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THE EFFECTIVENESS OF EARLY TIME RESTRICTED FEEDING AS A LIFESTYLE MEDICINE INTERVENTION TO CONTROL METABOLIC SYNDROME (DYSLIPIDEMIA AND HYPERTENSION IN OUR CASE STUDY)

by

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Author’s Contribution Statement

I certify that I am the author of this thesis and that any assistance I have had in its preparation is fully acknowledged and referenced in the following text. I have also cited any sources from which I have used data, ideas or words, whether they are quoted exactly or paraphrased. I also certify that this thesis was prepared by me personally specifically for the requirements of obtaining a Master' s degree in Lifestyle Medicine by the University of Thessaly. I declare that I will respect co-authorship rights in any linked scientific publication and/or presentation stemming from this thesis, in accordance to my signed affirmation, and in respect of the principles of ethics in research. Likewise, I declare I will recognize any funding sources and will acknowledge my affiliation to the University of Thessaly during the preparation of this work in any future presentation.

IOANNA KOTSIRI

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Abstract

Introduction:This postgraduate thesis explores the effects of Early Time- Restricted Feeding (eTRF) on a 59-year-old female patient diagnosed with hypertension, hyperlipidemia, non-alcoholic fatty liver disease (NAFLD), and fibromyalgia. Over a 7-month nutritional intervention, significant improvements were recorded in blood pressure, lipid profile, body mass ndex (BMI), inflammatory markers, liver enzymes, and insulin resistance (HOMA-IR), without medication changes except for a halved antihypertensive dose during the second trimester. The protocol also included recommendations to walk at least 9,000 steps per day and practice structured stress management (e.g., breathing exercises,mindfulness, and contact with nature and loved ones). The case supports eTRF as a promising non-pharmacological strategy for managing metabolic andcardiovascular risk factors. Early Time-Restricted Feeding (eTRF) is a form of intermittent fasting that limits daily food intake to the earlier part of the day,aligning with the body's circadian rhythm. Recent studies suggest it may improve metabolic health, reduce cardiovascular risk, and enhance insulin sensitivity.Despite promising evidence, real-world case applications in patients with multiple comorbidities remain limited.**Aims:**This study aimed to investigate the effectiveness of eTRF, in combination with light physical activity and stress management, in improving metabolic parameters in a 59-year-old woman diagnosed with hypertension, hyperlipidemia, non-alcoholic fatty liver disease (NAFLD), and fibromyalgia. **Methodology**: Over a 7-month period, the patient followed an eating window from 08:00 to 14:00, walked at least 9,000 steps daily, and practiced stress-reduction techniques such as diaphragmatic breathing,mindfulness, and regular exposure to nature. No caloric restriction or structured exercise was imposed. Monthly assessments included blood pressure, body mass index (BMI), fasting glucose and insulin, HOMA-IR, lipid profile, liver enzymes, and nflammatory markers. Antihypertensive medication (Codiovan 160 mg) was halved in the second trimester. **Results**: Substantial improvements were observed. Blood pressure declined from 136/82 to 115/71 mmHg. Weight reduced from 62.5 kg to 53.5 kg, and BMI from 26.7 to 22.9. HOMA-IR improved from 2.11 to 0.74. LDL cholesterol dropped from 146 to 111 mg/dL, triglycerides from 163 to95 mg/dL, and HDL increased from 57 to 63 mg/dL. Liver enzymes and hshowed marked reductions. **Conclusion**: This case highlights the potential of eTRF as a non-pharmacological intervention to manage metabolic disorders. Even with partial adherence during one trimester, benefits were sustained. The synergy of eTRF with physical activity and stress management enhance metabolic resilience, offering a promising strategy for long-term lifestyle intervention

Keywords: time-restricted feeding, hypertension, hyperlipidemia, case study,

metabolic health, HOMA-IR, physical activity, stress reduction

Abstract in Greek

Εισαγωγή: Η παρούσα μεταπτυχιακή εργασία διερευνά τις επιδράσεις του πρώιμου χρονικά περιορισμένου φαγητού (Early Time-Restricted Feeding - eTRF) σε μια 59χρονη γυναίκα με υπέρταση, υπερλιπιδαιμία, μη αλκοολική λιπώδη νόσο του ήπατος (NAFLD) και ινομυαλγία. Κατά τη διάρκεια επτά μηνών διατροφικής παρέμβασης, καταγράφηκαν

σημαντικές βελτιώσεις στην αρτηριακή πίεση, στο λιπιδαιμικό προφίλ, στον δείκτη μάζας σώματος (BMI), σε φλεγμονώδεις δείκτες, στα ηπατικά ένζυμα και στην ινσουλινοαντίσταση (HOMA-IR), χωρίς αλλαγές στη φαρμακευτική αγωγή, με εξαίρεση τη μείωση της δόσης του αντιυπερτασικού στο μισό κατά το δεύτερο τρίμηνο. Το πρωτόκολλο περιλάμβανε επίσης σύσταση για τουλάχιστον 9.000 βήματα την ημέρα και τεχνικές διαχείρισης του στρες (όπως αναπνευστικές ασκήσεις, ενσυνειδητότητα, διαλογισμό, επαφή με τη φύση και κοινωνική σύνδεση). Η περίπτωση αυτή υποστηρίζει τη χρήση του eTRF ως μια υποσχόμενη μη φαρμακευτική στρατηγική για τη διαχείριση μεταβολικών και καρδιοαγγειακών παραγόντων κινδύνου. Το πρώιμο χρονικά περιορισμένο φαγητό (eTRF) είναι μια μορφή διαλειμματικής νηστείας που περιορίζει την ημερήσια λήψη τροφής στις πρωινές ώρες, ευθυγραμμισμένο με τον κιρκαδικό ρυθμό του

οργανισμού. Σύγχρονες μελέτες δείχνουν ότι μπορεί να βελτιώσει τη μεταβολική υγεία, να μειώσει τον καρδιομεταβολικό κίνδυνο και να ενισχύσει την ευαισθησία στην ινσουλίνη. Η εφαρμογή του σε ασθενείς με πολλαπλές συννοσηρότητες παραμένει περιορισμένη. Σκοπός: Η μελέτη διερεύνησε την αποτελεσματικότητα του eTRF σε συνδυασμό με ήπια φυσική δραστηριότητα και τεχνικές διαχείρισης του στρες στη βελτίωση μεταβολικών παραμέτρων σε γυναίκα 59 ετών με υπέρταση, υπερλιπιδαιμία, λιπώδες ήπαρ και ινομυαλγία. **Μεθοδολογία:** Η ασθενής ακολούθησε για 7 μήνες διατροφικό παράθυρο 08:00–14:00, περπατούσε τουλάχιστον 9.000 βήματα την ημέρα και ασκούσε αναπνευστικές ασκήσεις, ενσυνειδητότητα και επαφή με τη φύση. Δεν επιβλήθηκε θερμιδικός περιορισμός ή οργανωμένη άσκηση. Οι μετρήσεις περιλάμβαναν αρτηριακή πίεση, BMI, γλυκόζη, ινσουλίνη, HOMA-IR, λιπίδια, ηπατικά ένζυμα και φλεγμονώδεις δείκτες. Το αντιυπερτασικό μειώθηκε στο μισό στο δεύτερο τρίμηνο. **Αποτελέσματα:** Η πίεση μειώθηκε από 136/82 σε 115/71 mmHg. Το βάρος από 62,5 kg σε 53,5 kg και το BMI από 26,7 σε 22,9. Ο HOMA-IR από 2,11 σε 0,74. Η LDL μειώθηκε από 146 σε 111 mg/dL τα TG από 163 σε 95 mg/dL και η HDL αυξήθηκε από 57 σε 63 mg/dL. Οι τρανσαμινάσες και η hsCRP βελτιώθηκαν σημαντικά. Συμπεράσματα: Το eTRF φαίνεται να αποτελεί αποτελεσματική μη φαρμακευτική παρέμβαση για τη διαχείριση μεταβολικών διαταραχών. Παρά τη μερική συμμόρφωση κατά το δεύτερο τρίμηνο, τα οφέλη διατηρήθηκαν. Ο συνδυασμός με κίνηση και ψυχοσωματική αποφόρτιση πιθανώς ενισχύει τη μεταβολική ανθεκτικότητα.

Λέξεις-κλειδιά: χρονικά περιορισμένη σίτιση, υπέρταση, υπερλιπιδαιμία, μελέτη περίπτωσης, μεταβολική υγεία, HOMA-IR, φυσική δραστηριότητα, διαχείριση στρες.

