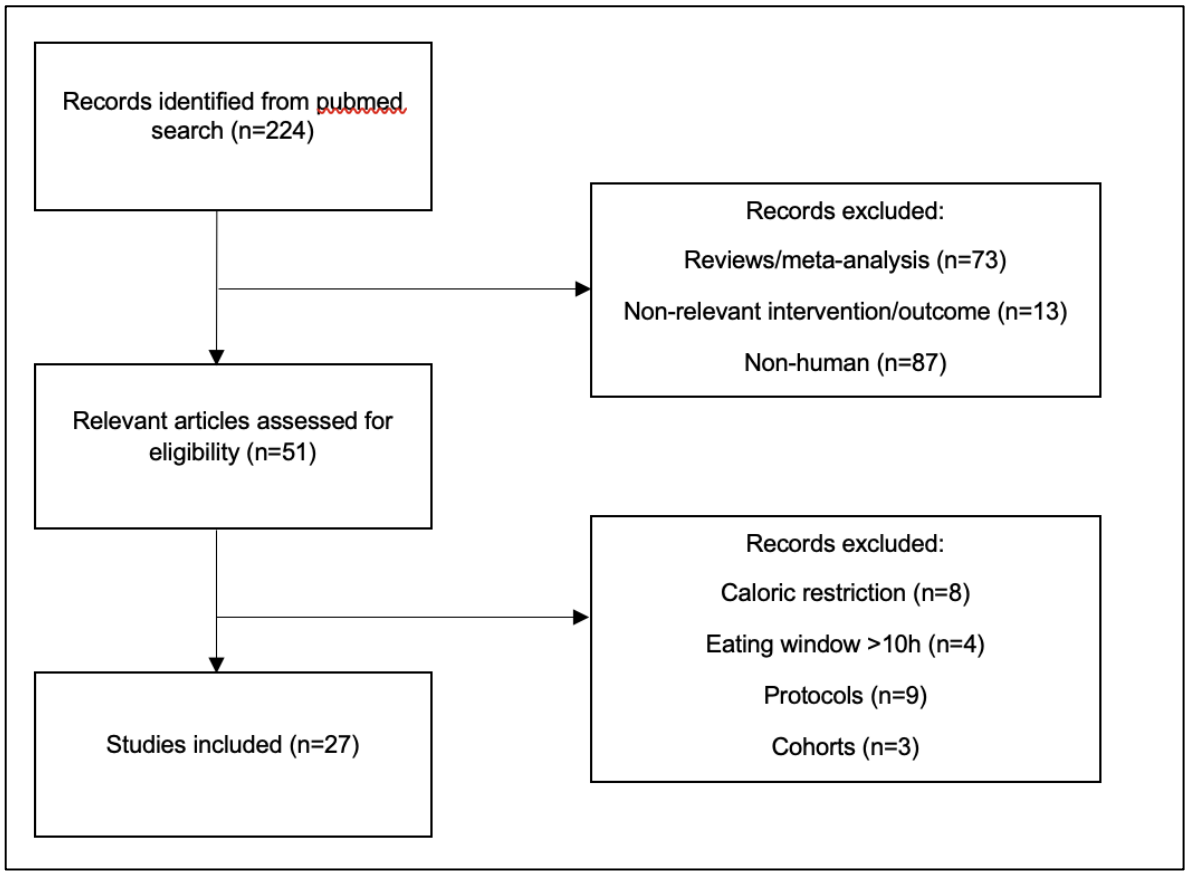

Figure 1: Flow chart of results from the systematic review.

2.3 Inclusion and exclusion criteria

The inclusion criteria for this review were as follows: (1) studies must be interventional studies; (2) interventions must not involve caloric restrictions; (3) the eating window must be set to <10 hours in the methods; (4) studies must have outcomes correlated with metabolic syndrome or health markers associated with it.

Inclusion criterion 1 was chosen to focus on the results of interventional studies, as observational studies, such as cohort studies, often have greater recall bias. Inclusion criterion 2 was selected to examine the impact of time-restricted eating independent of calorie restrictions since several health benefits can be attributed solely to calorie restrictions. Inclusion criterion 3 was chosen to emphasize the difference between ad libitum eating and time-restricted eating, as several studies show a baseline eating duration of 12-14 hours (Manoogian et al., 2021). Inclusion

criterion 4 was chosen because this thesis focuses on outcomes related to metabolic syndrome or health markers associated with it.

The exclusion criteria were: (1) animal studies; (2) trials that have not yet been published; (3) studies with other types of fasting, including 5:2 diets, alternative fasting, and sunrise to dawn fasting; (4) other studies that did not meet the inclusion criteria.

Exclusion criterion 1 was chosen as this thesis aims examine results in humans. Exclusion criterion 2 ensured that only studies with actual results were included, rather than those based on hypotheses. Exclusion criterion 3 was chosen to focus on the specific results of time-restricted eating/feeding.

Based on these inclusion and exclusion criteria, from the 224 records identified, 51 were further assessed for eligibility. From those 51, only 27 were included, based on their abstract and full text, and the inclusion and exclusion criteria described.

2.4 Data extraction and analysis

The 27 included studies were thoroughly reviewed to extract relevant data from their results. Only results pertinent to the thesis aim were considered. The extracted results were briefly summarized in a table, and the studies were grouped based on similarities in their interventions of patient populations. The results of studies with similar interventions or patient groups were then compared to each other in the results section.

3. Results

3.1 Early, late and midday time restricted Eating

Of the 27 studies identified in the literature search, five studies investigated if the timing of the eating window in TRE differentially affected outcomes related to metabolic parameters. Early time-restricted eating (eTRE) was therefore compared to those that were confined to late or midday time-restricted eating (lTRE or mTRE) and control groups with an *ad libitum* meal pattern (Table 1). Hutchison et al., compared early time restricted feeding (TRFe) with delayed time restricted feeding (TRFd) (Hutchison et al., 2019). Kim & Song, and Zhang et al., assessed eTRE and lTRE, with Zhang et al. also including a control group (Kim & Song, 2023; Zhang et al., 2022). Sutton et al., examined eTRF and a control group, while Xie et al., compared eTRF with mTRF and a control group (Sutton et al., 2018; Xie et al., 2022).

Hutchison et al. (2019) examined the effects of 9-hour TRF commencing at 08:00 or 12:00 on glucose tolerance in men at risk of type 2 diabetes, dividing participants into two groups, TRFe and TRFd for 5 weeks. Fifteen men, aged 55 ± 3 years were included in the study, with a hypothesis that TRF would improve glycemic control, and TRFe would have greater improvements than TRFd. The participants in both the TRFe and the TRFd significantly improved their glucose tolerance compared to baseline assessed by a standard glucose tolerance test in which Area under the curve (AUC) of glucose concentration over 2h was calculated. However, the eTRF group had a more pronounced improvement (36% reduction in AUC; -1.6 ± 0.4 mmol/L/h) than the TRFd (21% % reduction; 0.87 ± 0.5 mmol/L/h). However, fasting glucose were not affected by mealtime or TRF. Both TRF groups decreased fasting triglycerides without any mealtime effect. Mean fasting glucose assessed by continuous glucose monitoring (CGM) was lower during TRFe compared to baseline but not in TRFd, and no differences were observed between TRF treatments. In TRFe, mean blood glucose concentration for the three hours preceding the first meal of the day was reduced compared to baseline, and a similar trend was observed in TRFd, but no significant difference was found between treatments (Hutchison et al., 2019).

Kim & Song (2023) examined whether 8-hour TRE had an effect on body composition and cardiometabolic risk factors among 34 young adults, aged 18-39, with typically late bedtime, dividing into eTRE and lTRE groups for 4 weeks. They found that body composition measures, like body weight, BMI and waist circumference decreased only in the eTRE group. The eTRE group showed improvements in glucose (89.8 ±9.4 mg/dL pre, 86.1 ±6.5 mg/dL post) and insulin (10.9 ± 5.5 μU/mL pre, 8.6 ±4.7 μU/mL post) parameters, while the lTRE group did not. Both groups experienced a decrease in serum TG (100.6 ± 65.2 mg/dL pre, 79.3 ±46.2 mg/dL post), but HDL cholesterol decreased only in the eTRE group (63.1 ±16.9 mg/dL pre, 58.9 ± 13.7 mg/dL post). Blood pressure did not differ between groups and baseline values. (Kim & Song, 2023).

