REVIEW ARTICLE

# Role of Chrononutrition in Modulating Metabolic and Cardiovascular Health

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## Abstract

Maintaining optimal cardiovascular and metabolic health depends on aligning dietary practices with the body's intrinsic circadian rhythms. Chrononutrition is a rapidly advancing research area that explores how the timing of food intake influences physiological health outcomes. Unlike conventional nutritional strategies that emphasise food quantity and composition, chrononutrition highlights meal timing as a critical regulator of metabolic processes, including glucose metabolism, insulin responsiveness and lipid regulation. Accumulating evidence indicates that unfavourable eating behaviours, particularly late-day or nighttime food consumption, are closely associated with metabolic impairments and an increased risk of conditions such as obesity, type 2 diabetes and cardiovascular disease. By integrating principles of nutrition with chronobiology, chrononutrition offers a promising approach for reducing the burden of chronic diseases. This review evaluates the role of chrononutrition in metabolic and cardiovascular health, with particular emphasis on time-restricted eating (TRF), consistency in meal timing and the underlying molecular mechanisms responsible for the observed health benefits. Overall, the findings suggest that dietary strategies synchronised with biological clocks may represent an effective approach for chronic disease prevention.

**Key words:** Nutritional sciences; Circadian rhythm; Health; Metabolism; Cardiovascular system; Fasting; Intermittent fasting.

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## Introduction

Eating behaviours play a crucial role in synchronising the circadian rhythm, which functions as the body's internal biological clock, as emphasised by the emerging field of chrononutrition.[1] In contrast to traditional nutritional approaches that primarily focus on dietary composition and caloric intake, chrononutrition recognises meal timing as a fundamental determinant of physiological health. Growing evidence demonstrates that disrupted eating schedules and circadian misalignment adversely affect metabolic regulation, thereby increasing susceptibility to obesity, type 2 diabetes and cardiovascular disease. Examining how the timing of meals influences core physiological mechanisms, including insulin sensitivity and glucose homeostasis, provides novel opportunities for improving metabolic and cardiovascular outcomes. Beyond metabolic regulation, chrononutrition also plays an important role in coordinating additional physiological systems.[2] Circadian alignment has been shown to influence immune function, cognitive performance and sleep regulation. Consuming food at biologically appropriate times may help modulate inflammatory pathways, potentially reducing the risk of autoimmune conditions, atherosclerosis and other chronic inflammatory disorders.[3] Furthermore, evidence suggests that adherence to circadian-aligned eating patterns is associated with improved mental health outcomes. Studies indicate that synchronising food intake with circadian rhythms supports emotional well-being, enhances mood stability and improves cognitive function. Together, these findings position chrononutrition as a comprehensive strategy for optimising metabolic and cardiovascular health while also supporting overall physiological balance.[4] While several studies report improvements in insulin sensitivity with time-restricted feeding, the majority are limited by small sample sizes and short intervention durations, which may restrict the generalisability of findings. Additionally, inconsistencies exist across studies, particularly regarding the magnitude of metabolic improvements, possibly due to variations in study design, population characteristics and adherence to dietary protocols.

Chrononutrition also significantly influences body weight regulation and sleep quality. Aligning food intake with circadian rhythms can promote energy expenditure and appetite control, both of which are essential for maintaining a healthy body weight. Research indicates that allocating a greater proportion of daily caloric intake to earlier hours of the day, particularly during breakfast, enhances satiety, reduces cravings later in the day and limits excessive evening food consumption. Early energy intake further supports efficient glucose regulation and lipid metabolism, thereby lowering the risk of adiposity and weight gain. In contrast, irregular eating patterns or breakfast omission have been linked to metabolic disturbances, increased late-day hunger and a greater likelihood of obesity.[5] Figure 1 illustrates the interaction between environmental cues, such as light–dark cycles and meal timing, with the central and peripheral circadian clocks. It highlights how these factors regulate biological rhythms, including sleep–wake cycles, hormonal secretion, food intake and metabolic processes.

In addition to metabolic effects, chrononutrition has been associated with improved sleep outcomes. Late-night food consumption can disrupt circadian rhythms and impair sleep quality, particularly by interfering with the initiation of melatonin secretion.[6] Conversely, appropriately timed

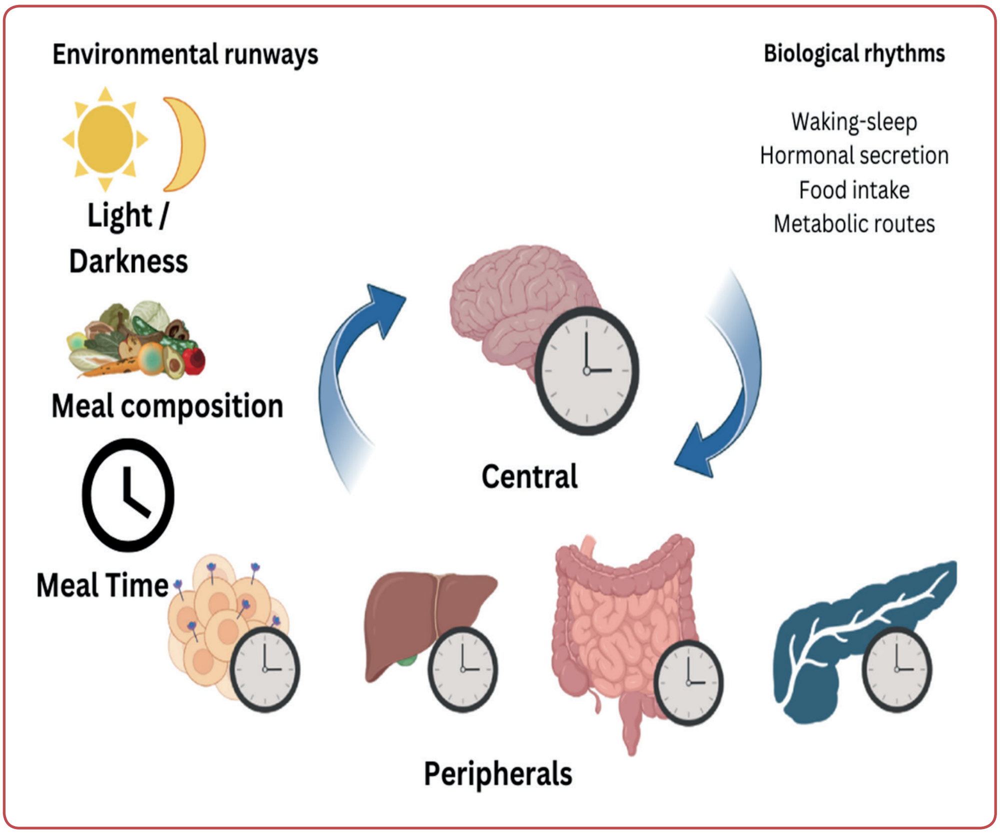


*Figure 1: Chrononutrition and regulation of the dietary circadian rhythm*

meals especially early time-restricted feeding (eTRF) have been associated with reduced systemic inflammation, enhanced sleep quality and improved metabolic health.[7] Collectively, these findings suggest that meal timing may be as critical as dietary composition in preventing obesity and promoting overall health. Accordingly, this review aimed to evaluate the role of chrononutrition in metabolic and cardiovascular health and to assess its potential contribution to chronic disease prevention.