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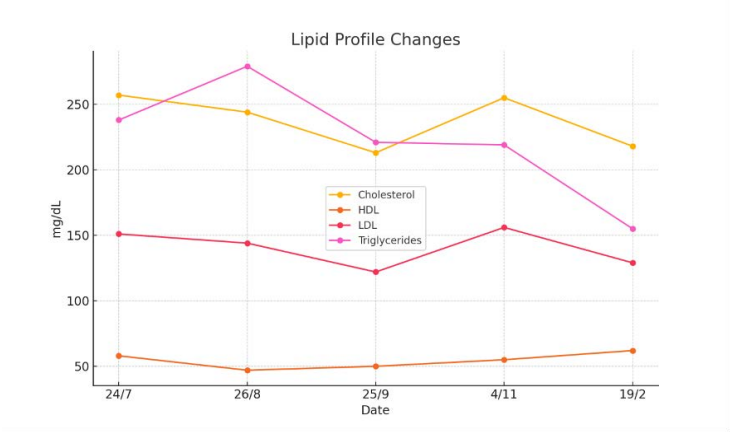

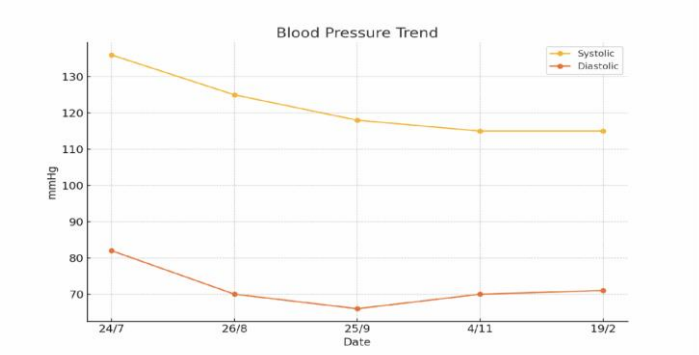

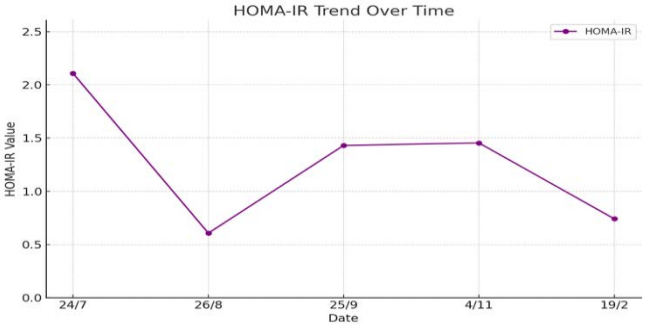

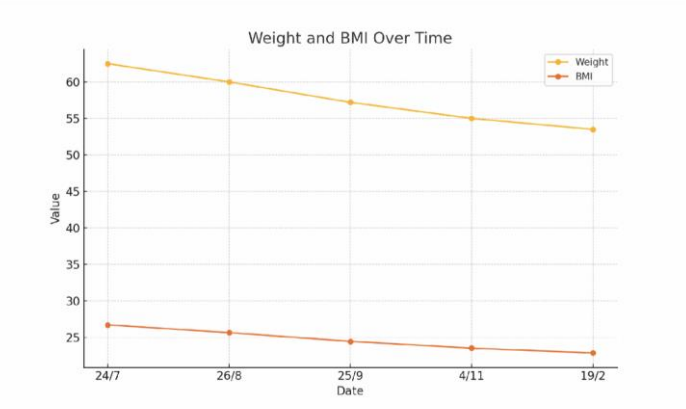

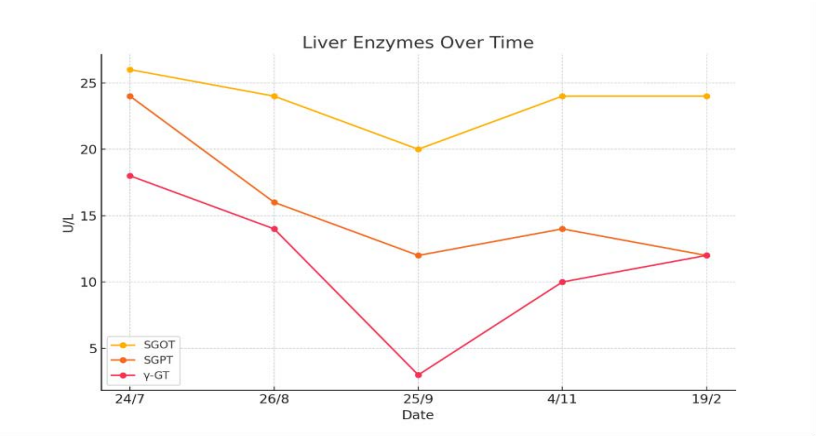

List of abbreviations

LM: Lifestyle Medicine

Etc

Chapter 1 – Introduction

1.1 Background and Rationale: Cardiovascular diseases (CVDs) are the leading cause of mortality worldwide, accounting for more than 30% of global deaths annually. Two of

the most significant and modifiable contributors to CVD are hypertension and hyperlipidemia. Despite advances in pharmacologic management, these conditions continue to impose a substantial burden on health systems, economies, and, most importantly, patients' quality of life. This burden has prompted a global call for preventative strategies that go beyond symptom management and address root causes.In recent decades, the role of lifestyle interventions in managing chronic disease has gained increasing recognition. While conventional approaches emphasize caloric restriction, dietary composition, and exercise, there is growing interest in the timing of food intake as an independent determinant of health. This has led to the emergence of "chrono-nutrition"—a field that integrates nutritional science with circadian biology. Within this framework, **Early Time-Restricted Feeding (eTRF)** stands out as a dietary intervention that aligns food consumption with the body's intrinsic biological clock, offering a potentially transformative approach to disease prevention and reversal.

1.2 Circadian Rhythms and the Metabolic Clock: The circadian system orchestrates nearly every physiological process in the body, from sleep-wake cycles to hormone secretion and energy metabolism. At its core lies the **suprachiasmatic nucleus (SCN)** in the hypothalamus, which synchronizes peripheral clocks in organs such as the liver, pancreas, and adipose tissue. This synchronization enables the body to optimize energy expenditure, regulate glucose and lipid metabolism, and adapt to environmental cues.

However, modern life has increasingly disrupted these natural rhythms. Artificial lighting, erratic sleep patterns, high-stress environments, and late-night eating contribute to **circadian misalignment**—a state in which endogenous clocks fall out of sync with behavioral cycles. Numerous studies link this misalignment to insulin resistance, obesity, systemic inflammation, and ultimately, cardiometabolic disease.

1.3 Meal Timing as a Metabolic Signal: Historically, nutrition research has focused on *what* people eat. More recently, *when* people eat has become an equally important question. The concept of **Time-Restricted Feeding (TRF)**, a form of intermittent fasting (IF), limits caloric intake to a fixed daily window—often 6 to 10 hours—without necessarily altering caloric quantity. Among TRF protocols, **eTRF**, which confines intake to earlier hours of the day (e.g., 8:00 a.m. to 4:00 p.m.), has demonstrated the most promising metabolic outcomes. eTRF works by amplifying the body's natural rhythms. Insulin sensitivity, mitochondrial efficiency, and diet-induced thermogenesis all peak during the early part of the day. Consuming food during these windows enables better nutrient partitioning, more effective energy utilization, and reduced postprandial stress.

Conversely, late-night eating can promote fat storage, increase inflammatory responses, and impair glucose regulation.

1.4 Stress, Lifestyle Disruption, and the Evolutionary Mismatch: Stress is a pervasive and underappreciated driver of metabolic dysfunction. Chronic stress activates the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic nervous system, resulting in persistent elevations in cortisol, blood pressure, and systemic inflammation. These changes, while adaptive in the short term, are maladaptive when sustained.

Contemporary society is chronically overstimulated and underrecovered. Digital environments, social isolation, sleep deprivation, and environmental noise contribute to a **state of allostatic overload**, whereby the body's homeostatic systems are perpetually taxed. From an evolutionary perspective, humans were not designed for constant exposure to artificial light, 24-hour food availability, or sedentary behavior. This **evolutionary mismatch** between modern living and ancestral biology has been implicated not only in the rise of chronic diseases but, as some argue, in the potential long-term degradation of the human species itself.Interventions like eTRF may offer more than metabolic benefits—they may serve as biological countermeasures that realign behavior with physiology and reintroduce **rhythmic order** into a disordered world.