Xie et al. (2022) performed a study to compare eTRF (8-hour between 06:00 and 15:00) with mTRF (8-hour between 11:00 and 20:00), in 90 healthy individuals with a mean age of 31, without obesity for 5 weeks. A control group was also included. They observed changes in fasting glucose between the eTRF (Δ = -0.59 ± 0.84 mmol/L) and control group (Δ = 0.16 ± 0.38 mmol/L), but not between the mTRF and control groups or between the TRF groups. Reductions in body mass in the eTRF group (Δ = -1.6 ± 1.4 kg) compared with the control group (Δ = 0.3 ± 1.2 kg), and in body fat and body fat mass between eTRF (Δ = -0.60 ± 1.22% and Δ = -0.76 ± 1.01 kg, respectively) and control (Δ = 0.42 ± 1.16% and Δ = 0.41 ± 0.89 kg, respectively) were observed, but again there were no differences between mTRF and control, and between the TRF groups. Blood pressure did not differ between the groups, and no differences in triglycerides and HDL were observed (Xie et al., 2022).

Zhang et al. (2022) performed a trial to compared the effects of 6-hour eTRE (from 07:00 to 13:00), 6-hour lTRE (from 12:00 to 18:00), and a control group, on body weight loss and cardiometabolic outcomes in 60 young adults (mean age 23) with overweight and obesity for 8 weeks. The hypothesis was that the eTRE group would have greater weight loss and improvements in cardiometabolic parameters compared with the lTRE and control groups. Both eTRE (-4.6% [95%CI: -5.5 to -3.8]) and lTRE (-3.7% [95%CI: -4.6 to -2.9]) led to a decrease in body weight. Waist circumference was also decreased compared to the control group, with eTRE (-5.6 cm) showing a greater reduction than lTRE (-3.9 cm). Mean glucose levels decreased in the eTRE

group by -2.3 mg/dL, while both lTRE and control groups showed an increase of 2.5 mg/dL. No improvements in fasting glucose levels were observed in any of the groups. In terms of blood pressure, eTRE reduced systolic blood pressure (-5.5 mmHg), while no significant changes were seen in the lTRE group (-1.6 mmHg) or control group (0.9 mmHg). Diastolic blood pressure did not differ significantly among the groups. TG, and HDL cholesterol levels showed no significant differences (Zhang et al., 2022).

Sutton et al. (2018) conducted a study on 12 men with prediabetes (aged 56 ± 9) , comparing a 6-hour eTRF with dinner before 15:00 to a control group (eating 12-hours daily) for 5 weeks to examine whether time-restricted feeding can improve cardiometabolic health and have a benefit independent on weight loss. They hypothesized that eTRF would improve glycemic control and vascular function and reduce inflammation markers and oxidative stress, without weight loss. They found that eTRF did not influence fasting glucose or mean glucose. Morning levels of systolic and diastolic blood pressure were lowered by 11 ± 4 mm Hg and 10 ± 4 mm Hg compared to the control group. However, no effects were observed on HDL cholesterol (Sutton et al., 2018).

In summary, the studies investigating the effects of early time-restricted eating (eTRE) compared to late or midday time-restricted feeding (lTRE or mTRE) or control groups have demonstrated various impacts on body composition, glucose and insulin levels, and cardiovascular parameters. eTRE has shown to be more effective in reducing body weight, BMI, and waist circumference compared to lTRE and control groups. While improvements in glucose and insulin parameters were generally more pronounced in eTRE groups, both eTRE and lTRE demonstrated reductions in serum triglycerides. Blood pressure reductions were observed in some eTRE groups, but the effects on HDL and LDL cholesterol levels were inconsistent across studies. Overall, these findings suggest that eTRE may be more beneficial for weight loss and cardiometabolic health compared to lTRE or mTRE, although the outcomes may vary depending on the study population and specific interventions.

Table 1. An overview of the study design, main results and conclusions of the studies included in section 3.1 Early Time Restricted Eating vs Late or Midday Time Restricted Eating, alphabetically.

Study	Study design	Main results	Conclusion
Hutchison et al. (2019	Randomized crossover trial. 7days baseline assessment, 7 days of 9h TRFe and TRFd, separated by 2 weeks washout. Metabolic testing conducted on day 0 and 7 of each intervention, and continuous glucose monitoring. Men with risk for type 2 diabetes, 15 participants.	TRF improved glucose tolerance, fasting triglycerides. No significant differences in the two TRF groups were made. No effect of TRF on fasting and postprandial insulin, nonesterified fatty acids and gastrointestinal hormones. Only TRFe lowered mean fasting glucose.	1 week of TRF improves glucose response to meals, regardless of when the TRF is commenced.
Kim & Song (2023)	Pre-post Single-Arm Intervention. 4 weeks TRE (8h window). Divided into starting before (eTRE) or after (lTRE) noon. Body comp measured weekly, blood samples at baseline and after intervention. Healthy young adults, 34 participants.	Body weight and fat mass significantly reduced only in eTRE. eTRE showed improvements in glucose and insulin, while lTRE did not. TG were decreased in both groups. eTRE had increased LDL and decreased HDL. No differences in blood pressure.	8h TRE may be a good strategy for managing body weight and cardiometabolic risk factors, even for those with late chronotype, without altering sleep-wake cycle.
Sutton et al. (2018)	Randomized, crossover, isocaloric and eucaloric controlled feeding trial. 5 weeks of either eTRF (6h window) or control, then a 7week washout before switching schedule. Men with prediabetes. 3h OGTT at baseline and after each intervention. 12 participants.	eTRF improved insulin sensitivity, B-cell responsiveness, blood pressure, oxidative stress and appetite. No change in HDL and LDL cholesterol.	eTRF improved all the stated previously, even when food was matched to control arm, and without weight loss.
Xie et al. (2022)	Randomized controlled trial. 5 weeks of either eTRF (early,8h window), mTRF (midday, 8h window) or control. Healthy adults without obesity. Anthropometrics, body composition, blood samples were measured. 90 participants.	eTRF was more effective than mTRF in improving insulin sensitivity. eTRF improved fasting glucose, reduced total body mass, reduced inflammation and increased gut microbial diversity.	eTRF showed greater benefits for insulin resistance and metabolic parameters than mTRF.
Zhang et al. (2022)	Randomized controlled trial. 2 weeks baseline followed by 8 weeks of either eTRE (6h window), lTRE (late, 6h window) or control. Overweight and obese young adults. Body composition, blood samples and questionnaires were collected. 60 participants.	eTRE reduced systolic blood pressure, mean glucose, fasting insulin, insulin resistance, leptin, and thyroid axis activity. lTRE only reduced leptin. Both produced weight loss.	eTRE had greater cardiometabolic health improvements than lTRE, but both are good when it comes to weight loss.

3.2 Time restricted eating in healthy adults

Of the 27 studies included in the literature search, 10 studies were conducted on healthy participants (Table 2). Brady et al., did their study on endurance athletes, while Moro et al., conducted both their studies on resistance-trained males (Brady et al., 2021; Moro et al., 2016; Moro et al., 2021) . Kesztyüs et al., Kim & Song, Martens et al., McAllister et al., Park et al., and Xie et al., included only healthy adults (Kesztyüs et al., 2021; Kim & Song, 2023; Martens et al., 2020; McAllister et al., 2020; Park et al., 2021; Xie et al., 2022). Manoogian et al., conducted their study on firefighters with health risks within a healthy range, however 71% of participants had at least one cardiometabolic risk factor (Manoogian et al., 2022).

Brady et al. (2021) performed a study on 23 endurance athletes (aged 36.4 ± 7.4) divided into a TRE group (8-h eating window) and a habitual dietary control group for 8 weeks, to investigate the effects on body composition, energy and macronutrient intakes, indices of endurance performance and markers of metabolic health. Their hypothesis was that this intervention would not influence body mass and their chosen secondary outcomes. The participants maintained their normal training routines during the intervention. The TRE group experienced a significant reduction in body mass (mean difference of -1.92 kg), while fat mass did not differ significantly between the groups. There were no differences in fasting glucose and fasting triglycerides between the groups (Brady et al., 2021).