Despite the growing body of literature on chrononutrition, several critical gaps remain. Many existing reviews primarily focus either on epidemiological associations or isolated clinical outcomes, with limited integration of mechanistic pathways and translational relevance. Furthermore, there is insufficient synthesis of how circadian biology, meal timing and metabolic regulation interact across molecular, physiological and clinical domains. This review aimed to bridge these gaps by providing a comprehensive and integrative perspective on chrononutrition, emphasising (i) underlying circadian and metabolic mechanisms, (ii) clinical implications for cardiometabolic health and (iii) potential applications in disease prevention strategies. By consolidating evidence from observational, interventional and mechanistic studies, this review offers a more holistic understanding of how meal timing influences metabolic and cardiovascular outcomes.

## Background and definition of chrononutrition

Chrononutrition is an interdisciplinary framework that integrates nutritional science with chronobiology to examine how the timing of food intake influences human health. This concept is based on the understanding that many physiological and biochemical processes governing energy expenditure and metabolism are regulated by endogenous circadian rhythms. These rhythms follow a 24-hour cycle and are shaped by environmental cues such as light exposure, ambient temperature and patterns of food consumption. Circadian regulation plays a central role in controlling digestive function, glucose and lipid metabolism and the secretion of key metabolic hormones, including cortisol and insulin.[8] The primary objective of chrononutrition is to align eating schedules with these biological rhythms in order to optimise metabolic efficiency and promote overall health. Increasing scientific attention has highlighted the importance of meal timing due to its substantial impact on metabolic outcomes. Evidence indicates that consuming food during the biological night or late in the day when the body is physiologically prepared for rest can impair insulin sensitivity, glucose tolerance and lipid handling. Such metabolic disturbances contribute to the development of obesity, type 2 diabetes and cardiovascular disease.[4] These adverse effects are partly explained by daily variations in metabolic capacity, which is highest during the morning hours and progressively declines toward the evening. Eating when metabolic efficiency is reduced may therefore lead to metabolic dysregulation and increased systemic stress.

Meal frequency and regularity represent additional key components of chrononutrition. Inconsistent eating behaviours, including skipped meals or food intake at irregular times, can disrupt circadian alignment and adversely affect metabolic and cardiovascular health.[9] This disruption is particularly evident among shift workers, who often consume meals at biologically inappropriate times and consequently face a higher risk of metabolic syndrome and cardiovascular disorders due to prolonged circadian misalignment.

Chrononutrition also includes time-restricted feeding (TRF), a dietary strategy in which food consumption is confined to specific daily time windows. Research has demonstrated that eTRF, in which meals are consumed earlier in the day within a shortened eating period, can enhance insulin sensitivity, lower blood pressure and reduce oxidative stress, even in the absence of weight loss.[7] Collectively, these findings emphasise that both meal timing and dietary composition play critical roles in shaping metabolic and cardiovascular health outcomes.

At the molecular level, circadian rhythms are regulated by a central pacemaker located in the suprachiasmatic nucleus (SCN) of the hypothalamus. This master clock coordinates peripheral clocks present in multiple tissues, including the liver, pancreas and adipose tissue, ensuring synchronisation of metabolic activity across the body. These peripheral clocks respond to external signals, particularly food intake and play a

*Table 1: Importance of metabolic and cardiovascular health*

| Aspect of health | Definition | Significance | Supporting evidence |
|---|---|---|---|
| **Metabolic health** | Maintenance of optimal glucose, lipid levels, blood pressure and waist circumference without medication. | Prevents obesity, type 2 diabetes and metabolic syndrome; supports cardiovascular (CV) health and longevity. | Katzmarzyk et al[12] reported lower chronic disease risk in metabolically healthy individuals. |
| **Insulin sensitivity** | Efficiency of the body's response to insulin for glucose regulation. | Reduces risk of type 2 diabetes and metabolic syndrome; improves CV outcomes. | Al-Badrani et al[13] showed improved insulin sensitivity lowers metabolic and CV risk. |
| **Lipid metabolism** | Processes involved in fat utilisation for energy, hormones and cell structure. | Maintains cholesterol balance and prevents atherosclerosis, reducing CV risk. | Bays et al[14] identified lipid metabolism disruption as a key CV risk factor. |
| **Cardiovascular health** | Proper functioning of the heart and blood vessels. | Prevents hypertension, heart disease and stroke; promotes longevity. | Benjamin et al[15] highlighted its role in reducing mortality. |
| **Blood pressure regulation** | Maintenance of normal arterial pressure levels. | Lowers risk of heart disease, stroke and organ damage. | Sharman et al[16] emphasised its importance in preventing CV events. |
| **Inflammatory response** | Immune response to injury or infection. | Chronic inflammation increases CV risk; control supports metabolic health. | Laera et al[17] showed anti-inflammatory strategies reduce CV disease risk. |

critical role in regulating tissue-specific metabolic processes such as glucose and lipid metabolism. When meal timing aligns with the intrinsic rhythmic activity of these peripheral clocks, metabolic efficiency is enhanced, leading to improved cardiovascular function, better energy balance and reduced inflammatory responses. Chrononutrition exerts significant effects on both cardiovascular and metabolic health outcomes. Evidence indicates that consuming meals late in the day or concentrating most daily caloric intake into a single large meal can elevate postprandial glucose levels and increase blood pressure, thereby raising cardiovascular risk.[10, 11] In contrast, dietary patterns synchronised with circadian rhythms have been associated with improved lipid metabolism, reduced cholesterol levels and attenuation of inflammatory processes. Such metabolic improvements contribute to a lower risk of atherosclerosis and other cardiovascular disorders. Table 1 summarises key aspects of metabolic and cardiovascular health, outlining their definitions, clinical significance and supporting evidence. It highlights the interconnected roles of metabolic regulation, insulin sensitivity, lipid metabolism, blood pressure control and inflammation in maintaining overall cardiometabolic health and reducing disease risk.