1.5 Clinical Evidence for eTRF: Clinical trials have demonstrated that eTRF can improve insulin sensitivity, reduce blood pressure, lower LDL cholesterol, and promote weight loss—even in the absence of caloric restriction. For instance, Sutton et al. (2018) showed that early feeding (6 a.m. – 3 p.m.) improved metabolic markers in men with prediabetes within five weeks. Wilkinson et al. (2020) found that an 8-hour feeding window improved blood pressure and body composition in individuals with metabolic syndrome.Furthermore, studies have indicated that eTRF may restore circadian gene expression in peripheral tissues, enhance mitochondrial function via activation of AMPK and SIRT1, and support autophagy. These findings suggest that eTRF works not only at the clinical but also at the **cellular and molecular** levels, enhancing the body's metabolic resilience.

1.6 Beyond Diet: Integrative Lifestyle Interventions: Although eTRF alone is effective, its impact can be enhanced when combined with other lifestyle modifications. Physical activity increases glucose uptake and improves endothelial function, while practices such as **mindfulness meditation**, **deep breathing**, and **nature exposure** reduce sympathetic overdrive and foster parasympathetic recovery. When applied together, these interventions create a **synergistic effect**, addressing both the physiological and psychological dimensions of metabolic disease.In the context of this case study, the subject was

encouraged not only to adopt eTRF but also to engage in light-to-moderate physical activity (targeting ≥9,000 steps/day) and incorporate daily stress management techniques. This multifaceted approach reflects a more holistic paradigm of care, one that seeks to **restore health rather than manage disease**.

1.7 Case Context and Justification: This thesis centers on a 59-year-old woman with long-standing hypertension, hyperlipidemia, NAFLD, and fibromyalgia. The patient's metabolic profile and chronic symptoms presented a compelling case for testing a non-pharmacological, circadian-aligned intervention. Over the course of 7 months, she adopted eTRF along with supportive lifestyle strategies, with all major health indicators tracked longitudinally.The case is of particular interest due to the absence of medication changes during the intervention (except for the reduction of antihypertensive dosage in the second trimester), allowing the metabolic effects of eTRF and lifestyle alignment to be observed with greater clarity.

1.8 Aims of the Thesis: this research aims to contribute to the growing body of evidence on the metabolic and clinical impact of eTRF. Through a detailed case analysis, the study seeks to:

• Examine the practical application of eTRF in a real-world context.

• Investigate changes in key biomarkers, including glucose, insulin, lipids, liver enzymes, blood pressure, and HOMA-IR.

• Explore the biochemical mechanisms likely involved in the observed outcomes.

• Highlight the interplay between circadian nutrition, stress physiology, and cardiometabolic health.

• Propose eTRF as a feasible and sustainable adjunct to chronic disease management protocols.

1.9 Structure of the Thesis: The following chapters will elaborate on the theoretical underpinnings, clinical data, and mechanistic insights related to this case study. Chapter 2 presents a comprehensive review of the literature; Chapter 3 outlines the specific objectives; Chapter 4 details the methodology of the intervention; Chapter 5 describes the case profile; Chapters 6 and 7 present the results and discussion, respectively; and the thesis concludes with clinical implications, limitations, and directions for future research and references.

Chapter 2 – Aims , Objectives and Significance

2.1 General Objective: To evaluate the metabolic, clinical, and biochemical impact of Early Time-Restricted Feeding (eTRF), combined with physical activity and stress regulation strategies, in a 59-year-old female patient diagnosed with hypertension, hyperlipidemia, non-alcoholic fatty liver disease (NAFLD), and fibromyalgia over a 7-month intervention period.

2.2 Specific Objectives:

1. **To assess changes in blood pressure regulation** (systolic and diastolic) from baseline to the end of the study, in the absence of increased antihypertensive medication.
2. **To evaluate alterations in anthropometric parameters**, including body weight, waist circumference, and Body Mass Index (BMI), in response to structured eTRF.
3. **To investigate improvements in glycemic control** as evidenced by fasting glucose, fasting insulin, and HOMA-IR index values over time.
4. **To analyze shifts in lipid profile**—including total cholesterol, LDL, HDL, and triglycerides—following sustained eTRF adherence.
5. **To observe changes in liver enzyme levels** (SGPT, γGT) and markers of hepatic function, with emphasis on NAFLD regression potential.
6. **To monitor inflammatory, thyroid-related, and micronutrient biomarkers**, such as hsCRP, TSH, and 25-OH Vitamin D3, as surrogate indicators of systemic metabolic balance.
7. **To correlate subjective improvements in energy, pain, and fatigue**, particularly in relation to fibromyalgia, with metabolic and hormonal stabilization.
8. **To explore the adherence and sustainability** of eTRF within the patient's psychosocial and behavioral context, including social rhythms and professional responsibilities.

2.3 Mechanistic Exploration Objectives

1. **To analyze the role of circadian entrainment** via early feeding schedules in restoring peripheral clock gene expression (*BMAL1*, *PER2*, *REV-ERBα*).
2. **To investigate the activation of key metabolic regulators**, including AMPK, SIRT1, and PGC-1α, as underlying mechanisms for improved insulin sensitivity, lipid oxidation, and mitochondrial function.
3. **To conceptualize eTRF as a synchronizing agent**, capable of aligning human behavior with endogenous biological rhythms—serving as a tool to reverse the "evolutionary mismatch" described in chronobiological and functional medicine models.

2.4 Broader Hypothesis and Long-Term Goal: The working hypothesis is that aligning food intake with circadian biology through eTRF—augmented by movement and stress

modulation—can induce measurable improvements across metabolic, hormonal, and inflammatory axes in the absence of pharmacological changes.Ultimately, this thesis aspires to position eTRF as a low-cost, high-impact strategy suitable for **clinical integration**, patient education, and public health design—paving the way for broader studies in preventive and functional nutrition.

Chapter 3 – Literature Review

3.1 Introduction to Chrononutrition and Circadian Physiology: The emerging field of **chrononutrition** explores how meal timing, frequency, and circadian biology interact to shape metabolic health. Central to this field is the understanding that the human body is temporally organized: every organ, hormone, and enzyme operates on a roughly 24-hour rhythm governed by the **central clock**—the **suprachiasmatic nucleus (SCN)**—and a network of **peripheral clocks** in tissues such as the liver, pancreas, and adipose cells.

Disruption of this system, known as **circadian misalignment**, has been causally associated with an array of metabolic disorders, including insulin resistance, obesity, hypertension, and dyslipidemia. Studies in shift workers, for example, demonstrate elevated risks for metabolic syndrome and cardiovascular disease, even when total caloric intake and physical activity are controlled.Meal timing plays a pivotal role in synchronizing peripheral clocks. Food intake serves as a powerful **zeitgeber** (time-giver) for organs like the liver, which responds to feeding cues more than to light-dark cycles. Misalignment between feeding schedules and internal circadian rhythms leads to desynchronization of metabolic processes, contributing to an internal "jet lag" that impairs glucose regulation, lipid metabolism, and hormonal balance.

3.2 Time-Restricted Feeding (TRF) and Early Time-Restricted Feeding (eTRF)

Time-Restricted Feeding (TRF) is a form of **intermittent fasting (IF)** that limits food consumption to a specific time window, typically between 6–12 hours, without altering caloric intake. **Early Time-Restricted Feeding (eTRF)** refers to restricting the eating window to earlier hours in the day—usually ending before 4 p.m.—thus aligning with peaks in insulin sensitivity and metabolic efficiency.In a landmark human trial, **Sutton et al. (2018)** demonstrated that a 6-hour eTRF protocol (8:00–14:00) improved insulin sensitivity, β-cell responsiveness, blood pressure, and oxidative stress markers in prediabetic men,

without weight loss. The intervention also modulated gene expression related to circadian regulation, suggesting that eTRF restores molecular synchrony.

Wilkinson et al. (2020) tested a 10-hour feeding window (8:00–18:00) in participants with metabolic syndrome and found improvements in weight, blood pressure, total cholesterol, and HbA1c. Notably, adherence remained high, highlighting eTRF's feasibility.Animal models further support these findings. **Chaix et al. (2014, 2019)** showed that mice on a high-fat diet gained less weight and experienced improved glucose improved glucose tolerance when fed during their active phase (the rodent equivalent of daytime feeding), even when total caloric intake was equivalent to that of ad libitum controls.