Moro et al. (2016) examined TRF in 34 healthy, resistance-trained males (aged 29.21 ± 3.8) over 8 weeks, dividing participants into TRF (8-hour eating window, feeding 13:00, 16:00 and 20:00) or normal diet (eating at 08:00, 13:00 and 20:00) groups. The intention was to investigate the effects of TRF during resistance training with the hypothesis that TRF would lead to greater fat loss and improvements in health-related biomarkers than a typical eating schedule. The TRF group experienced a significant decrease in fat mass (-16.4% vs -2.8% in ND). Blood glucose decreased only in the TRF group (96.64 ± 5.1 mg/dL to 85.92 ± 7.13 mg/dL). No significant changes were observed in lipids such as HDL, but TG decreased in the TRF group (123.78 ± 15.12 mg/dL to 115.23 ± 11.77 mg/dL) (Moro et al., 2016).

In a follow-up study, Moro et al. (2021) divided 20 healthy resistance-trained males (same age as previously) to either TRE or ND, to examine the same parameters as previously, but for 12 months. In this study the hypothesis was that 12 months of TRE would lead to lower body mass and a reduction in inflammatory and metabolic markers, compared with a normal diet. After 12 months, TRE decreased total body mass by 3.36% (82.22 ± 5.92 kg pre; 80.33 ± 4.76 kg post) and fat mass by -11.81% (9.79 ± 3.32 kg pre; 8.11 ±1.61 kg post). Glucose concentrations were lower in the TRE group after 12 months with -9.26% (95.10 ± 5.30 mg/dL pre; 86.50 ± 3.72 mg/dL post). HDL cholesterol significantly improved in the TRE group with 15.39% (53.70 ± 2.67 mg/dL pre; 61.80 ± 3.97 mg/dL post). No changes were observed in the ND group. TG levels were also reduced by 20.98% in the TRE group (123.20 ± 6.94 mg/dL pre; 97.10 ± 3.03 mg/dL post)(Moro et al., 2021).

Kesztyüs et al. (2021) examined the feasibility and adherence of TRE (8/9- hours eating window) in 40 healthy adults, aged 47.8 ± 10.5 years, for three months, observing moderate reductions in weight (-1.3 ± 2.3 kg) and waist circumference (-1.7 ± 3.22 cm). There were no significant changes in HDL, or TG (Kesztyüs et al., 2021).

In the study by Kim & Song (2023) on healthy adults, the authors found that eTRE had a more pronounced effect on various outcomes compared to lTRE. However, both eTRE and lTRE led to a decrease in several cardiometabolic parameters, such as serum TG and HDL cholesterol (Kim & Song, 2023). The results of the study have been summarized in section 3.1.

Martens et al. (2020) investigated the feasibility and tolerability of 6 weeks of TRF (<8-hour eating window) without weight loss in 24 healthy, non-obese middle-aged and older adults, between 55 and 79 years. The study found that TRF did not negatively body mass nor did it affect resting blood pressure. TRF did not influence fasting blood glucose but did lower glucose area under the curve (AUC) (Martens et al., 2020).

McAllister et al. (2020) conducted a study on 22 healthy men (age 22 ± 2.5), who were divided into ad libitum TRF or isocaloric TRF groups, both with 8-hour eating

window for 4 weeks. The hypothesis was that following ad libitum TRF would reduce caloric intake and therefore improve cardiometabolic health, compared to isocaloric TRF. No changes in blood glucose levels or differences between the groups regarding HDL cholesterol were observed. Nonetheless, both groups experienced an increase in HDL cholesterol: 2.9 mg/dL for the ad libitum group and 4.8 mg/dL for the isocaloric group. Both groups experienced a significant decrease in body mass (ad libitum pre 23.8 ± 12.2% pre; post 22.9 ± 12.5% post, isocaloric 21.7 ± 8.6% pre; 20.6 ±9.4% post), fat mass (ad libitum 26.1 ±20.6kg pre; 25.3 ±20.7kg post, isocaloric 17.9 ±8.3kg pre; 17 ±8.9kg post) ,as well as a significant reduction in systolic (119 ± 11mmHg pre; 113± 10mmHg post) and diastolic (75± 10mmHg pre; 65± 8mmHg post) blood pressure (McAllister et al., 2020).

Park et al. (2021) conducted a study on 33 healthy young adults aged 18-28, mainly active at night, implementing 4 weeks of 8-hour TRE to examine the effects on body weight and cardiometabolic risk factors. Significant changes were observed in body weight (-1.0 ± 1.4 kg), BMI (-0.4 ± 0.5 kg/m2), and percent body fat (-0.4 ± 1.9%). These changes were more prominent in women than in men. Based on weight change after 4 weeks, participants were divided into weight loss or weight gain groups. The weight loss group experienced changes ranging from -4.1 to -0.4 kg, with significant reductions in body weight and fat mass. The weight gain group experienced changes ranging from 0 to 1.1 kg and showed increases in body weight but no increase in fat mass. HDL cholesterol (-4.3 ± 7.7 mg/dL) was lower in the weight loss group. In the weight gain group, HDL cholesterol levels increased after intervention, but the changes were not significant (Park et al., 2021).

Xie et al. (2022) conducted a study on healthy participants without obesity, with the intention of comparing eTRF with mTRF. The study has been summarized in section 3.1. The researchers observed that eTRF had a greater impact on several metabolic parameters compared to mTRF and a control group (Xie et al., 2022).

Lastly, the study conducted by Manoogian et al. (2022) focused on the feasibility of TRE and its effects on cardiometabolic health in 24-hour shift workers (137 participants, age 21-59), specifically firefighters. The participants were randomized into standard-of-care (SOC) or 10-hour TRE groups, both following a Mediterranean

diet, for 12 weeks. The hypothesis was that a self-selected 10-hour TRE was feasible in this group and result in modest reduction in cardiometabolic risks. The study found that regarding glucose regulation, there were no significant changes. However, for those who started with elevated fasting glucose (>100 mg/dL) there was a decrease in both groups (SOC = -4.64 mg/dL and TRE = -6.00 mg/dL), but there was not a significant difference between the groups. There were no significant differences in TG for either group. Diastolic blood pressure significantly decreased in TRE group (-2.00 mmHg), but not in SOC. For the participants with elevated systolic blood pressure at baseline, it was decreased both with SOC (-8.38mmHg) and TRE (-7.67mmHg), but there were no differences between the groups. For those with elevated diastolic blood pressure at baseline, it was decreased only in TRE group (-12.15mmHg). The TRE group experienced a significant decrease in body weight (-1.1%, -0.94kg) and BMI (-0.26kg/m^2) compared to the SOC group, but no significant changes in body fat percentage (Manoogian et al., 2022).

In summary, the studies conducted on healthy adults suggest that time-restricted eating can lead to improvements in various health outcomes, such as reductions in body weight, fat mass, and waist circumference, as well as improvements in glucose regulation, lipid profiles, and blood pressure. However, the extent of these improvements varies among the studies and may be influenced by factors such as the population studied, the specific TRE protocol used, and the study duration. Overall, these findings indicate that TRE can be a feasible and beneficial dietary intervention for healthy adults, potentially leading to improved cardiometabolic health and body composition.

Table 2. An overview of the study design, main results and conclusions of the studies included in section 3.2 Time-restricted eating in healthy adults, alphabetically.