# Chronobiology: understanding biological rhythms

## Overview of circadian rhythms

Circadian rhythms are endogenous biological cycles with an approximate 24-hour periodicity that regulate a broad range of physiological and behavioural functions. These rhythms are present in nearly all organisms, including humans and are shaped by both internal mechanisms and external environmental cues such as light and temperature. The primary regulator of circadian rhythms is an internal "biological clock" located in the hypothalamic SCN.[8] The SCN functions as the central coordinator, synchronising peripheral clocks in organs such as the liver, pancreas, heart and adipose tissue. These peripheral clocks play a vital role in controlling metabolic processes, hormone secretion and overall energy balance.[18] Circadian rhythms enable physiological processes to occur in alignment with predictable environmental changes across the day-night cycle. Key functions governed by the circadian system include body temperature regulation, sleep–wake patterns, hormone release such as cortisol and melatonin and daily feeding behaviours.[19] Disruptions to circadian organisation, whether caused by shift work, irregular sleep schedules, or excessive exposure to artificial light during nighttime hours, have been associated with a wide range of adverse health outcomes, including cancer, metabolic disorders and cardiovascular diseases.[20] A central function of circadian rhythms is the regulation of metabolic homeostasis. The circadian clock influences insulin sensitivity, glucose utilisation and lipid storage, processes that are strongly affected by the timing of food intake. Eating during periods that conflict with the body's natural biological rhythms such as late at night can result in metabolic imbalance and elevate the risk of obesity and type 2 diabetes. Circadian rhythms also contribute significantly to cardiovascular regulation by influencing blood pressure, heart rate and hormone-mediated vascular function.[21] Persistent circadian misalignment has been linked to an increased incidence of hypertension and other cardiovascular disorders, particularly among individuals engaged in shift work.

Beyond physical health, circadian rhythms exert a substantial influence on mental and cognitive functioning. Proper synchronisation between internal biological clocks and external environmental cues is essential for mood stability, cognitive performance and psychological well-being.[18] Disruption of circadian timing has been associated with an elevated risk of mental health conditions, including depression, bipolar disorder and anxiety. These observations highlight the critical importance of maintaining circadian integrity, demonstrating that the precise timing of physiological processes plays a key role in both physical and mental health outcomes.

### Influence of light, sleep and hormones on biological rhythms

Light is the most powerful external cue, or zeitgeber, responsible for synchronising circadian rhythms with the external environment. Exposure to natural daylight plays a central role in regulating the hypothalamic SCN, which aligns the body's internal clock with the 24-hour light–dark cycle.[22] Specialised retinal photoreceptors, known as melanopsin-containing retinal ganglion cells, detect changes in light intensity and relay this information to the SCN. In response, the SCN modulates the secretion of key hormones, including melatonin, which facilitates sleep onset and cortisol, which promotes wakefulness and alertness.[23] Disruption of natural light exposure, particularly through excessive artificial lighting at night, can desynchronise circadian rhythms and has been linked to adverse health outcomes such as sleep disturbances, metabolic dysfunction and elevated cardiovascular risk.[24] Sleep represents another essential component in maintaining circadian stability. While sufficient sleep supports circadian alignment, circadian rhythms also regulate sleep timing, duration and quality. Proper circadian synchronisation promotes restorative sleep at night and sustained alertness during daytime hours. In contrast, irregular sleep schedules, including those associated with shift work or trans-meridian travel, can impair sleep quality and lead to cognitive deficits, metabolic disturbances and increased susceptibility to chronic diseases such as obesity and diabetes.[23] Evidence further suggests that inconsistent sleep patterns may intensify circadian misalignment and disrupt normal hormonal secretion.[6]

Hormonal rhythms are closely intertwined with circadian regulation and play a crucial role in metabolic and cardiovascular homeostasis. Melatonin, secreted by the pineal gland, follows a nocturnal pattern that facilitates sleep initiation, with concentrations peaking during the night and gradually declining toward morning.[25] In contrast, cortisol exhibits a diurnal rhythm characterised by a pronounced increase upon awakening, known as the cortisol awakening response, which supports alertness and energy mobilisation.[26] Precise temporal regulation of these hormonal cycles is essential for maintaining metabolic balance and cardiovascular health. Chronic stress, sleep deprivation, or circadian disruption can alter hormone secretion patterns, contributing to immune dysfunction, metabolic irregularities and heightened cardiovascular disease risk.

## Chrononutrition: timing of food intake

Disruption of biological rhythms, particularly circadian cycles, can exert significant adverse effects on human health. Circadian misalignment arises when the body's internal biological clock becomes desynchronised from external environmental signals such as light–dark cycles, ambient temperature and social or behavioural routines. Although multiple factors can interfere with biological timing, contemporary lifestyle patterns represent a major driving force behind circadian disruption. Shift work, irregular sleep-wake schedules, frequent trans-meridian travel resulting in jet lag and extended exposure to artificial light especially blue light emitted from electronic devices during nighttime hours are among the most prominent contributors.[27] Shift workers are especially susceptible, as their occupational demands often require alertness and activity during nighttime periods when the circadian system is physiologically programmed for rest.

The consequences of circadian disruption are widespread and multifaceted. One of the earliest and most common outcomes is impaired sleep quality. Circadian misalignment can lead to fragmented sleep, insomnia and irregular sleep-wake cycles, which in turn contribute to cognitive dysfunction, reduced concentration and the development of mood disturbances such as anxiety and depression.[23] Prolonged circadian disruption has also been strongly associated with metabolic abnormalities, including insulin resistance, impaired glucose tolerance and dyslipidaemia, all of which increase the risk of obesity and type 2 diabetes.[28] Individuals engaged in evening or night work, as well as those with inconsistent eating and sleeping habits, exhibit a higher prevalence of metabolic syndrome, characterised by elevated blood glucose levels, hypertension and central adiposity.[29]