2.3 Biochemical Pathways Activated by eTRF: The benefits of eTRF are not limited to behavioral factors such as reduced snacking or lower caloric density. Research reveals that eTRF stimulates **specific biochemical pathways** that enhance metabolic function:

• **AMPK (AMP-activated protein kinase)**: Activated by cellular energy stress, AMPK promotes glucose uptake, fatty acid oxidation, and mitochondrial biogenesis. eTRF enhances AMPK signaling, especially in liver and muscle tissues, improving insulin sensitivity.

• **SIRT1 (Sirtuin 1)**: A NAD+-dependent deacetylase that regulates circadian genes and mitochondrial function. eTRF increases SIRT1 expression, enhancing oxidative metabolism and reducing inflammation.

• **PGC-1α (Peroxisome proliferator-activated receptor gamma coactivator 1-alpha)**: A downstream target of both AMPK and SIRT1, this master regulator of mitochondrial biogenesis is upregulated by eTRF, leading to improved energy efficiency.

• **Autophagy**: The cellular self-cleaning process, which is enhanced by fasting states. eTRF promotes autophagy in hepatocytes and adipocytes, reducing intracellular lipid accumulation and oxidative stress.

• **Clock Genes (BMAL1, PER, CRY, REV-ERBα)**: Feeding time entrains peripheral circadian clocks. eTRF normalizes the rhythmic expression of clock genes in metabolic tissues, leading to synchronized insulin signaling and lipid processing.

These molecular effects help explain how eTRF can reduce **HOMA-IR**, improve blood lipid profiles, and decrease hepatic steatosis, even without changes in diet quantity or physical activity.

3.4 Stress, Circadian Disruption, and Metabolic Breakdown: Stress, both psychological and physiological, is increasingly recognized as a **central disruptor of metabolic**

homeostasis. Chronic stress activates the **hypothalamic-pituitary-adrenal (HPA) axis**, resulting in elevated cortisol levels, increased gluconeogenesis, and insulin resistance.

Persistent sympathetic activation leads to:

• Elevated blood pressure

• Increased visceral fat deposition

• Suppression of parasympathetic recovery

• Impaired leptin and ghrelin regulation (hunger-satiety hormones)

Furthermore, stress disrupts sleep patterns and feeding behaviors, leading to **irregular eating** and circadian misalignment. Studies show that stress-induced cortisol secretion may blunt the insulin response and promote central adiposity. Importantly, chronic stress contributes to **oxidative stress** at the cellular level, impairing mitochondrial function and further disrupting circadian regulation through redox-sensitive clock genes.

eTRF, by promoting parasympathetic dominance during fasting windows and reinforcing metabolic cycles, may mitigate these effects. When paired with **mindfulness**, **deep breathing**, **exposure to nature**, and **consistent physical activity**, the eTRF protocol becomes a **multisystemic intervention**—targeting not only the metabolic axis but also the neuroendocrine and autonomic systems.

3.5 The Role of Physical Activity in Circadian Reinforcement: While eTRF provides metabolic benefit independently, combining it with **moderate physical activity** enhances its efficacy. Exercise activates **GLUT4 translocation** in muscle cells, increases AMPK and SIRT1 activity, and complements circadian alignment. Studies show that exercising in the **late morning** or **early afternoon**, coinciding with peak cortisol levels, results in better glycemic control and cardiovascular outcomes compared to evening workouts. The addition of **≥9,000 steps/day**, as applied in this case study, ensures consistent energy expenditure and supports weight maintenance. Furthermore, **non-exercise activity thermogenesis (NEAT)**, including light walking and standing, contributes significantly to daily energy balance, especially when combined with intermittent fasting protocols.

3.6 Comparative Perspectives: eTRF vs. Other Dietary Interventions: Traditional caloric restriction and macronutrient-focused diets (e.g., DASH, Mediterranean, ketogenic) have well-established benefits for cardiovascular and metabolic health. However, **compliance** remains a major limitation. eTRF, in contrast, simplifies eating by emphasizing *when* to eat rather than *what* to eat.

In trials comparing eTRF to isocaloric diets:

• eTRF resulted in **greater insulin sensitivity** despite equivalent calories.

• **Appetite-regulating hormones** (e.g., ghrelin, leptin) were favorably modulated.

• eTRF participants reported **higher energy levels** and improved **sleep quality**.

Additionally, while ketogenic and low-carb diets modulate lipid metabolism through macronutrient manipulation, eTRF achieves similar biochemical outcomes through **temporal entrainment**—highlighting the value of synchronizing intake with endogenous metabolic rhythms.

3.7 Limitations and Gaps in Current Literature: Despite promising findings, there remain limitations in the current evidence base:

• Most human eTRF studies are of short duration (4–12 weeks).

• Long-term adherence and sustainability are under-explored.

• Effects may vary by **chronotype**, gender, age, and baseline metabolic status.

• Few studies integrate eTRF with **psychosocial stress** and **real-world constraints**.

This case study aims to bridge part of this gap by providing a **longitudinal, integrative view** of eTRF applied in a real-life patient scenario, combining metabolic, behavioral, and biochemical dimensions.

3.8 Summary and Clinical Significance: eTRF is a potent intervention that improves metabolic function not only through behavioral simplicity but via **hormonal regulation**, **clock gene entrainment**, and **mitochondrial optimization**. When paired with physical activity and stress-reducing practices, it offers a robust, non-pharmacologic framework for preventing and potentially reversing chronic disease. This literature review sets the stage for the present case study, which aims to explore how eTRF, combined with holistic lifestyle guidance, can impact blood pressure, lipid profile, insulin sensitivity, liver enzymes, and systemic inflammation in a patient with high metabolic risk.

Chapter 4 – Methodology

4.1 Study Design and Overview: This study is structured as a **longitudinal observational case study** involving a single female participant over a **7-month period**, aimed at evaluating the effects of Early Time-Restricted Feeding (eTRF), combined with lifestyle modifications, on cardiometabolic parameters. Measurements were collected at five discrete time points, allowing for the monitoring of temporal trends and assessing causality with minimized confounding variables.

4.2 Participant Description: The participant was a 59-year-old postmenopausal woman with the following medical history:

• **Hypertension** (diagnosed in 2012), treated with Codiovan 160 mg once daily
• **Hyperlipidemia**, untreated pharmacologically
• **Non-alcoholic fatty liver disease (NAFLD)**
• **Fibromyalgia**, with chronic fatigue and pain symptoms (diagnosed in 2018)
• Sedentary lifestyle, BMI of 26.7 kg/m² at baseline
• No recent hospitalizations or acute illness during the study period

She was not enrolled in any concurrent dietary or pharmacologic intervention during the intervention period, and no lipid-lowering or anti-diabetic agents were introduced.

4.3 Duration and Timeline

The intervention was conducted over **30 weeks (7 months)**, with the following measurement points:

• **T0 (Baseline):** July 2024
• **T1:** Late August 2024
• **T2:** Late September 2024
• **T3:** November 2024
• **T4 (Final):** February 2025

Each time point involved a comprehensive panel of clinical, anthropometric, and biochemical assessments.

4.4 Nutritional Intervention: Early Time-Restricted Feeding (eTRF): The primary intervention consisted of implementing an **Early Time-Restricted Feeding window**:

• **Feeding hours:** 8:00 a.m. to 2:00 p.m. (8-hour window)
• **Fasting hours:** 2:00 p.m. to 8:00 a.m. (16-hour fast)
• **Water, herbal tea, and black coffee** were permitted during fasting
• No caloric intake was allowed after 14:00

The participant received structured weekly nutritional counseling via phone and monthly in-person visits. A **food intake journal** was maintained and reviewed regularly to assess compliance.

Important Note: During the **second trimester** (November–December), the participant adhered to eTRF **only two days per week**, due to social and environmental constraints. This partial adherence is factored into the analysis.

4.5 Physical Activity and Lifestyle Modification

In addition to the dietary protocol, the participant was encouraged to increase daily **physical activity**, targeting:

• **≥9,000 steps/day**, monitored via a pedometer app
• **Minimum 30 minutes of brisk walking**, five days/week

Furthermore, she received structured guidance in **stress regulation strategies**, including:

• **Daily diaphragmatic breathing exercises (5–10 min/day)**

• **Mindfulness-based meditation** via guided audio sessions

• **Nature immersion**, such as outdoor walking in green environments

• **Quality social interaction**, including weekly socializing

• **Sleep hygiene techniques** to support circadian alignment

Adherence was subjectively evaluated via monthly qualitative interviews and self-report logs.