Study	Study design	Main Results	Conclusion
Brady et al. (2021)	Randomized controlled trial. 8 weeks of TRE (8h window, ad libitum) compared with control. Exercise test before and after 8 weeks, including fasting blood samples. 23 participants.	TRE gave reduction in body mass, and lower self-reported energy intake. TRE did not influence the exercise testing or blood sample.	Decrease in body mass but did not alter indices of endurance running performance or metabolic health.
Kesztyüs et al. (2021)	Pre-post design. 3 months TRE (8-9h window). Anthropometrics, questionnaire and blood samples at baseline and follow-up. Healthy individuals. 40 participants.	Moderate reduction in weight and waist circumference. Improved health related quality of life.	TRE is well accepted, may improve health related quality of life. May help reduce obesity and abdominal obesity.
Kim & Song (2023)	Pre-post Single-Arm Intervention. 4 weeks TRE (8h window). Divided into starting before (eTRE) or after (lTRE) noon. Body comp measured weekly, blood samples at baseline and after intervention. Healthy young adults, 34 participants.	Body weight and fat mass significantly reduced only in eTRE. eTRE showed improvements in glucose and insulin, while lTRE didn't. TG were decreased in both groups. eTRE had increased LDL and decreased HDL. No differences in blood pressure.	8h TRE may be a good strategy for managing body weight and cardiometabolic risk factors, even for those with late chronotype, without altering sleep-wake cycle.
Manoogian et al. (2022)	Randomized controlled trial. 12week TRE (10h window) or SOC (standard of care). Firefighters working 24h shifts. Blood glucose, blood samples and anthropometrics measured at baseline and end of 12 weeks. 137 participants.	TRE significantly decreased VLDL size. Those with cardiometabolic risk at baseline had a significant reduction in TRE in HbA1C and blood pressure. TRE also reduced body weight and BMI.	TRE is feasible and can improve cardiometabolic health in those with increased risk.
Martens et al. (2020)	Randomized controlled, crossover trial. 12 weeks with 6week TRF (8h window) and 6-week control, switching halfway. Healthy, non-obese midlife and older adults. Blood samples, blood pressure, OGTT, motor and cognitive test at baseline, switch, and end. 24 participants.	TRF did not influence lean mass, bone density and nutrient intake. Cardiovascular function was not improved, but functional capacity and glucose tolerance were improved.	Short-term TRF is safe and well tolerated. TRF was not associated with any of the adverse effects of conventional Calorie reduction. TRF may improve endurance capacity and glucose tolerance.
McAllister et al. (2020)	Randomized trial pre-post study. 4 weeks of either ad libitum TRF or isocaloric TRF (both 8h window). Healthy men. Blood samples, blood pressure and body composition were measured before and after intervention. 22 participants.	HDL-c levels were increased in both groups, as well as adiponectin. Reduction in body mass and fat percentage in both groups. Reduction in blood pressure in both groups.	TRF can improve markers of cardiometabolic health.

Moro et al. (2016)	Randomized controlled trial. 8 weeks of TRF (8h window) or ND (normal diet). Kilocalories were matched with baseline. Resistance-trained males. Anthropometrics, blood samples, respiratory ratio, resting energy expenditure and strength were measured before and after intervention. 34 participants.	Decrease in fat mass in TRF. Fat-free mass, muscle areas, max strength were maintained in both groups. Testosterone, IGF-1, blood glucose and insulin levels decreased in TRF. Adiponectin increased in TRF. No significant changes in the other markers.	TRF with 8h window can be beneficial for resistance trained individuals to improve biomarkers and decrease fat mass without losing muscle mass.
Moro et al. (2021)	Single-blind randomized study. Based on Moro et al, 2016. 12 months of TRE (8h window) or ND, along with resistance training. Kilocalories were matched with baseline. Healthy, resistance trained males. All measurements were taken at baseline, 2 months, and 12 months. 20 participants.	Body mass, fat mass, IGF-1 and testosterone were significantly lower in TRE than in ND. Inflammatory markers, insulin resistance and lipid profile were significantly improved in TRE compared with ND.	Long-term TRE combined with resistance training is effective in reducing inflammatory markers and risk factors of cardiovascular and metabolic disease.
Park et al. (2021)	Feasibility study. 4 weeks of TRE (8h window). Young adults mainly active at night. Body composition measured at baseline, 2weeks and 4 weeks. Blood samples measured at baseline and 4 weeks. 33 participants.	Significant changes in bodyweight, body mass, body fat. In weight loss group fasting insulin, HOMA-IR significantly lowered. LDL were higher and HDL lower in weight loss group after intervention.	8h TRE can be a strategy to manage bodyweight and cardiometabolic risk factors among young adults with late chronotypes.
Xie et al. (2022)	Randomized controlled trial. 5 weeks of either eTRF (early,8h window), mTRF (midday, 8h window) or control. Healthy adults without obesity. Anthropometrics, body composition, blood samples were measured. 82 participants.	eTRF was more effective than mTRF in improving insulin sensitivity. eTRF improved fasting glucose, reduced total body mass, reduced inflammation, and increased gut microbial diversity.	eTRF showed greater benefits for insulin resistance and metabolic parameters than mTRF.

3.3 Time restricted eating in overweight and obese adults

TRE has gained considerable attention as a potential strategy to manage overweight and obesity in adults, and out of the 27 studies included in the literature search, the following 8 studies explore the effects of TRE on glycemic control, body composition, and cardiometabolic health in this population (Table 3). Various eating windows have been tested in these studies, ranging from 4-hour in Cienfuegos et al., 8-hour in Chow et al., Kesztyüs et al., Lowe et al., and Schroder et al., to 10-hour windows in Che et al., Haganes et al., and Prasad et al. (Che et al., 2021; Chow et al., 2020; Cienfuegos et al., 2020; Haganes et al., 2022; Kesztyüs et al., 2019; Lowe et al., 2020; Prasad et al., 2021; Schroder et al., 2021).

In the study conducted by Cienfuegos et al. (2020), the researchers sought to compare the weight loss and cardiometabolic effects of 4-hour and 6-hour TRF regimens in 54 adults (mean age 46) with obesity for 8 weeks. A control group was included. The results of the study showed that both the 4-h and 6-h TRF interventions led to comparable weight loss (Δ = -3.2% ± 0.4% and Δ = -3.2% ± 0.4% respectively), compared to control, with no significant differences between the two groups. Visceral fat mass was not significantly different between the groups. Fasting glucose, blood pressure, TG and HDL cholesterol did not change significantly (Cienfuegos et al., 2020).

Chow et al. (2020) conducted a feasibility study to investigate the effects of TRE (8-hour eating window) on body composition and metabolic measures in 20 individuals with overweight or obesity, with a mean age of 45. The study participants were randomized into TRE or non-TRE groups for 12 weeks. Results showed that the TRE group experienced a significant reduction in body weight (-3.7%) and visceral fat (-11-1%; 1.7kg to 1.4kg) compared to the non-TRE group. TRE lowered fasting glucose by -7.7% (95 mg/dL to 87 mg/dL), and fasting TG by -23.6% (144 mg/dL to 106 mg/dL). Blood pressure changes were not changed significant in either group (Chow et al., 2020).

Kesztyüs et al. (2019), conducted a pre-post pilot study without a control group to evaluate the adherence to TRF (8/9-hour eating window) for 3 months, and its impact on abdominal obesity in 40 primary care patients, aged 49.1 ± 12.4, with one or more components of metabolic syndrome. They hypothesized that TRF can be suitable as a low-threshold intervention in a primary care setting. Participants experienced a moderate weight loss (-1.7 ± 2.5 kg) and a reduction in waist circumference (-5.3 ± 3.1 cm). Consequently, three participants (7.5%) were no longer classified as abdominally obese. No significant changes in TG, HDL cholesterol (Kesztyüs et al., 2019).

The study by Lowe et al. (2020) focused on the effects of TRE (8-hour eating window) on weight loss and other metabolic parameters in 116 men and women, aged 18-64, with overweight and obesity for 12 weeks, including a consistent meal timing group (CMT), eating 3 structured meals per day. The hypothesis was that TRE

in individuals with overweight and obesity would lead to weight loss and improvements in metabolic markers, compared to the CMT group. Results showed a significant decrease in weight in the TRE group (-0.94 kg) and a nonsignificant decrease in weight in the CMT group (-0.68 kg). However, there was no significant difference in weight change between the groups. In the in-person there was a significant decrease in weight in the TRE group using the in-person weight measurements (-1.70 kg) but not in the CMT group. There were no significant changes in whole body fat mass. No significant changes in fasting glucose, TG, HDL cholesterol and blood pressure between groups was observed. There was a significant change in diastolic blood pressure in the TRE group (-4.08 mmHg), but not significantly different between groups (Lowe et al., 2020).

In the study conducted by Schroder et al. (2021), the effects of 8-hour TRF on body composition and weight loss associated with metabolic syndrome, and cardiovascular risk were investigated in 32 obese women (mean age 39), over a period of 3 months. A control group was included. The results demonstrated that the TRF group experienced a reduction in body weight (83.62 ± 3.95kg to 80.24±3.87kg) and waist circumference (101.13±2.42cm to 97.15±2.21cm). Systolic blood pressure (126.7±3.4 mmHg to 121.3±3.1 mmHg), and diastolic blood pressure (86.9± 2.1 mmHg to 83.5± 2.1 mmHg) were also reduced. However, no significant changes were observed in blood biomarkers like glucose, HDL cholesterol and TG (Schroder et al., 2021).