Cardiovascular health is similarly compromised by circadian misalignment. Disrupted sleep patterns and altered internal timing have been linked to elevated blood pressure, reduced heart rate variability and heightened systemic inflammation key contributors to cardiovascular disease risk.[28] As a result, shift workers and individuals experiencing chronic circadian disruption demonstrate a greater incidence of myocardial infarction, stroke and other cardiovascular events, likely due to sustained physiological stress placed on the cardiovascular system. In addition, circadian rhythms play an essential role in regulating immune function and their disruption can weaken immune responses, increasing vulnerability to infections and inflammatory conditions.[30]

Beyond somatic health, circadian disruption has profound implications for mental and emotional well-being. Misalignment of biological rhythms has been associated with impairments in memory, learning capacity and executive functioning, as well as an elevated risk of neurodegenerative disorders such as Parkinson's and Alzheimer's disease.[31] Emotional regulation is also affected, with circadian disturbances contributing to the development and exacerbation of mood disorders, including bipolar disorder and major depression. Evidence suggests that these effects may be mediated through alterations in the rhythmic release of neurotransmitters such as serotonin and dopamine, which are critical for maintaining emotional stability and cognitive balance.[23, 32] Although current evidence supports the beneficial effects of chrononutrition, several limitations must be acknowledged. Many studies are short-term interventions with limited sample sizes, reducing the strength of causal inference. Additionally, heterogeneity in study designs, meal timing protocols and participant characteristics contributes to inconsistent findings. These limitations highlight the need for large-scale, long-term randomised controlled trials to establish robust clinical guidelines.

## Definition and principles of chrononutrition

Chrononutrition is an integrative discipline that combines nutritional science with chronobiology the study of biological rhythms to examine how the timing of food intake influences health outcomes, disease susceptibility and metabolic regulation. To enhance metabolic efficiency, optimise energy utilisation and lower the risk of chronic conditions such as obesity, type 2 diabetes and cardiovascular disease, dietary intake should be synchronised with the body's circadian rhythms.[33] Circadian rhythms are endogenous 24-hour cycles that govern key physiological processes, including metabolism, hormonal secretion and sleep–wake patterns, with light exposure and feeding behaviour acting as primary regulatory cues. These rhythms are coordinated by a central pacemaker located in the SCN of the brain, along with peripheral clocks distributed across metabolic tissues such as the liver, pancreas and adipose tissue. Chrononutrition therefore emphasises aligning meal timing with these biological oscillations to promote optimal physiological function. Accumulating evidence suggests that food consumption during daytime hours when metabolic activity is naturally elevated results in more favourable metabolic outcomes compared to eating during the night.[34] Intake of calorie-dense or carbohydrate-rich meals earlier in the day has been shown to improve glycaemic control and reduce the likelihood of insulin resistance, as insulin sensitivity is highest in the morning and gradually declines as the day progresses.[35] Similarly, lipid metabolism and fat oxidation operate more efficiently during day-

*Table 2: Meal timing and its impact on metabolism*

| Meal timing | Effects on metabolism | Supporting studies |
|---|---|---|
| **Morning** (breakfast) | Enhances insulin sensitivity, improves glucose control and increases fat oxidation; skipping is linked to higher appetite and poor glycaemic control. | Flanagan et al (2021)[35] reported improved glycaemic outcomes and reduced metabolic syndrome risk. |
| **Afternoon** (lunch) | Aligns with circadian rhythm, supporting digestion and energy balance; skipping increases evening hunger. | Garaulet et al (2014)[33] linked late lunch to higher body mass index (BMI) and reduced weight loss. |
| **Evening** (dinner) | Late eating impairs glucose tolerance, reduces insulin sensitivity and promotes fat storage. | Almoosawi et al (2019)[9] associated late meals with poor lipid metabolism and weight gain. |
| **Time-restricted feeding (TRF)** | Daytime eating window improves insulin sensitivity, fat oxidation and metabolic health. | Sutton et al (2018)[7] showed improved glycaemic control and reduced BP and inflammation. |
| **Irregular meal timing** | Disrupts circadian rhythm, impairs glucose regulation and increases metabolic risk. | Katsi et al (2022)[34] linked irregular eating to metabolic dysfunction and CVD risk. |
| **Mid-morning snack** | Stabilises glucose and maintains energy levels. | Qian et al (2016)[10] showed improved glucose stability with protein/fibre snacks. |
| **Early afternoon snack** | Sustains energy and reduces overeating later in the day. | Pot (2018)[38] reported benefits for metabolic balance and glucose control. |
| **Mid-afternoon snack** | Improves satiety and reduces evening overeating. | Almoosawi et al (2019)[9] found improved satiety and reduced caloric intake. |
| **Early evening snack** | Helps appetite control without disrupting circadian rhythm. | Garaulet et al (2014)[33] showed reduced late-night eating. |
| **Nighttime eating restriction** | Avoiding late meals improves glucose metabolism and sleep quality. | McHill et al (2014)[6] demonstrated reduced metabolic disruption and better circadian alignment. |

light hours, whereas nighttime eating has been associated with increased fat storage and weight gain.[9] Chrononutrition also underscores the importance of meal consistency and regularity, as irregular eating behaviours such as skipping meals or consuming food at atypical times can disrupt internal circadian clocks and impair metabolic regulation. Such patterns have been linked to elevated blood pressure, a higher prevalence of metabolic syndrome and disturbances in glucose metabolism.[36]

One of the most widely adopted chrononutrition strategies is TRF, which confines daily food intake to a defined eating window, typically during daytime hours. TRF has demonstrated benefits in improving metabolic indicators such as body weight, lipid profiles and insulin sensitivity, even in the absence of intentional caloric restriction.[7] In addition to metabolic improvements, synchronising eating patterns with circadian rhythms also supports cardiovascular health. Studies indicate that circadian-aligned meal timing can contribute to reductions in blood pressure, improvements in cholesterol levels and enhanced endothelial function, collectively lowering the risk of cardiovascular disease.[33, 37] Table 2 summarises the effects of different meal timing patterns on metabolic health, highlighting how alignment with circadian rhythms improves glucose regulation, energy balance and overall metabolic function, while late or irregular eating patterns are associated with adverse metabolic outcomes.

## Dietary patterns aligned with chrononutrition

Dietary practices that respect circadian biology emphasise not only what is consumed but also when food is eaten. Meal timing is closely linked to circadian rhythms, which regulate key physiological processes such as metabolism, digestion and the sleep–wake cycle. Chrononutrition aims to enhance metabolic health and lower disease risk by synchronising food intake with these endogenous biological rhythms. One of its core principles is concentrating energy intake earlier in the day, when metabolic efficiency and insulin sensitivity are highest. Evidence indicates that consuming larger meals in the morning and early afternoon, while reducing evening intake, improves glycaemic control, decreases appetite and increases fat oxidation, thereby reducing the risk of metabolic conditions including obesity and type 2 diabetes.[39] Consistency in meal timing is another essential component of chrononutrition.