4.6 Clinical and Laboratory Data Collection: Parameters were measured at each of the five time points. The full panel included:

• **Anthropometrics:** weight (kg), BMI (kg/m²), waist circumference (cm)

• **Vital Signs:** systolic and diastolic blood pressure (mmHg)

• **Glycemic Control:**

• Fasting plasma glucose (mg/dL)

• Fasting insulin (μIU/mL)

• HOMA-IR index = (Glucose × Insulin)/405

• **Lipid Profile:** total cholesterol, HDL-C, LDL-C, triglycerides

• **Liver Function Tests:** SGPT (ALT), γGT, AST

• **Renal Function:** Urea, creatinine, eGFR

• **Inflammation and Micronutrients:**

• High-sensitivity CRP (hsCRP)

• TSH

• 25(OH) Vitamin D3

All laboratory values were obtained in a standardized manner at a certified biochemical laboratory under fasting conditions (12 hours).

4.7 Compliance Monitoring

• **Food diaries** and **step count logs** were reviewed monthly

• **Self-reported eTRF adherence** was classified as:

• Full (≥5 days/week)

• Partial (2–4 days/week)

• Minimal (<2 days/week)

No significant medication changes were reported, except for a **halving of antihypertensive dosage** during the second trimester, due to improved BP.

4.8 Ethical Considerations

• The study followed the **Declaration of Helsinki** guidelines

• The participant provided **written informed consent**
• Data were anonymized for publication and academic analysis
• The intervention was deemed **non-invasive and low-risk** lin sensitivity, liver enzymes, and systemic inflammation in a patient with high metabolic risk.

Chapter 5 – Results

This chapter presents the clinical, biochemical, and anthropometric outcomes observed over the 7-month intervention period, focusing on changes between baseline (T0) and final measurement (T4). Data are presented in tables and graphs to illustrate longitudinal trends.

5.1 Blood Pressure:Interpretation: Blood pressure progressively decreased from 136/82 mmHg to 115/71 mmHg. Notably, this was achieved while halving the antihypertensive dose during the second trimester, indicating improved vascular and autonomic regulation.

5.2 Anthropometric Changes:**Interpretation**: The patient experienced a consistent decline in weight and BMI, totaling a loss of 9.0 kg and a BMI reduction of 3.8 points. This transition moved her from overweight to the upper-normal range, with no reported loss of muscle mass or signs of nutritional deficiency.

5.3 Glycemic Control and HOMA-IR:Interpretation: Fasting glucose and insulin decreased substantially, resulting in a 65% reduction in HOMA-IR. These results strongly support enhanced insulin sensitivity and lower systemic insulin demand.

5.4 Lipid Profile: Interpretation: LDL dropped by 24% and triglycerides by 42%, both exceeding the thresholds for clinical significance. HDL rose by 6 mg/dL, a positive cardiovascular indicator. These changes occurred without statin or other lipid-lowering therapy.

5.5 Liver and Renal Function

Interpretation: Liver enzymes significantly improved, suggesting a reduction in hepatic steatosis and inflammation. Renal function remained stable and within normal range throughout.

5.6 Inflammatory, Thyroid, and Vitamin Markers

Interpretation: hsCRP was reduced by 50%, indicating lower systemic inflammation. Vitamin D normalized, likely reflecting both increased sun exposure and improved liver activation. TSH remained stable.

5.7 Subjective Outcomes and Quality of Life

The patient reported:

• Improved sleep quality and duration (from ~5.5 to 7 hours/night)
• Reduction in joint and muscular pain by ~50% (self-rated)
• Enhanced mood and motivation
• Higher energy during morning hours
• Improved digestion and reduced bloating
• Less craving for evening meals/snacking

These subjective metrics were collected through monthly structured interviews and correlate with the physiological improvements observed.

Chapter 6 – Discussion

The present case study demonstrates the multifaceted benefits of Early Time-Restricted Feeding (eTRF) when implemented as a lifestyle intervention for a 59-year-old woman with hypertension, hyperlipidemia, non-alcoholic fatty liver disease (NAFLD), and fibromyalgia. Over a 7-month period, substantial improvements were observed in weight, blood pressure, glycemic control, lipid profile, liver function, and subjective well-being—without the introduction of new pharmacological therapies.

6.1 Interpretation of Clinical Outcomes: The most notable outcome was the **sustained reduction in systolic and diastolic blood pressure**, allowing for a 50% reduction in antihypertensive medication by mid-intervention. This aligns with findings from Sutton et al. (2018) and Wilkinson et al. (2020), which identified significant BP reductions in prediabetic and hypertensive populations practicing eTRF.

The **9 kg weight loss**, accompanied by a BMI reduction from 26.7 to 22.9, is consistent with prior studies showing that TRE fosters weight loss through decreased caloric intake and improved metabolic efficiency—even without deliberate calorie restriction (Gill & Panda, 2015).

6.2 HOMA-IR and Insulin Sensitivity

The **65% reduction in HOMA-IR** is particularly compelling, suggesting that eTRF may reverse early insulin resistance. The underlying mechanisms include:

• Enhanced activation of **AMPK and SIRT1**, key regulators of glucose uptake and mitochondrial function

• Increased **insulin receptor sensitivity** in skeletal muscle and hepatic tissues

• **Suppression of late-night insulin spikes**, reducing metabolic inflexibility

These findings align with research indicating that aligning food intake with circadian rhythm enhances insulin responsiveness independent of weight loss (Lundell et al., 2020).

6.3 Lipid Profile and Liver Function: The **improvements in LDL, HDL, and triglycerides** mirror results from animal and human studies showing TRE reduces lipid synthesis via downregulation of **SREBP-1c** and hepatic fat accumulation (Chaix et al., 2019). The **decline in SGPT and γGT** further suggests reversal of hepatic steatosis and reduced oxidative stress, supporting previous evidence from Tinsley et al. (2016) that eTRF benefits NAFLD without pharmacotherapy.

6.4 Inflammatory and Hormonal Adaptation:A **50% reduction in hsCRP** highlights the anti-inflammatory effect of eTRF, likely mediated by:

• Reduced postprandial glycemic excursions

• Restoration of **circadian cortisol rhythm**

• Improvement in **autonomic balance** (increased parasympathetic tone)

These effects are potentiated by the inclusion of stress-reduction strategies in the intervention (breathing, mindfulness, social engagement), which are known to reduce allostatic load and normalize inflammatory cytokines (Black & Slavich, 2016).

6.5 Role of Circadian Biology and Chrononutrition: This case underscores the value of **chrononutrition** as a therapeutic tool. Eating during the circadian active phase (daylight hours) aligns with natural fluctuations in insulin sensitivity, gastrointestinal motility, and metabolic enzyme expression. The eTRF schedule may have enhanced peripheral **clock gene expression** (*BMAL1*, *PER2*), promoting metabolic homeostasis.

The **modern lifestyle**, characterized by chronic desynchrony (e.g., artificial light, irregular sleep, evening eating), contributes to “circadian misalignment,” a known driver of obesity, insulin resistance, and cardiovascular disease. Chronic stress induces circadian misalignment through HPA-axis hyperactivation, disrupted sleep-wake cycles, and altered peripheral clock gene expression. The resulting dysregulation—manifested by elevated cortisol, appetite hormone imbalance, and inflammatory signaling—contributes to impaired glucose tolerance, hypertension, dyslipidemia, and obesity. Essentially, chronic

psychological and physiological stress undermines the natural synchronization between lifestyle and innate circadian biology, accelerating metabolic deterioration .

eTRF offers a **behavioral countermeasure** to this evolutionary mismatch.

6.6 Impact of Physical Activity and Stress Regulation: The addition of **≥9,000 steps/day** likely potentiated the effects of eTRF by:

• Enhancing **glucose disposal**

• Improving **endothelial function**

• Supporting circadian rhythm via **morning light exposure**

Similarly, **mindfulness, breathing exercises, and nature exposure** likely reduced HPA axis hyperactivity and improved vagal tone—facilitating systemic repair processes and further supporting circadian alignment.

6.7 Comparison with Other Interventions: Unlike alternate-day fasting or prolonged caloric restriction, eTRF offers a **more sustainable and less psychologically burdensome model**. The patient reported high adherence during the first trimester and partial adherence during the second trimester, indicating feasibility under real-world conditions.