The randomized controlled trial by Che et al. (2021) aimed to determine the effectiveness of a TRF intervention in improving glycemic control and weight changes in 120 overweight patients with type 2 diabetes (age 18-70), with either 10-hour TRF group or a control group for 14 weeks with 12 weeks intervention. They hypothesized that the TRF group would lose 5% of their body weight and the control group would lose 2%. Results demonstrated that the TRF group experienced significant reductions in fasting plasma glucose (-1.47±0.25 mmol/L), body weight (-2.98±0.43kg) and BMI (-1.64±0.38 kg/m^2) compared to the control group. TG was significantly reduced in TRF group with -0.23±0.08 mmol/L compared to 0.13±0.06 mmol/L in the control group. TRF did not affect the level of HDL cholesterol (Che et al., 2021).

In the randomized controlled trial by Haganes et al. (2022), the researchers examined the effects of TRE (<10-hour eating window), high-intensity interval training (HIIT), and a combination of both (TREHIIT), compared to an non-intervention control group for 7 weeks on glycemic control, body composition, and cardiometabolic health in 131 women with overweight or obesity (mean age 36). The hypothesis was that isolated and combined TRE and HIIT would improve glycemic control, and that the combination would induce greater improvements. The results revealed that neither isolated TRE nor HIIT, nor the combined TREHIIT, led to significant improvements in fasting glucose compared to the control group. All intervention groups experienced decreases in body weight (TRE -2-1kg, HIIT -1.7kg and TREHIIT -3.6kg) and visceral fat area (TRE -8.0cm^2, HIIT – 9.2cm^2 and TREHIIT -16.8cm^2) compared to the control group, with TREHIIT showing significantly greater reductions than isolated TRE and HIIT. Blood pressure did not change significantly. No significant differences were found in HDL cholesterol and TG for any intervention group compared to the control group (Haganes et al., 2022).

In the pilot study by Prasad et al. (2021), they investigated the impact of a smartphone intervention promoting TRE (10-hour window) on feasibility in 50 adults with overweight and obesity, aged 30-75, for 3 months. No control group was included. The results showed that body weight significantly decreased from 91.6 ± 17.1 kg to 90.1 ± 19.1 kg. Waist circumference also significantly decreased from 98.9 ± 10.7 cm to 96.9 ± 7.5 cm. Systolic blood pressure significantly decreased from 124.0 ± 27.5 mmHg to 114.0 ± 17.3 mmHg, with 66.7% of participants experiencing a reduction of ≥10 mmHg. Diastolic blood pressure did not significantly decrease (Prasad et al., 2021).

The studies investigating TRE in overweight and obese adults have shown promising results, with many reporting significant reductions in body weight, waist circumference, and fasting glucose levels. Some studies also demonstrated improvements in other cardiometabolic parameters such as triglycerides and blood pressure, though these findings were not consistent across all studies. The varying eating windows and intervention durations make it difficult to draw definitive conclusions, but overall, TRE appears to have potential as a weight management strategy in this population.

Table 3. An overview of the study design, main results and conclusions of the studies included in section 3.3 Time restricted eating in overweight and obese adults, alphabetically.

Study	**Study design**	**Main Results**	**Conclusion**
Che et al. (2021)	Randomized controlled trial. 12 weeks of TRE (10h window, ad libitum) or control. Overweight adults with diabetes type 2. Blood samples at baseline and at 12 weeks. 120 participants.	Significant reduction in HbA1c, fasting plasma glucose, body weight, BMI and HOMA-IR, and significant increase of HOMA-B in TRE group compared to control.	TRE improves blood glucose, insulin sensitivity, weight loss, and reduces the dosage of hypoglycemic drugs.
Chow et al. (2020)	Randomized controlled trial. 12 weeks of TRE (8h window ad libitum) or non-TRE. Adults with overweight/obesity. Weight, body composition, lipids, blood pressure, glucose tolerance, 2week glucose monitoring, 2 weeks physical activity were measured during pre and end intervention periods. 20 participants.	TRE group decreased weight, lean mass, fat mass and visceral fat. Also reduced eating window and eating occasions. No changes in physical activity and metabolic measures.	TRE reduces eating occasions and is associated with weight loss.
Cienfuegos et al. (2020)	Randomized parallel-arm trial. 8 weeks of 4h and 6h TRF, ad libitum and controls. Adults with obesity. Body weight assessed every week, body composition and metabolic risk factors at baseline and 8 weeks. 58 participants.	4h does not produce superior changes in body weight compared to 6h. They also produce similar reduction in fasting insulin and insulin resistance, also a reduction in oxidative stress. It did not influence other risk factors.	4 and 6h have similar outcomes and the benefits are reduction in fasting insulin, insulin resistance and oxidative stress. Also, a reduction in body weight.
Haganes et al. (2022)	Randomized controlled trial. 7 weeks of TRE (<10h window), HIIT, a combination of the two, and control. Women with overweight/obesity. Fasting blood samples, blood pressure, body composition, Vo2 test at baseline and after intervention. 131 participants.	TRE and TREHIIT did not improve glycemic control during OGTT, but TRE and TREHIIT had improvements in secondary glycemic control outcomes (long-term glycemic control, OGTT peak glucose, 30-min insulin concentration, 24h glucose). TREHIIT had effects on fat mass loss.	All 3 groups reduce visceral fat, while TREHIIT improves HbA1c. TRE combined with HIIT can induce several health benefits and decrease metabolic disease risk in women with overweight/obesity.
Kesztyüs et al. (2019)	Pre-post design.3 months TRF (8-9h window). Participants with one or more components of MetS. Questionnaires, anthropometrics and blood samples at baseline and follow-up. 40 participants.	Moderate weight loss and changes in BMI. Weight-to-height-ratio reduced. Weight loss correlated with percentage of fasting target reached.	TRF has a good adherence and may help reduce abdominal obesity. This might prevent cardio-metabolic disease.

Lowe et al. (2020)	Randomized clinical trial. 12 weeks of TRE (8h window, ad libitum) or CMT (consistent meal timing). Adults with overweight/obesity. Daily weighting and blood pressure. Metabolic testing. 116 participants.	Significant decrease in weight in TRE, but no significant change between the groups. Significant difference in appendicular lean mass between groups. No other significant changes.	TRE is more effective in weight loss than consistently eating during the day.
Prasad et al. (2021)	Feasibility study. Open label, non-randomized intervention. Using smartphone application. 2 week "run-in" period followed by 90 days TRE (10h window). Adults with overweight/obesity. Anthropometrics and questionnaires before and after TRE. 50 participants.	TRE group decreased eating window from 16h to 11h 54m. Also decreased bodyweight, waist circumference and systolic blood pressure.	90 days TRE intervention is feasible for adults with overweight and obesity.
Schroder et al. (2021)	Non-randomized controlled clinical trial. 3 months of either TRF (8h window) or control. Obese women. Anthropometrics, body composition, blood biomarkers, cardiovascular risk and quality of life evaluated at baseline and after 3 months. 32 participants.	TRF reduced weight, BMI, body fat and waist circumference. TRF reduced cardiovascular risk in 30 years. No significant changes in blood biomarkers.	TRF reduces body weight without changing biomarkers related to MetS.

3.4 Time restricted eating in adults with type 2 diabetes

TRE has shown promise as a potential intervention for glycemic control and weight management in adults with type 2 diabetes. In this subsection, 3 studies out of the 27 included in this thesis, are reviewed that investigate the impact of TRE on adults with type 2 diabetes (Table 4). These studies have different intervention durations, ranging from 2-weeks in Parr et al., to 14 weeks in Che et al., and Andriessen et al., with a crossover 3 weeks on each intervention separated by a wash out period (Andriessen et al., 2022; Che et al., 2021; Parr et al., 2020).