Eating behaviours such as skipping breakfast, consuming meals late at night, or following irregular eating schedules can disrupt circadian regulation and adversely affect metabolic function. Research suggests that these irregular patterns interfere with glucose homeostasis and are associated with a higher risk of metabolic syndrome and cardiovascular disease.[5] In contrast, regular and predictable meal timing supports metabolic stability, particularly when meals are aligned with circadian rhythms.

TRF represents a dietary approach that closely follows chrononutrition principles. Studies by Gabel et al[40] demonstrate that restricting food intake to a defined daily window typically during periods of peak metabolic activity can improve insulin sensitivity, reduce body weight and decrease inflammation. By confining eating to a shorter timeframe and extending the overnight fasting period, TRF helps reinforce circadian alignment and promote metabolic health. Notably, the benefits of TRF have been observed independently of total caloric intake, highlighting the importance of meal timing beyond calorie reduction alone.

Conversely, eating late in the evening or at night is considered incongruent with circadian physiology and may negatively influence metabolic processes. Late-night meals have been shown to exacerbate insulin resistance, impair glucose metabolism and contribute to weight gain, as metabolic activity naturally declines during nighttime hours.[28] Therefore, chrononutrition advocates for earlier and lighter evening meals to support efficient digestion and optimal metabolic function.

## Chrononutrition and metabolic health

Chrononutrition is a key determinant of metabolic health because circadian rhythms govern essential physiological processes, including insulin responsiveness, glucose handling and lipid metabolism. Both meal timing and dietary composition significantly influence metabolic status, which is characterised by balanced blood glucose, lipid profiles and insulin levels. Evidence suggests that synchronising eating behaviours with circadian phases when the body is most efficient at nutrient uptake and energy utilisation leads to improved metabolic outcomes.[7] Accordingly, chrononutrition advocates for higher energy intake earlier in the day, when insulin sensitivity

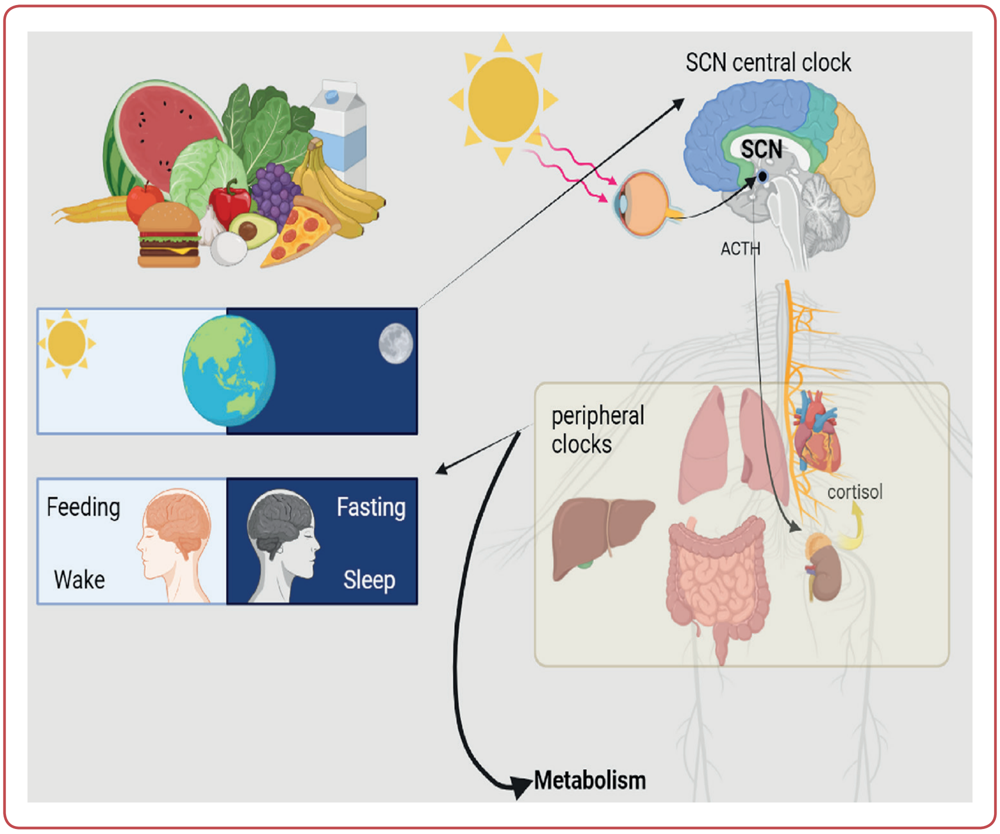


*Figure 2: Chrononutrition and healthy ageing*

is greatest and reduced food consumption in the evening and nighttime, when metabolic activity declines. This approach helps prevent metabolic disorders such as obesity and type 2 diabetes, lowers insulin resistance and supports effective glucose regulation.[41, 42] Disruptions in circadian-aligned eating patterns, such as consuming a large proportion of daily calories in the evening or late at night, have been shown to disturb metabolic homeostasis. Collectively, evidence suggests that alignment of food intake with endogenous circadian rhythms, particularly through earlier meal timing supports optimal metabolic function. Conversely, late-night eating disrupts circadian regulation and is consistently associated with adverse metabolic outcomes. To avoid redundancy, these concepts are discussed integratively across subsections with emphasis on distinct physiological mechanisms. The circadian system optimally regulates glucose and lipid metabolism during the morning and early afternoon and is modulated by both feeding behaviour and light exposure. Studies demonstrate that consuming a substantial breakfast can enhance metabolic health by promoting fat oxidation, suppressing appetite and facilitating weight control.[39] TRF has emerged as a prominent chrononutrition-based dietary intervention due to its favourable metabolic effects. Research indicates that limiting food intake to a 6–10-hour window during daylight hours can reduce circulating insulin levels, improve glucose tolerance and decrease the risk of metabolic diseases. By aligning meal timing with circadian rhythms, TRF supports metabolic regulation and attenuates inflammatory responses. In contrast, extended nighttime eating and irregular meal schedules can disrupt circadian organisation, reduce metabolic efficiency and promote metabolic dysfunction. Additionally, meal timing has a significant impact on lipid metabolism, as evening or late-night food consumption can increase triglycerides concentrations and enhance fat storage, thereby elevating the risk of obesity and cardiovascular disease. Figure 2 provides a schematic overview of how circadian rhythms regulate metabolic processes through the interaction between the central and peripheral clocks. Light signals entrain the central clock located in the SCN, which in turn coordinates peripheral clocks in key metabolic organs such as the liver, gut and kidneys via hormonal pathways, including cortisol and ACTH signalling. In parallel, behavioural cues such as feeding–fasting cycles and sleep–wake patterns further influence peripheral clock activity. The integration of these environmental and physiological signals ensures the synchronisation of biological rhythms, ultimately regulating metabolic functions such as energy balance, glucose metabolism and overall homeostasis.