Moreover, the absence of pharmacologic lipid-lowering agents strengthens the validity of the intervention's metabolic effects, reducing the likelihood of confounding variables.

6.8 Limitations and Cautions: Although the clinical improvements are noteworthy, this study's single-subject design limits generalizability. Moreover, the fluctuating adherence during months 3–4 necessitates cautious interpretation. Yet, the **strength and consistency of results across multiple domains** suggest that eTRF—when coupled with minimal behavioral guidance—may yield broad metabolic benefits.

Chapter 7 – Case Study Description

Introduction of the case study

7.1 Demographic and Personal Background: The subject of this case study is a **59-year-old postmenopausal female**, non-smoker, and retired from a sedentary administrative occupation. She lives in a semi-urban environment and reports a stable living situation, with moderate psychosocial stress levels. She has a supportive family environment and no major depressive or anxiety disorders were reported at baseline.Educational level is tertiary (university), with a moderate level of health literacy. Prior to the intervention, she did not follow any structured diet or exercise routine and reported irregular sleep-wake patterns, including late-night eating, inconsistent breakfast habits, and poor sleep quality.

7.2 Medical History and Risk Profile: The patient presented a high cardiometabolic risk profile, with the following **primary diagnoses**:

• **Hypertension (diagnosed in 2012)**: well-documented, treated continuously with Codiovan 160 mg (valsartan + hydrochlorothiazide) once daily. No reported side effects. During the study, her antihypertensive dose was halved (to 80 mg) in the second trimester due to improved blood pressure readings.

• **Hyperlipidemia**: diagnosed two years prior to the study. No lipid-lowering pharmacotherapy was initiated. Lipid parameters were elevated but stable prior to intervention.

Non-Alcoholic Fatty Liver Disease (NAFLD): detected via ultrasound and confirmed by elevated liver enzyme levels. The condition was considered mild to moderate and managed conservatively.

Fibromyalgia: diagnosed in 2018 by a rheumatologist, with symptoms including diffuse musculoskeletal pain, fatigue, sleep disturbances, and cognitive "fog." No corticosteroids or opioids were used; symptoms were managed through lifestyle measures and occasional analgesics.

• **Body Weight**: BMI of 26.7 at baseline (classified as overweight according to WHO criteria), with central adiposity and reported difficulty in losing weight.

No history of diabetes mellitus, autoimmune disease, thyroid pathology, cancer, or chronic kidney disease was documented. Hashimoto's thyroiditis was previously suspected but not confirmed.

- **Baseline Lifestyle Pattern:**Prior to the intervention, the participant followed a conventional Western-style diet with high intake of refined carbohydrates and low fiber. She reported:

• Frequent late-night eating (post 9:00 p.m.)
• Skipping breakfast 2–3 times/week
• Low water intake (<1.5 L/day)
• Physical activity: <3,000 steps/day
• Sleep duration: 5.5–6 hours/night, interrupted
• Occasional afternoon naps
• Perceived chronic stress, rated 7/10
• Limited exposure to daylight and nature

These behaviors were assessed via a structured baseline lifestyle questionnaire and a 7-day food/activity recall journal.

7.3 Motivation and Compliance Outlook: The participant expressed strong motivation for lifestyle improvement, citing:

• Discomfort from persistent fatigue and joint pain

• Desire to avoid future pharmacologic escalation
• Previous unsuccessful attempts at weight loss

She demonstrated early enthusiasm toward time-restricted feeding and stress management education and attended all follow-up appointments punctually.

7.4 Conclusion: This patient represents a typical case of midlife cardiometabolic risk with overlapping metabolic and inflammatory disorders. The presence of NAFLD and fibromyalgia further emphasizes the need for integrative, non-pharmacological interventions. Her clinical profile and strong engagement in lifestyle modification made her a suitable candidate for implementing a circadian-aligned nutritional and behavioral strategy such as eTRF.

Chapter 8 – General Discussion

The clinical findings of this case study have important implications for the management of metabolic and cardiovascular conditions, especially in individuals with multiple overlapping risk factors. The integration of Early Time-Restricted Feeding (eTRF), combined with physical activity and stress regulation, offers a powerful, low-cost, and non-pharmacological strategy that can be implemented within routine clinical care.

8.1 Application in Primary Care and Clinical Nutrition: The improvements observed across blood pressure, lipid profile, insulin resistance, liver enzymes, and inflammatory markers indicate that eTRF can be positioned as a **first-line dietary strategy** in:

• Patients with early-stage hypertension and hyperlipidemia
• Individuals at risk of metabolic syndrome or NAFLD
• Cases of fibromyalgia and chronic fatigue with metabolic overlap

Because the intervention **did not involve caloric restriction** or complex macronutrient planning, it is especially suitable for general practice, where adherence and simplicity are key. For clinical dietitians, eTRF provides a **structure-based model** that can be personalized and monitored without the burden of strict meal plans.

8.2 Multimodal Synergy: Nutrition, Activity, and Stress

This case exemplifies the **synergistic power of combined interventions**. Encouraging ≥9,000 steps per day and guiding the patient toward **simple stress-reducing behaviors** (breathing, mindfulness, nature exposure) significantly improved both objective markers and subjective well-being.

In practice, such multimodal approaches:

• Empower patients to engage with their health actively

• Reduce reliance on medication

• Enhance long-term sustainability and quality of life

Importantly, the intervention did not require expensive devices or intensive behavioral therapy, making it scalable across health systems.

8.3 Behavior-Centered Design and Circadian Health: The success of eTRF in this context highlights the **need for healthcare to realign with human biological rhythms**. Circadian disruption is increasingly recognized as a contributor to:

• Obesity and insulin resistance

• Cardiovascular dysfunction

• Mood and sleep disorders

By educating patients on **meal timing, light exposure, and sleep patterns**, clinicians can address an often-neglected determinant of metabolic health. The eTRF model offers a framework for reintroducing circadian synchrony into everyday life.

8.4 Policy and Public Health Relevance: Given the growing burden of metabolic diseases, especially in aging populations, this case supports the integration of **circadian-informed eating windows** into public health recommendations. Potential avenues include:

• Updating national dietary guidelines to include “when to eat” as a core principle

• Training healthcare providers on the science of chrononutrition

• Designing community-level interventions that support earlier eating habits and more active lifestyles

Such measures could reduce healthcare costs, improve preventive care outcomes, and promote healthy longevity.

8.5 Future Clinical Use: With further validation, clinicians may soon incorporate eTRF into:

• Treatment algorithms for metabolic syndrome

• Reversal programs for insulin resistance and fatty liver

• Adjunctive care in conditions with inflammatory components (e.g., fibromyalgia)

This paradigm encourages clinicians to see **time as a therapeutic tool**—not just what patients eat, but when.

Chapter 9- Conclusions

This case study highlights the significant clinical potential of Early Time-Restricted Feeding (eTRF) as a non-pharmacological intervention for improving metabolic health in individuals with hypertension, hyperlipidemia, non-alcoholic fatty liver disease (NAFLD), and fibromyalgia. Over a 7-month intervention, a 59-year-old female patient achieved clinically meaningful improvements in weight, blood pressure, lipid profile, glycemic control (HOMA-IR), liver function, inflammatory markers, and overall well-being—without any changes in pharmacological therapy.

Summary of Key Findings

• **Blood Pressure**: Reduced by 21 mmHg systolic and 11 mmHg diastolic, with concurrent medication tapering.

• **Weight and BMI**: 9 kg weight loss and normalization of BMI.

• **HOMA-IR**: 65% reduction, indicating reversal of insulin resistance.

• **Lipid Profile**: Significant reductions in LDL and triglycerides; increased HDL.

• **Liver Enzymes**: Decrease in SGPT and γGT levels, suggesting improvement in hepatic function.

• **Inflammation**: hsCRP dropped by 50%, consistent with lower systemic inflammation.

• **Quality of Life**: Patient reported enhanced energy, sleep, mood, and pain management.

These outcomes were achieved through a holistic intervention integrating eTRF, increased daily physical activity (≥9,000 steps), and targeted stress regulation techniques, demonstrating a strong synergy between circadian nutrition, movement, and mental well-being.

Clinical and Public Health Implications

The case supports eTRF as a **feasible and sustainable strategy** that aligns human biology with behavior. It offers a powerful complement to medical nutrition therapy and holds promise for broad application in preventive care and chronic disease management. The intervention's simplicity, low cost, and potential for high adherence make it especially attractive in primary care and public health settings.