The study by Andriessen et al. (2022) aimed to investigate the effects of 10-hour TRE on glucose homeostasis and insulin sensitivity in 14 adults with type 2 diabetes, aged 50-75. Participants underwent two 3-week intervention, one TRE intervention and one control intervention, separated by a wash-out period of ≥4 weeks. Results showed that the TRE group had lower fasting plasma glucose than the control group (8.0±0.3 mmol/L vs. 8.9±0.5 mmol/L). There was no difference in TG levels between the groups. A small, but significant weight loss occurred in the TRE group (-1.0±0.3kg), but not in the control group (Andriessen et al., 2022).

The study by Che et al. (2021), was done on participants with type 2 diabetes, with the intention to explore the effects of 10-hour TRF on glycemic regulation and weigh changes. The results showed that weight decreased in TRF group, relative to the control group. There were also reductions in fasting glucose and TG in the TRF group (Che et al., 2021). The results have been summarized in section 3.3.

In the study by Parr et al. (2020), the researchers investigated the feasibility of TRE (9-hour window) in 20 individuals with type 2 diabetes, mean age 50 ± 9, hypothesizing that TRE would be feasible and acceptable for those with type 2 diabetes, with no adverse outcomes and reactions. Participants followed their habitual eating patterns for 2-weeks and then underwent a 4-week TRE intervention. No control group was included. The results showed no significant differences in fasting glucose, HDL cholesterol or TG between the habitual eating period and the TRE period. Additionally, no significant differences were found in body mass or blood pressure measures between the habitual period and the end of the TRE intervention period (Parr et al., 2020).

The studies on TRE in adults with type 2 diabetes present mixed results. While Andriessen et al. (2022) reported significant improvements in fasting plasma glucose and a modest weight loss in the TRE group compared to the control group, Parr et al. (2020) found no significant differences in fasting glucose, HDL cholesterol, TG, body mass, or blood pressure between the habitual eating period and the end of the TRE intervention. Che et al. (2021) observed reductions in weight, fasting glucose, and TG in the TRF group compared to the control group. Overall, the evidence suggests that TRE may have some benefits for glycemic control and weight management in individuals with type 2 diabetes, but further research is needed to establish more definitive conclusions and recommendations.

Table 4. An overview of the study design, main results and conclusions of the studies included in section 3.4 Time restricted eating in adults with type 2 diabetes, alphabetically.

Study	Study design	Main Results	Conclusion
Andriessen et al. (2022)	Randomized crossover trial. Two 3 weeks of TRE (10h window) and control with 4week washout between. Adults with type 2 diabetes. Main outcomes measured at baseline and end of interventions. 14 participants.	Hepatic glycogen, hepatic and peripheral insulin sensitivity were not affected by TRE. TRE increased time spent in normoglycemic range, decreased fasting glucose and 24h glucose.	Daytime 10h TRE decreases glucose levels and prolongs time in normoglycemia.
Che et al. (2021)	Randomized controlled trial. 12 weeks of TRE (10h window, ad libitum) or control. Overweight adults with diabetes type 2. Blood samples at baseline and at 12 weeks. 120 participants.	Significant reduction in HbA1c, fasting plasma glucose, body weight, BMI, and HOMA-IR, and significant increase of HOMA-B in TRE group compared to control.	TRE improves blood glucose, insulin sensitivity, weight loss, and reduces the dosage of hypoglycemic drugs.
Parr et al. (2020)	Feasibility study. Pre-post, non-randomized intervention. 2 weeks of habitual eating followed by 4 weeks TRE (9h window). Adults with type 2 diabetes. Questionnaires/interviews at end of intervention. Blood samples, physiological and psychological outcomes pre and post intervention. 20 participants.	TRE did not significantly improve glycemic control or reduce body mass. No other significant changes in biochemical measures. No difference in daily energy intake.	4 weeks of 9h TRE is feasible and achievable for adults with type 2 diabetes.

3.5 Time restricted eating in adults with other underlying conditions

Out of the 27 studies included in this thesis, 5 studies have been conducted focusing on a specific condition, using different TRE windows and intervention durations. The study by Cai et al., involved patients with non-alcoholic fatty liver disease (NAFLD), while He et al., and Wilkinson et al., examined adults with metabolic syndrome (MetS) (Cai et al., 2019; He et al., 2022; Wilkinson et al., 2020). Li et al., targeted women with anovulatory polycystic ovary syndrome (PCOS), while Sutton et al., investigated men with prediabetes (Li et al., 2021; Sutton et al., 2018).

In a randomized controlled trial conducted by Cai et al. (2019), the effects of alternate day fasting (ADF) and 8-hour TRF on body weight and lipid profile in 271 patients, aged 18-75, with non-alcoholic fatty liver disease (NAFLD) were investigated for 12 weeks. A control group was included. The ADF and TRF groups experienced significant decreases in body weight (4.56±0.41kg and 3.62±0.65kg respectively) but no significant change in waist circumference was observed. TG decreased

significantly in the ADF group (0.64±0.06mmol/L) TRF group (0.58±0.07mmol/L) compared to the control group. However, there were no significant differences in fasting glucose, HDL cholesterol and blood pressure among the groups (Cai et al., 2019).

In the study by He et al. (2022), a 3-month RCT was conducted to investigate the effects of a low-carbohydrate diet (LCD), 8-hour TRE (choosing eTRE or lTRE), and their combination on body weight, abdominal fat area and cardiometabolic outcomes in 169 adults (mean age 41) with metabolic syndrome (MetS). The study results show that LCD (-2-2±0.3kg), TRE (-3.4±0.4kg), and their combination (-5.0±0.4kg) all significantly reduced body weight in adults with MetS, with the combination giving the highest reduction. Abdominal visceral fat area was only reduced by TRE (-13±5cm^2) and combination treatment (-10±3cm^2). TRE and combination treatment significantly improved fasting blood glucose (-0.18mmol/L and -0.21mmol/L respectively). In terms of lipid profiles, LCD did not cause any significant differences in TG and HDL cholesterol. In contrast, TRE, and combination treatment significantly reduced TG levels (-0.30mmol/L and -0.51mmol/L respectively). The combination treatment significantly changed HDL cholesterol by 0.09±0.02mmol/L. Regarding blood pressure, none of the treatments had benefits on systolic blood pressure, but diastolic blood pressure was significantly reduced by combination treatment with -5±2mmHg (He et al., 2022).

In the study conducted by Wilkinson et al. (2020), the researchers aimed to investigate the effects of 10-hour TRE intervention on 19 individuals (aged 59 ± 11.14) with MetS, over a period of 12 weeks with no control group. They hypothesized that TRE would result in significant improvements in mean blood glucose, fasting insulin, TG and inflammatory markers, in patients with MetS. Notably, there were reductions in body weight (-3.30±3.20kg) visceral fat rating (-0,58±0.77) waist circumference (-4.46±6.72cm), and both systolic (-5.12±9.51mmHg) and diastolic (-6.47±7.94mmHg) blood pressure. Changes in HDL cholesterol and TG was not significant. There was a trend towards improvement in fasting glucose, but it was not significant. However, the study found improvements in fasting glucose levels in those participants who initially presented elevated levels at baseline (-8.67±16.26mg/dL) (Wilkinson et al., 2020).

Li et al. (2021) study investigated the impact of TRF (8-hour window) on endocrine and metabolic profiles in 18 women, aged 18-31, with anovulatory polycystic ovary syndrome (PCOS), for 6 weeks. The results showed that participants lost a modest amount of weight (74.70 to 73.40kg), and there were significant reductions in visceral fat area (168±39.45cm^2 to 154.7±41.42cm^2). No significant changes were observed in fasting glucose and TG (Li et al., 2021).

The study by Sutton et al. (2018) investigated 6-hour eTRE versus a control group on 12 men with prediabetes, with the intention to test the benefits of TRE independent of weight loss, for 5 weeks. The results showed that eTRF did not influence fasting glucose or HDL cholesterol, but blood pressure was lowered. (Sutton et al., 2018). The results have been summarized in section 3.3.

In various studies examining the effects of TRE on different conditions, significant results were observed. Cai et al. (2019) found that in patients with non-alcoholic fatty liver disease (NAFLD), both alternate day fasting (ADF) and 8-hour TRE led to significant decreases in body weight and triglycerides. He et al. (2022) reported that in adults with metabolic syndrome (MetS), a low-carbohydrate diet (LCD), 8-hour TRE, and their combination all reduced body weight, with the combination yielding the highest reduction. Wilkinson et al. (2020) discovered that a 10-hour TRE intervention for individuals with MetS reduced body weight, visceral fat rating, waist circumference, and blood pressure. In women with anovulatory polycystic ovary syndrome (PCOS), Li et al. (2021) found that an 8-hour TRE window led to modest weight loss and significant reductions in visceral fat area. Lastly, Sutton et al. (2018) reported that a 6-hour early TRE did not influence fasting glucose or HDL cholesterol in men with prediabetes but did lower blood pressure.