## Mechanistic insights: how chrononutrition modulates health

The cardiovascular advantages of chrononutrition an approach that aligns eating behaviours with endogenous circadian rhythms are increasingly supported by scientific evidence. The circadian clock plays a fundamental role in cardiovascular regulation by controlling daily fluctuations in blood pressure, heart rate and hormonal release. Disruption of these rhythms, including food intake that occurs outside normal biological timing, can contribute to adverse cardiovascular outcomes such as hypertension, atherosclerosis and elevated risk of heart disease.[28] Adhering to chrononutrition principles, particularly consuming food during daylight hours when cardiovascular efficiency is greatest, may help reduce these risks and support overall cardiac health. Dietary timing has a direct influence on cardiovascular function. Studies indicate that consuming large or energy-dense meals in the evening or late at night is associated with increased triglyceride concentrations, impaired glucose tolerance and higher postprandial blood pressure, all of which contribute to greater cardiovascular risk.[43] As the body's ability to metabolise fats and carbohydrates declines in the evening, late eating may promote lipid accumulation and arterial plaque development. In contrast, allocating a greater proportion of daily caloric intake to earlier in the day when metabolic activity is heightened—has been linked to lower blood pressure, improved glycaemic control and reduced systemic inflammation, thereby favouring cardiovascular health.

TRF is a well-studied chrononutrition strategy that has demonstrated cardiovascular benefits. Early time-restricted feeding, in which meals are consumed primarily during the morning and early afternoon, has been shown to improve blood pressure regulation and decrease oxidative stress, both of which are critical in the prevention of cardiovascular disease.[7] Additionally, TRF has been associated with enhanced endothelial function, reduced arterial stiffness and improved synchronisation between meal timing and circadian rhythms key indicators of cardiovascular protection.[40]

Beyond its effects on glucose regulation and vascular function, chrononutrition also supports cardiovascular health through improved lipid metabolism. Eating in accordance with circadian timing has been shown to reduce circulating triglycerides and low-density lipoprotein (LDL) cholesterol, two major contributors to atherosclerosis and heart disease.[9] Conversely, nighttime eating linked to circadian disruption can elevate these lipid markers and increase cardiovascular risk. Chrononutrition also influences inflammatory pathways, which play a central role in cardiovascular pathology. Circadian misalignment resulting from late or irregular eating patterns can intensify inflammatory responses, accelerating atherosclerotic processes. Aligning food intake with circadian rhythms has been associated with lower levels of inflammatory markers, thereby reducing the likelihood of cardiovascular events such as myocardial infarction and stroke.[34]

## Molecular mechanisms

At the molecular level, chrononutrition modulates the circadian system, which controls physiological functions through complex feedback mechanisms involving clock genes, hormonal signals and metabolic pathways. The master circadian pacemaker located in the suprachiasmatic nucleus (SCN) of the hypothalamus synchronises peripheral clocks in metabolic organs such as the liver, pancreas and adipose tissue, thereby coordinating metabolic activity with the light–dark cycle.[44] In addition, chrononutrition plays an important role in hormonal regulation, as the timing of food intake influences the rhythmic secretion of key circadian-associated hormones, including insulin, cortisol and melatonin. Insulin sensitivity is highest in the morning and progressively decreases over the course of the day, indicating that earlier meal timing better matches the body's physiological capacity to metabolise carbohydrates and maintain glycaemic stability. Cortisol, a hormone with a pronounced diurnal rhythm, contributes to the mobilisation of glucose and lipids to meet energy demands. By optimising the temporal coordination between hormonal rhythms and metabolic processes, chrononutrition supports improved glucose homeostasis and limits excess fat storage.[44]

Beyond hormonal and metabolic regulation, chrononutrition also influences health through pathways related to oxidative stress and mitochondrial function. Circadian control of enzymes involved in energy production, such as cytochrome c oxidase, along with regulation of mitochondrial biogenesis, affects cellular energy efficiency and overall metabolic performance.

## Hormonal regulation

Hormonal regulation is a core component of chrononutrition, as the timing of food intake directly affects the release and function of hormones that control metabolism, energy homeostasis and overall physiological health. Circadian rhythms drive daily variations in hormones such as ghrelin, insulin, cortisol and melatonin, which respond to external signals including light exposure and feeding patterns.[45] Synchronising meals with these hormonal rhythms can improve glycaemic control, enhance metabolic efficiency and lower the risk of metabolic diseases. Among these hormones, insulin has been extensively examined in the context of chrononutrition. Insulin sensitivity is highest in the morning and progressively decreases throughout the day, making early-day food consumption more favourable for effective glucose uptake. Studies demonstrate that carbohydrate-rich meals consumed in the morning improve glucose tolerance and reduce the likelihood of insulin resistance, whereas identical meals eaten in the evening result in elevated insulin and blood glucose responses.[29] These effects reflect circadian regulation of metabolic pathways, including the insulin receptor gene (Insr), which exhibits optimal activity during the body's active phase. Consequently, concentrating caloric intake earlier in the day supports hormonal equilibrium and aligns eating behaviour with endogenous circadian timing. Cortisol, often referred to as the "stress hormone," follows a well-defined circadian pattern known as the cortisol awakening response, characterised by a morning peak followed by a gradual decline over the day. This hormone plays a critical role in energy metabolism by modulating appetite, lipid mobilisation and hepatic glucose production.[46] Chrononutrition promotes food intake during periods of naturally elevated cortisol to facilitate efficient energy mobilisation and minimise metabolic strain. In contrast, consuming food late at night can disrupt this hormonal balance, as lower evening cortisol levels are associated with reduced metabolic efficiency and increased fat deposition.[28]

Melatonin, the primary regulator of the sleep-wake cycle, also exerts important effects on metabolic processes. Its levels rise in the evening to promote sleep and signal a reduction in insulin secretion and other metabolic activities.[25] Because melatonin inhibits insulin release, eating during periods of elevated melatonin such as late at night can impair glucose metabolism and increase the risk of insulin resistance.[33] This highlights the importance of scheduling meals earlier in the day, when melatonin concentrations are low and metabolic activity is higher.