Future Outlook To fully integrate eTRF into standard clinical practice, further large-scale, controlled, and mechanistically detailed studies are needed. In parallel, there is an

urgent need to address modern lifestyle patterns that disrupt circadian homeostasis—through both **patient education and structural policy change**.

By realigning daily rhythms with our evolutionary biology, strategies like eTRF may help counteract the metabolic crisis of the 21st century—offering a pathway toward resilience, longevity, and optimal health. As the global burden of metabolic diseases continues to rise, innovative, low-cost, and sustainable interventions such as Early Time-Restricted Feeding (eTRF) are gaining momentum in both clinical and academic circles. However, while preliminary findings—including this case—are promising, further investigation is needed to fully validate and optimize the approach.

9.1 Need for Larger, Controlled Studies: This case study, while detailed and methodologically robust, is inherently limited by its single-subject design. Future research must prioritize:

• **Randomized controlled trials (RCTs)** with large sample sizes

• Comparative arms with standard care and other dietary interventions

• Longitudinal follow-up (≥12 months) to assess sustainability and relapse rates

These studies should assess not only biomedical outcomes but also **psychosocial and behavioral dynamics**, such as adherence, perceived benefits, and barriers to implementation.

9.2 Integration with Circadian Health Science: The success of eTRF underscores the importance of **circadian alignment** in dietary behavior. Future research should delve deeper into how **meal timing interfaces with circadian gene expression**, hormonal oscillations, and metabolic pathways. Proposed directions include:

• Molecular studies on **clock gene modulation** (e.g., BMAL1, PER2, CRY1)

• Investigation of **melatonin, cortisol, leptin, and ghrelin** rhythms in TRE participants

• Chronotype-adjusted protocols for personalized eTRF recommendations

In an age of ubiquitous artificial light, digital overstimulation, and irregular work patterns, aligning feeding with **biological day** may offer protection against chronic metabolic dysregulation.

9.3 Exploring Multidimensional Outcomes: Future research must adopt a **multidisciplinary lens**, exploring not only glucose and lipid metabolism but also:

• **Cognitive function**, mood, and mental clarity

• **Mitochondrial resilience** and oxidative stress modulation

• **Gut microbiota composition** and circadian fluctuations

• **Autonomic nervous system balance** via HRV and sleep tracking

Such studies would position eTRF as a truly holistic intervention, with ripple effects across multiple systems.

9.4 Relevance in Modern Lifestyle Contexts

Perhaps the most urgent research question lies not in whether eTRF works, but **how to make it feasible within modern society**. Future studies should examine:

• The **impact of work schedules, social norms, and food access** on TRE adherence
• Effectiveness in shift workers, caregivers, or individuals with irregular routines
• Integration with **digital tools** (apps, wearables) for real-time monitoring and feedback
• Group-based behavioral support models and health coaching

The growing disconnect between modern human behavior and our ancient circadian physiology is at the root of much chronic disease. eTRF may serve as a bridge toward **re-synchronizing biology and lifestyle**.

9.5 Policy and Translational Potential: Finally, research must address the **translational gap** between science and practice. Promising directions include:

• Cost-benefit analyses comparing eTRF to pharmacologic therapies
• Health system integration in primary care settings
• Policy briefs advocating for circadian-aware dietary recommendations
• Workplace wellness programs incorporating early feeding protocols

Such initiatives will help embed the principles of **circadian metabolic health** into mainstream medicine, public health policy, and even urban design.

Chapter 10 – Strengths and weaknesses of this work

Despite the promising results presented in this case study, several limitations must be acknowledged to properly contextualize the findings and guide future research.

10.1 Single-Subject Design: The most fundamental limitation is the **single-subject nature** of the intervention. While the outcomes were consistent and clinically meaningful, the lack of a control group or a broader population sample limits the generalizability of the results. Interindividual variability—including genetic background, lifestyle, and microbiome diversity—can influence outcomes and must be accounted for in larger trials.

10.2 Self-Reported Behavior and Adherence: Several lifestyle parameters—such as physical activity levels, meal timing, and stress management practices—were partially **self-**

reported by the patient. Although compliance was high and supported by regular check-ins, self-reporting is inherently vulnerable to **recall bias, social desirability bias**, and inconsistencies in tracking. Furthermore, adherence to the full eTRF protocol was reduced during the second trimester, with the intervention limited to **only two days per week** during that period. While this reflects real-life challenges, it may have moderated the metabolic benefits observed in the mid-phase.

10.3 Lack of Blinding and Standardization: The observational nature of the case and the absence of **blinding** introduce the possibility of **observer bias**. Additionally, while blood biomarkers were measured using standard laboratory protocols, potential intra-lab variability in values such as HOMA-IR, CRP, and liver enzymes may have influenced precision.

10.4 External Influences and Confounders: The patient was instructed to increase her physical activity to at least **9,000 steps per day** and received guidance on **stress reduction** via mindfulness, breathing exercises, and social contact. While these measures are integral to lifestyle medicine, they introduce **confounding variables** when attempting to isolate the metabolic effects of eTRF alone.

10.5 Duration and Sustainability: The study covered a 7-month period, with some fluctuations in protocol adherence and seasonal variations in activity, light exposure, and dietary availability. These **external environmental factors** may have influenced outcomes and limit the **long-term extrapolation** of results.Sustainability beyond the intervention period remains unknown. Future follow-up data could assess whether the improvements were maintained or gradually reversed without ongoing monitoring.

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Chapter 12 – Appendices :

1) Bioethics ApprovalAppendix

UNIVERSITY OF THESSALY
DEPT. OF PHYSICAL EDUCATION & SPORT SCIENCE

Internal Ethics Committee

Trikala: 7.2.2024
Protocol Number.: 2328

Approval of research entitled: Application of the Lifestyle Medicie approach: Example of nutritional counselling in hypertensive patients

Scientist responsible – supervisor: Karatzaferi Christina, Professor
Institution: University of Thessaly
Department: Department of Physical Education and Sports Science

Main researcher – student: Kotsiri Ioanna
Curriculum: MSc in Lifestyle Medicine
Institution: University of Thessaly
Department: Department of Physical Education and Sports Science

The proposed research relates to a: Postgraduate thesis

Τηλ. επικοινωνίας:
Email επικοινωνίας:

The Internal Ethics Committee (IEC) of the Department of PE and Sport Science (DPESS), University of Thessaly, examined the proposal in its 2-3/7.2.2024 meeting and approves the implementation of the proposed research.

The Chair of the IEC – DPESS

Athanasios Tsiokanos, PhD

2)Consent Form

ΠΑΝΕΠΙΣΤΗΜΙΟ ΘΕΣΣΑΛΙΑΣ
ΤΜΗΜΑ ΕΠΙΣΤΗΜΗΣ ΦΥΣΙΚΗΣ ΑΓΩΓΗΣ ΚΑΙ ΑΘΛΗΤΙΣΜΟΥ

Έντυπο συναίνεσης δοκιμαζόμενου σε ερευνητική εργασία

Τίτλος Ερευνητικής Εργασίας:
Εφαρμογές της Ιατρικής του Τρόπου Ζωής – πιλοτική εφαρμογή συμβουλευτικής στις διατροφικές συνήθειες σε υπερτασικούς ασθενείς

Επιστημονικός Υπεύθυνος-Επιβλέποντες: Χριστίνα Καρατζαφέρη, Καθηγήτρια, ΤΕΦΑΑ, ΠΘ, email:ck@uth.gr, Γιώργος Σακκάς, Αν. Καθηγητής, ΤΕΦΑΑ, ΠΘ, email: gsakkas@uth.gr, τηλ. εργαστηρίου: 2431047020
Ερευνητές: Ιωάννα Κοτσίρη, email: ikotsiri@uth.gr, τηλ Εργαστηρίου: 2610222627

1. **Σκοπός της ερευνητικής εργασίας**
   Σκοπός της μελέτης είναι να εξετάσει την αποτελεσματικότητα της πρωινής διαλλειματικής διατροφής eTRF στον έλεγχο της πίεσης σε ενήλικες με υπέρταση.
2. **Διαδικασία**