Table 5. An overview of the study design, main results and conclusions of the studies included in section 3.5 Time restricted eating in adults with other underlying conditions, alphabetically.

Study	Study design	Main Results	Conclusion
Cai et al. (2019)	Randomized controlled trial. 12 weeks of Alternate day fasting, TRF and control group. Patients with non-alcoholic fatty liver disease. Anthropometric measurements and plasma lipids were analyzed. 271 participants.	Significant decrease of body weight and fat mass TRF group, as well as in ADF. Both had significant reduction in serum triglycerides. Remaining parameters did not differ from TRF and control.	Both ADF and TRF can be effective for weight loss within a short time frame. ADF seems to have better results in certain parameters than TRF.
He et al. (2022)	Randomized trial. 3 months of 8h TRE alone, low-carbohydrate diet (LCD) or the two combined. Participants with Metabolic syndrome. Primary and secondary outcomes were measured at baseline and after 3 months. 169 participants.	All 3 groups reduced body weight and subcutaneous fat. TRE and TRE + LDC reduced abdominal visceral fat and diastolic blood pressure. TRE and TRE + LDC improved glycemic control and dyslipidemia.	All 3 groups reduce body weight and some cardiometabolic outcomes, but only TRE w/wo LCD reduces abdominal fat and improves glycemic control, largely improving metabolic disease risk.
Li et al. (2021)	Pre-post non-randomized design. 6-week TRF; 1w baseline stabilization, 5w intervention (8h window). Body composition, blood samples and oral glucose test at baseline and follow-up. Women with PCOS aged 18-31. 18 participants.	Modest weight loss, significant reduction in BMI. Significant decrease in fasting insulin, HOMA-IR, no significant difference in FG, TG, TC, LDL. Improvement in menstrual cycle irregularity.	TRF may have beneficial effects on menstruation, reducing weight, body fat, decreasing insulin resistance and chronic inflammation in PCOS women.
Sutton et al. (2018)	Randomized, crossover, isocaloric and eucaloric controlled feeding trial. 5 weeks of either eTRF (6h window) or control, then a 7week washout before switching schedule. Men with prediabetes. 3h OGTT at baseline and after each intervention. 12 participants	eTRF improved insulin sensitivity, B-cell responsiveness, blood pressure, oxidative stress and appetite. No change in HDL and LDL cholesterol.	eTRF improved all the stated previously, even when food was matched to control arm, and without weight loss.
Wilkinson et al. (2020)	Single-arm, paired-sample trial. 12 weeks of TRE (10h window). Participants with metabolic syndrome. Anthropometrics, body weight, Blood samples were measured. 19 participants.	Significant reduction in bodyweight, waist circumference, BMI, body fat, blood pressure, total cholesterol, LDL cholesterol and non-HDL cholesterol. Those with elevated fasting glucose and/or HbA1c at baseline had significant reduction. No significant improvement in the other measurements.	TRE intervention can be a good treatment for those with metabolic syndrome. Findings occurred without increased physical activity.

4. Discussion

In this thesis, we have investigated the effects of time-restricted eating (TRE) on body composition, glucose, and insulin parameters, and cardiometabolic markers in various populations. The review of the studies showed that early time-restricted eating (eTRE) generally had a more significant impact on weight reduction and glucose parameters compared to late time-restricted eating (lTRE). Both healthy adults and individuals with overweight or obesity experienced improvements in body composition and cardiometabolic health, while the results for individuals with underlying health conditions were more mixed.

Before delving into the discussion of the various findings, it is essential to note that the included studies varied in design, intervention duration, and eating windows, which could have affected the results and comparability between them. In this discussion section, we will examine the main findings from the different studies and compare them with existing literature. We will also discuss potential mechanisms that could explain the observed effects, as well as evaluate the strengths and limitations of the included studies. Finally, we will present some suggestions for future research to further elucidate how TRE can be optimized for different populations and how to understand the underlying mechanisms driving the observed benefits.

4.1 Importance of the timing of the eating window

Of the studies reviewed in this paper, five investigated the effects of different TRE protocols, such as eTRE, lTRE or mTRE, and control groups on body composition, glucose and insulin levels, and cardiovascular parameters. The main findings suggest that eTRE may be more effective in reducing body weight, BMI, and waist circumference compared to lTRE and control groups, as demonstrated by studies conducted by Kim & Song (2023), Xie et al. (2022) and Zhang et al. (2022). Additionally, improvements in glucose parameters were generally more pronounced in eTRE groups, as seen in the studies by Hutchison et al. (2019) and Kim & Song (2023). Both eTRE and lTRE demonstrated reductions in serum TG, as reported by Kim & Song (2023) and Zhang et al. (2022). Blood pressure reductions were observed in some of the eTRE groups, such as those in the studies by Zhang et al. (2022) and Sutton et al. (2018). However, the effects on HDL cholesterol levels were

inconsistent across studies, as shown by the mixed results from Kim & Song (2023), Xie et al. (2022), and Zhang et al. (2022).

When comparing the results of these studies, it is essential to consider the variations in the study designs, populations, and interventions. The duration of the interventions ranged from 4 to 8 weeks, and the populations included healthy individuals, those with overweight and obesity, and individuals at risk of type 2 diabetes or with prediabetes. These factors may contribute to the differences in the observed outcomes, as certain interventions may be more effective in specific populations or over longer periods.

In conclusion, the current evidence suggests that eTRE may be more beneficial for weight loss and cardiometabolic health compared to lTRE or mTRE, which correlates with what Hatori, and coworkers found in mice eating with regard to their circadian rhythm (Hatori et al., 2012). Further research is needed to confirm these findings and to better understand the underlying mechanisms and practical implications of TRE for weight management and cardiometabolic health.

4.2 Impact of TRE in healthy vs overweight and obese adults

The studies focusing on time restricted eating in healthy adults have consistently demonstrated the potential benefits of TRE in healthy adults, with improvements observed in body composition, cardiometabolic health, and overall well-being. The positive impact of TRE on weight loss and fat mass reduction was observed across multiple studies (Brady et al., 2021; McAllister et al., 2020; Moro et al., 2016; Moro et al., 2021; Park et al., 2021). Additionally, various studies have reported improvements in glucose regulation (Martens et al., 2020; Moro et al., 2016; Moro et al., 2021), lipid profiles (Kim & Song, 2023; McAllister et al., 2020; Moro et al., 2021), and blood pressure (Manoogian et al., 2022; McAllister et al., 2020).
On the other hand, studies investigating TRE in overweight and obese adults have also demonstrated promising results in terms of weight management and glycemic control. The significant reductions in body weight and waist circumference observed in many studies (Chow et al., 2020; Haganes et al., 2022; Prasad et al., 2021; Schroder et al., 2021) suggest that TRE may be an effective weight loss strategy for

this population. Moreover, the improvements in fasting glucose levels found in some studies (Che et al., 2021; Chow et al., 2020) indicate that TRE might also be beneficial for glycemic control, especially in overweight individuals with type 2 diabetes.

It is noteworthy that the positive effects of TRE were observed in both endurance athletes (Brady et al., 2021) and resistance-trained males (Moro et al., 2016; Moro et al., 2021), suggesting that the benefits of TRE are not limited to sedentary individuals.
Although most studies reported favorable outcomes, some inconsistencies were observed, particularly in the magnitude of the effects. For instance, the reduction in body weight observed by Brady et al., was not as substantial as that reported by Moro et al. (Brady et al., 2021; Moro et al., 2021). Similarly, the improvements in glucose regulation and lipid profiles were not uniform across studies (Kesztyüs et al., 2021; Manoogian et al., 2022; Martens et al., 2020). These discrepancies might be attributed to differences in study populations, TRE protocols, and intervention durations.