Ghrelin, commonly referred to as the "hunger hormone," also displays a circadian rhythm, with levels rising before meals and declining after food intake. Ghrelin plays a key role in regulating energy balance by signalling hunger to the central nervous system.[36, 47] Aligning eating times with these natural hormonal oscillations is a fundamental principle of chrononutrition, supporting efficient metabolism and balanced energy regulation.

### Molecular mechanisms: clock genes and epigenetic regulation

Circadian regulation at the molecular level is governed by core clock genes, including *CLOCK*, *BMAL1*, *PER* and *CRY*, which form transcriptional–translational feedback loops. These genes regulate metabolic pathways such as glucose homeostasis, lipid metabolism and mitochondrial function. Emerging evidence suggests that meal timing can influence the expression of these clock genes, thereby modulating metabolic outcomes. Additionally, epigenetic mechanisms, including DNA methylation and histone modification, play a crucial role in mediating gene–nutrient interactions. Chrononutrition may therefore exert long-term effects on metabolic health through epigenetic reprogramming, although this area remains underexplored and warrants further investigation.

## Clinical and epidemiological evidence

Chronic disorders such as obesity, diabetes and cardiovascular disease are closely linked to two interrelated biological processes: oxidative stress and inflammation. Growing evidence indicates that chrononutrition by synchronising meal timing with circadian rhythms can modulate these pathways and thereby attenuate oxidative stress and inflammatory responses. Circadian rhythms are fundamental to physiological homeostasis, as they regulate immune function and the generation of reactive oxygen species (ROS). Disruption of these rhythms through behaviours such as irregular eating schedules or late-night food consumption can impair this regulation, resulting in increased oxidative stress and sustained low-grade inflammation.[48] Although inflammation is an essential protective response to injury and infection, persistent low-level inflammation driven by metabolic imbalance is a major contributor to conditions such as atherosclerosis and type 2 diabetes. Evidence suggests that the timing of food intake plays a decisive role in shaping inflammatory processes, with irregular meals and nighttime eating being associated with elevated levels of pro-inflammatory cytokines, including interleukin-6 (IL-6) and tumour necrosis factor-α (TNF-α), which are linked to insulin resistance and cardiovascular pathology.

Oxidative stress represents another critical factor in the development of chronic disease and results from an imbalance between ROS generation and antioxidant defines systems. While ROS are inevitable byproducts of normal cellular metabolism, excessive accumulation can damage lipids, proteins and DNA, thereby promoting inflammation and cellular dysfunction.[49] Chrononutrition may reduce oxidative stress by improving mitochondrial function, as mitochondria the primary sites of cellular energy production are under circadian control and exhibit peak activity during the organism's active phase. Aligning food intake with periods of optimal mitochondrial efficiency can limit ROS overproduction and oxidative damage, whereas eating late at night, when mitochondrial activity is reduced, may exacerbate oxidative stress and increase susceptibility to chronic disease.[50]

In addition, chrononutrition enhances the body's intrinsic antioxidant defence systems, including glutathione and superoxide dismutase (SOD), whose expression and activity are also regulated by circadian rhythms and reach their highest levels during daytime hours.[45] Synchronising dietary intake with these endogenous rhythms helps preserve antioxidant capacity, offering further protection against oxidative injury and inflammation. Table 3 summarises observational studies showing that irregular meal timing and late-day energy intake are associated

*Table 3: Evidence linking meal timing with metabolic health outcomes*

| Study | Population | Key findings | Chrononutrition insights |
|---|---|---|---|
| Maukonen et al (2016)[5] | 5,000 Finnish adults | Irregular meals associated with higher BMI, waist circumference and metabolic syndrome. | Regular meal timing supports metabolic health. |
| Katsi et al (2022)[34] | 850 UK participants | Irregular eating linked to higher body weight and insulin resistance. | Circadian-aligned eating reduces metabolic risk. |
| Almoosawi et al (2019)[9] | 1,314 UK participants | Higher evening calorie intake associated with increased inflammation (CRP). | Late eating promotes inflammation and CVD risk. |
| Garaulet et al (2014)[33] | 420 overweight adults (Spain) | Late lunch linked to reduced weight loss and lower insulin sensitivity. | Early meal timing improves metabolic outcomes. |
| Shan et al (2020)[51] | 9,000 US adults | Breakfast skipping and late eating associated with higher BMI and diabetes risk. | Early eating supports glucose regulation and reduces diabetes risk. |

*BMI: body mass index; CRP: C-reactive protein; CVD: cardiovascular disease;*

*Table 4: Clinical evidence on time-restricted feeding (TRF) and metabolic health*

| Study | Population | Intervention | Key findings | Chrononutrition insights |
|---|---|---|---|---|
| Sutton et al (2018)[7] | 8 men with prediabetes | eTRF (8 am–2 pm) | Improved insulin sensitivity, BP and oxidative stress. | Early eating enhances metabolic health via circadian alignment. |
| Garaulet et al (2014)[33] | 420 overweight adults | Early vs late lunch timing | Early eaters showed better weight loss and insulin sensitivity. | Earlier meal timing improves metabolic outcomes. |
| Jamshed et al (2019)[52] | 11 overweight men | eTRF (6-hour window) | Improved insulin sensitivity, reduced hunger and BP. | eTRF reduces cardiovascular risk factors. |
| Hutchison et al (2019)[53] | 15 overweight adults | TRF (12 pm–8 pm) | Reduced glucose, fat mass and caloric intake. | Consistent TRF supports weight and metabolic control. |

*eTRF: early TRF; BP: blood pressure;*

with adverse metabolic outcomes, while circadian-aligned eating patterns support better metabolic health. Table 4 summarises clinical studies demonstrating that time-restricted feeding, particularly earlier eating patterns, improves metabolic parameters such as insulin sensitivity, blood pressure and body weight by aligning food intake with circadian rhythms.