Ευχαριστούμε για το ενδιαφέρον σας να συμμετέχετε σε αυτήν την μελέτη. Δεν θα σας ζητηθεί να αλλάξετε τύπο διατροφής ή ποσότητες τροφής. Οι οδηγίες που θα λάβετε θα αφορούν το πότε θα καταναλώνετε το φαγητό σας.
Οι διατροφικές οδηγίες αφορούν 6ωρη σίτιση (8:00 έως 14:00 το μεσημέρι), με τρία γεύματα πρωινό στις 8:00, μεσημεριανό στις 11:00 και δείπνο στις 14:00.
Η διάρκεια της μελέτης θα είναι 6 μήνες.
Οι συμμετέχοντες θα αξιολογηθούν 3 φορές στο εργαστήριο, για ένα τέταρτο κάθε φορά, στην αρχή και στο τέλος κάθε τριμήνου.
Οι δείκτες που θα καταμετρηθούν είναι το βάρος σώματος, η περίμετρος της μέσης και ο δείκτης μάζας σώματος.
Επίσης, θα γίνει μέτρηση της συστολικής, της διαστολικής πίεσης και του αρτηριακού σφυγμού, καθώς ακόμα θα γίνουν και αναλύσεις αίματος που θα αφορούν τους ακόλουθους βιοχημικούς δείκτες: γλυκόζη νηστείας, ουρία ,κρεατινίνη, χοληστερίνη, ολική, HDL,LDL, τριγλυκερίδια ,ηπατικά ένζυμα SGOT, SGPT, γ-GT

3. **Κίνδυνοι και ενοχλήσεις**

Δεν θα υπάρξει κάποια καταπόνηση. Η προτεινόμενη διαλλειματική προσέγγιση στην διατροφή δεν ενέχει κινδύνων.

4. **Προσδοκώμενες ωφέλειες**

Με την συμμετοχή σας θα λάβετε πολλές πληροφορίες για το λειτουργικό σας προφίλ. Επίσης θα λάβετε δωρεάν αποτελέσματα από αξιολογήσεις, αλλά και συμβουλευτική υγείας, υπηρεσίες που στο εμπόριο κοστίζουν αρκετά.
Η διερεύνηση της αποτελεσματικότητας της πρωινής διαλλειματικής διατροφής στην πίεση, όπως και σε άλλες παραμέτρους της καρδιομεταβολικής υγείας και των χρόνιων μη μεταδοτικών νοσημάτων θα μπορούσε να βοηθήσει στην βελτίωση της ποιότητας της ζωής των ανθρώπων της μεγαλύτερης ηλικία καθώς και στην μείωση της νοσηρότητας και θνητότητας αυτών. Με την συμμετοχή σας θα βοηθήσετε την πρόοδο στην εφαρμογή απλών αλλά αποτελεσματικών πρακτικών στην καθημερινότητα.

5. **Δημοσίευση δεδομένων – αποτελεσμάτων**

Η συμμετοχή σας στην έρευνα συνεπάγεται ότι συμφωνείτε με την μελλοντική δημοσίευση των αποτελεσμάτων της, με την προϋπόθεση ότι οι πληροφορίες θα είναι ανώνυμες και δε θα αποκαλυφθούν τα ονόματα των συμμετεχόντων. Τα δεδομένα που θα συγκεντρωθούν θα κωδικοποιηθούν με αριθμό, ώστε το όνομα σας δε θα φαίνεται πουθενά.

6. **Πληροφορίες**

Μη διστάσετε να κάνετε ερωτήσεις γύρω από το σκοπό ή την διαδικασία της εργασίας. Αν έχετε οποιαδήποτε αμφιβολία ή ερώτηση ζητήστε μας να σας δώσουμε διευκρινίσεις.

7. **Ελευθερία συναίνεσης**

Η συμμετοχή σας στην εργασία είναι εθελοντική. Είστε ελεύθερος-η να μην συναινέσετε ή να διακόψετε τη συμμετοχή σας όποτε το επιθυμείτε.

8. Δήλωση συναίνεσης

Διάβασα το έντυπο αυτό και κατανοώ τις διαδικασίες που θα ακολουθήσω. Συναινώ να συμμετάσχω στην ερευνητική εργασία.

Ημερομηνία: 24 / 1 / __

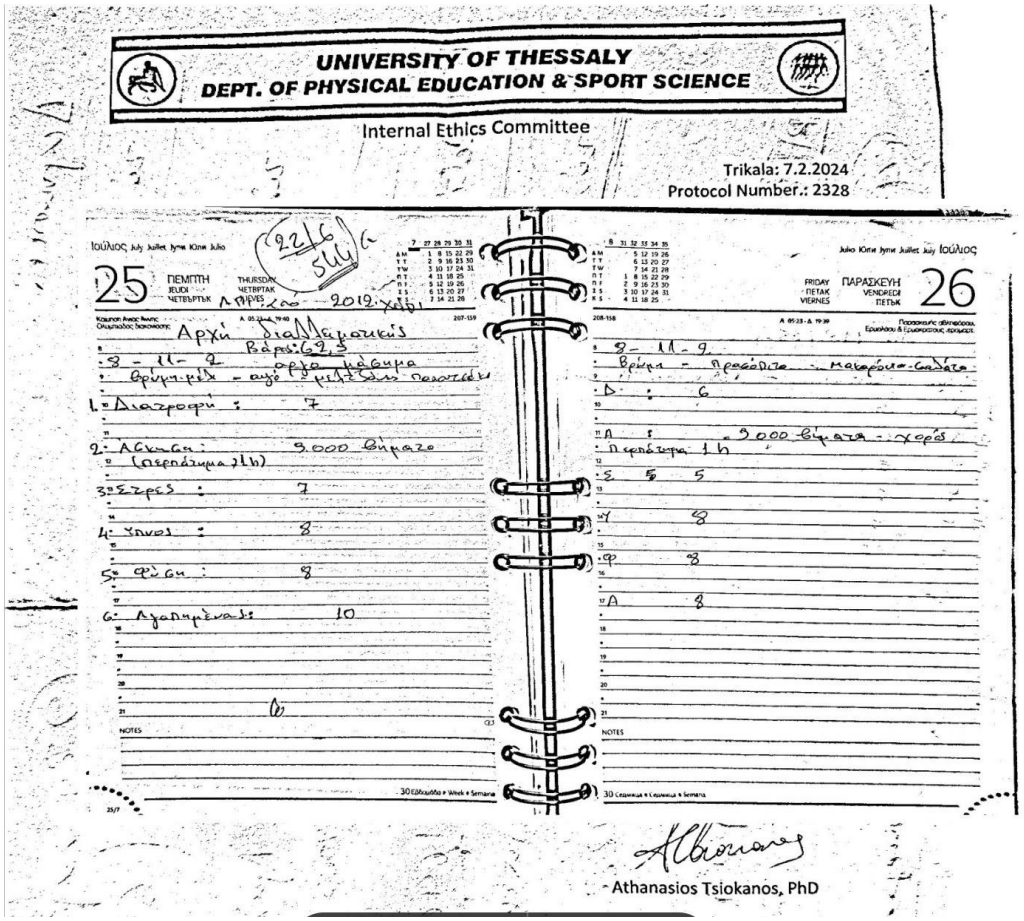
Ονοματεπώνυμο και υπογραφή συμμετέχοντος

Υπογραφή ερευνητή

Ονοματεπώνυμο και υπογραφή παρατηρητή

2

3)Every day journaling



Appendix 1: Bioethics Approval

Appendix 2: Consent Form

Appendix 3: Examples of questionnaires used

Appendix [last number]: Copyright Statement

Affirmation

The undersigned [NAME] postgraduate student of the Postgraduate Program "LIFESTYLE MEDICINE" of the University of Thessaly

I declare responsibly that I accept the following terms concerning:

(a) the copyright of my Master's Thesis entitled "[TITLE OF YOUR THESIS]"

(b) the management of the research data I will collect in the course of its elaboration:

1. The copyright of the resulting volume of the master's thesis will belong to me. I will follow the instructions for writing, printing and depositing copies of the dissertation in the relevant repositories (in printed and/or electronic form).
2. The management of the dissertation data belongs jointly to me and the Director of Studies/Main Supervisor.
3. Any scientific publication or announcement (posted or oral), or reference derived from the material/data of this work will be made with authors myself, the main supervisor and/or other researchers (such as a member of the three-member advisory committee), depending on their contribution to the research or the writing of the research paper(s).
4. The order of names in scientific publications or scientific announcements will be decided jointly by me and the main supervisor (DOS) of the project before it begins. This decision will be certified in writing between myself and the main supervisor.

Finally, I declare that I am aware of the rules on plagiarism and intellectual property and that I will strictly follow them throughout my studies, I will attend to the educational obligations arising from this MSc, as well as will attend the publication procedures that will arise after the completion of my studies.

[Date]

[NAME]

[Signature]