A notable difference between healthy adults and overweight/obese adults is the potential role of TRE in glycemic control. Although improvements in glucose regulation have been reported in healthy adults (Martens et al., 2020; Moro et al., 2016; Moro et al., 2021), the impact of TRE on glycemic control seems to be more pronounced in overweight/obese individuals, especially those with type 2 diabetes (Che et al., 2021; Chow et al., 2020). However, there are some inconsistencies in the observed effects on other cardiometabolic parameters such as TG and blood pressure. For example, Cienfuegos et al., and Lowe et al., did not find significant changes in triglycerides and blood pressure, while Chow et al., and Che et al., reported improvements in these parameters (Che et al., 2021; Chow et al., 2020; Cienfuegos et al., 2020; Lowe et al., 2020). These discrepancies could be attributed to the differences in the eating windows, intervention durations, or the population studied.

Therefore, it is important to note that the studies included in this review employed different eating windows and intervention durations, which could have impacted the

observed effects of TRE. For instance, Cienfuegos et al., utilized shorter eating windows of 4 and 6 hours, while Che et al., and Haganes et al., employed longer 10-hour eating windows (Che et al., 2021; Cienfuegos et al., 2020; Haganes et al., 2022). The intervention durations also varied from 3 weeks (Kesztyüs et al., 2019) to 12 months (Moro et al., 2021), indicating that the benefits of TRE can be observed in both short and long-term interventions. Also, the comparison of eTRF and mTRF by Xie et al., and Kim & Song revealed that eTRF might have a more pronounced effect on cardiometabolic parameters compared to mTRF or lTRE (Kim & Song, 2023; Xie et al., 2022). This finding suggests that the timing of the eating window may play a crucial role in determining the overall benefits of TRE, and this aspect should be investigated further in both healthy and overweight/obese populations.

In conclusion, the studies conducted on healthy adults suggest that TRE can be a feasible and effective dietary intervention, with potential benefits in weight management, cardiometabolic health, and overall well-being. Additionally, the available evidence on TRE in overweight and obese adults indicates that this dietary strategy has the potential to improve weight management and glycemic control, with some studies also showing improvements in other cardiometabolic parameters. Hatori et al., found in their mice study that the mice following a TRE protocol were largely protected against high-fat induced obesity and related metabolic illness, which can correlate to the human studies showing an improved weight management and glycemic control (Hatori et al., 2012).
However, further research is needed to determine the optimal eating window and intervention duration for TRE in this population, as well as to investigate the long-term effects of this intervention on weight management and cardiometabolic health.

4.3 TRE and impact in those with underlying conditions

The studies on TRE in individuals with type 2 diabetes and other underlying health conditions present mixed results, with variations in study design, intervention duration, and eating windows making it difficult to draw firm conclusions. Andriessen et al., and Che et al., observed improvements in fasting plasma glucose and weight loss in type 2 diabetes patients following a 10-hour TRE protocol (Andriessen et al., 2022; Che et al., 2021). However, Parr et al., found no significant improvements in

fasting glucose and other cardiometabolic parameters with a 9-hour TRE window (Parr et al., 2020). The shorter intervention period of 2 weeks in this study, compared to 14 weeks in Che et al., and 3 weeks in each intervention in Andriessen et al., could be a factor influencing the lack of significant improvements (Andriessen et al., 2022; Che et al., 2021). Additionally, the absence of a control group in the study by Parr et al., may have contributed to the observed results, as it did not allow for direct comparisons between the TRE and non-TRE conditions (Parr et al., 2020).

For other underlying health conditions, Cai et al., demonstrated that both ADF and 8-hour TRE interventions led to significant weight loss and reduced TG levels in patients with NAFLD, but no significant changes were observed for other metabolic parameters (Cai et al., 2019). Studies on MetS by He et al., and Wilkinson et al., showed significant weight loss and improvements in various cardiometabolic parameters (He et al., 2022; Wilkinson et al., 2020). However, the combination treatment in He et al., produced the most pronounced effects (He et al., 2022). Li et al., found that an 8-hour TRE window resulted in modest weight loss and significant reductions in visceral fat area in women with anovulatory PCOS, but no significant changes were observed in fasting glucose and TG levels (Li et al., 2021). Lastly, Sutton et al., studied the effects of a 6-hour early TRE on men with prediabetes, finding potential benefits for blood pressure management but not for glucose and lipid metabolism (Sutton et al., 2018).

In summary, the studies in this section provide evidence for the beneficial effects of TRE on weight management, lipid profile, and blood pressure in individuals with various underlying health conditions. However, the effects of TRE on fasting glucose and HDL cholesterol were inconsistent across the studies.

In conclusion, while some evidence suggests that TRE may have benefits for glycemic control and weight management in adults with type 2 diabetes and other underlying health conditions, the mixed results and heterogeneity in study designs warrant further investigation. Future research should focus on standardizing intervention protocols, exploring the long-term effects of TRE, and examining the potential interactions between TRE and other lifestyle interventions.

5. Future perspectives

In terms of future perspectives, more extensive, long-term studies with larger sample sizes are needed to assess the effectiveness of eTRE, lTRE, and mTRE interventions in various populations, and to understand the mechanisms underlying the observed effects of TRE on weight loss and cardiometabolic health. This could involve exploring the role of circadian rhythms, energy metabolism, hormone regulation, and the potential influence of TRE on gut microbiota.

Additionally, it is crucial to investigate the feasibility and sustainability of different TRE protocols in real-world settings, as well as potential barriers to adherence. By identifying strategies to support adherence and understanding individual preferences for specific TRE schedules, more personalized and effective dietary interventions can be developed. Optimizing TRE protocols for different populations, considering factors such as age, sex, and activity levels, will contribute to tailoring interventions to individual needs.

Randomized controlled trials with larger sample sizes and longer intervention periods are essential for confirming current findings and examining the long-term effects of TRE on weight management, cardiometabolic health, safety, and efficacy as a lifestyle intervention. Future studies should also investigate the optimal timing of the eating window and its interaction with factors such as sleep, circadian rhythm, and physical activity, to determine if a synergistic effect exists, as suggested by Haganes et al., (2022).

The heterogeneity in study designs and outcomes highlights the need for further research to understand the potential benefits of TRE for individuals with various underlying health conditions, including type 2 diabetes, and to establish definitive guidelines for TRE interventions in clinical practice. Future studies should aim to standardize intervention protocols, including eating windows and intervention durations, for more accurate comparisons between studies. Investigating the long-term effects of TRE on glycemic control, weight management, and overall health outcomes in individuals with various underlying health conditions will provide valuable insights into the potential applicability and sustainability of this dietary approach.

Finally, exploring the role of other lifestyle factors, such as physical activity and dietary composition, may help elucidate the specific effects of TRE in these populations.

6. Conclusion

The primary aim of this thesis was to explore the relationship between time-restricted eating (TRE) and metabolic syndrome, focusing on the potential benefits and drawbacks of implementing TRE interventions in individuals with or at risk of metabolic syndrome. The evidence from the studies reviewed in this thesis suggests that TRE, particularly early time-restricted eating (eTRE), has the potential to improve weight management and cardiometabolic health in various populations, including healthy adults, overweight and obese individuals, and those with underlying health conditions such as type 2 diabetes and metabolic syndrome.

While the majority of studies reported positive outcomes, some inconsistencies were observed, particularly in the magnitude of the effects and the specific cardiometabolic parameters impacted. These discrepancies can be attributed to differences in study designs, populations, TRE protocols, and intervention durations. Consequently, further research is needed to optimize TRE protocols for different populations and to better understand the underlying mechanisms driving the observed benefits.

Future studies should aim to conduct more extensive, long-term trials with larger sample sizes and standardized intervention protocols to confirm the findings from the current studies and investigate the long-term effects of TRE on weight management and cardiometabolic health. Additionally, research should explore the feasibility and sustainability of different TRE protocols in real-world settings, as well as the potential barriers to adherence. Moreover, it is crucial to investigate the role of other lifestyle factors, such as sleep, circadian rhythm, and physical activity, and their interactions with TRE, to develop more personalized and effective dietary interventions. Understanding these interactions could lead to better health outcomes in various populations. By addressing the specific objectives outlined in this thesis, this work contributes to the growing body of knowledge on the potential of time-restricted eating as a feasible dietary intervention for individuals with metabolic syndrome or at risk of developing the condition.

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