## Meta-analyses and systematic reviews

Meta-analyses and systematic reviews, which integrate findings from multiple individual studies, offer a robust and comprehensive evaluation of the health effects of chrononutrition. A prominent systematic review by Parr et al[54] examined the impact of meal timing on metabolic health and body weight regulation. Based on an analysis of ten intervention studies, the review reported that eTRF and earlier eating windows were generally associated with better glycaemic control, increased insulin sensitivity and improved weight management. These results highlight the significance of synchronising food intake with circadian rhythms, particularly for populations at elevated risk of metabolic disorders such as obesity and type 2 diabetes. The authors further noted that late-night eating was consistently linked to unfavourable metabolic outcomes, including higher body mass index (BMI) and increased risk of cardiovascular disease.

In a similar vein, a meta-analysis conducted by Davis et al[55] assessed the metabolic effects of TRF and intermittent fasting. Analysing data from 16 randomised controlled trials, the authors found that TRF was associated with significant reductions in body fat, improvements in lipid profiles and enhanced insulin sensitivity, even in the absence of deliberate caloric restriction. The findings suggest that limiting food intake to specific time windows can reduce cardiovascular risk factors and support effective weight management. Moreover, the analysis emphasised the critical role of appropriate meal timing in avoiding circadian misalignment, which is known to worsen metabolic dysfunction.

## Practical implications and recommendations

Chrononutrition provides practical insights for promoting health by synchronising food intake with the body's circadian rhythms. Eating patterns that emphasise a greater proportion of daily energy intake earlier in the day particularly during breakfast and lunch represent an effective strategy for supporting metabolic regulation and overall daily performance. This approach can improve metabolic efficiency, enhance insulin responsiveness and lower the risk of weight gain, type 2 diabetes and cardiovascular disease. In contrast, consuming large meals in the evening is discouraged, as the body's ability to digest and metabolise nutrients diminishes later in the day, increasing the likelihood of impaired glucose regulation and excess fat accumulation.

TRF is one of the most commonly recommended chrononutrition strategies and involves limiting food intake to a specific daily time window, ideally during daylight hours. This practice supports the synchronisation of internal circadian clocks, thereby promoting weight control and metabolic health. Regularity in meal timing is also essential, since inconsistent eating patterns can disrupt circadian organisation and increase susceptibility to metabolic disturbances. Furthermore, emphasis should be placed on the nutritional quality of morning meals, with a focus on nutrient-rich foods such as whole grains, lean protein sources and healthy fats. A well-balanced breakfast supplies key nutrients during periods of peak metabolic activity, helps maintain sustained energy levels and contributes to better appetite regulation throughout the day.

From a clinical perspective, chrononutrition offers a practical and non-pharmacological approach for the prevention and management of metabolic and cardiovascular diseases. Healthcare professionals may incorporate meal timing strategies, such as early time-restricted feeding and regular eating schedules, into patient counselling to improve glycaemic control, weight management and cardiovascular risk profiles. Furthermore, chrononutrition principles may be particularly beneficial for individuals with metabolic syndrome, type 2 diabetes and shift workers who experience circadian disruption. Integrating these strategies into clinical guidelines and lifestyle interventions could enhance patient outcomes and complement existing therapeutic approaches. Figure 3 presents an integrated overview of how chrononutrition and circadian rhythms interact to regulate cardiometabolic health. The central clock located in the SCN is synchronised by the light–dark cycle and regulates hormonal signals such as melatonin and

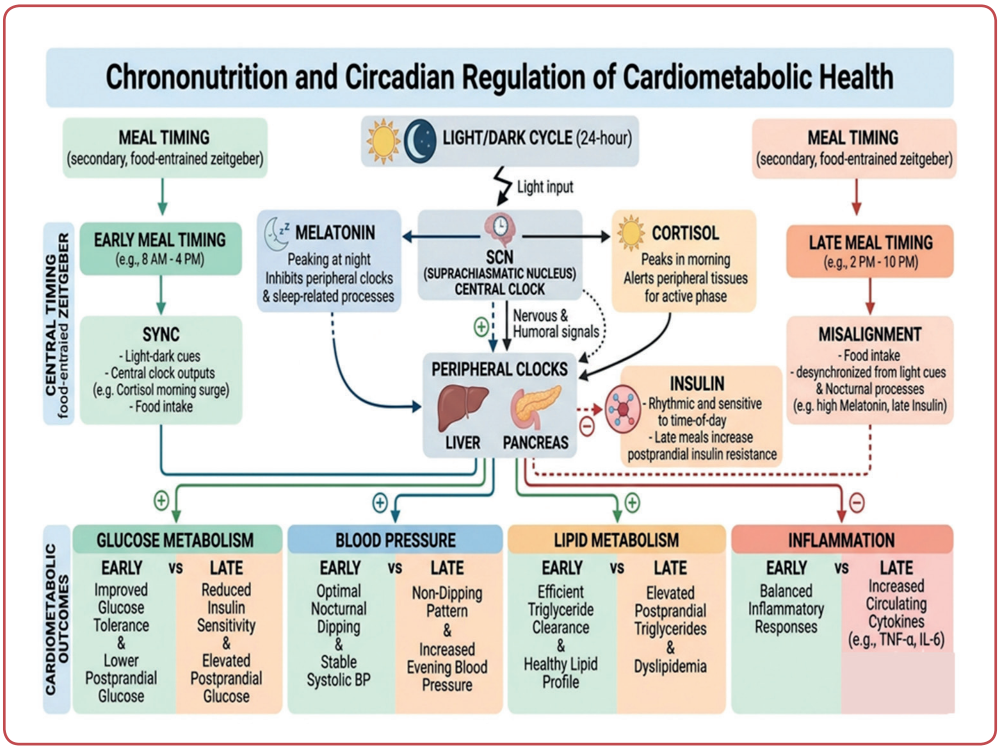


*Figure 3: Chrononutrition in cardiometabolic health: linking circadian biology with meal timing and metabolic outcomes*

cortisol. These signals coordinate peripheral clocks in metabolic organs, including the liver and pancreas. Meal timing acts as a secondary time cue (zeitgeber), influencing metabolic pathways through feeding–fasting cycles and insulin sensitivity. Early, circadian-aligned eating promotes synchronisation between central and peripheral clocks, leading to improved glucose metabolism, optimal blood pressure regulation, efficient lipid metabolism and balanced inflammatory responses. In contrast, late or irregular meal timing results in circadian misalignment, characterised by reduced insulin sensitivity, impaired glucose tolerance, dyslipidaemia, elevated blood pressure and increased inflammation. Overall, the figure highlights the importance of aligning dietary patterns with biological rhythms to support metabolic and cardiovascular health.[56-58]

## Future perspectives

Chrononutrition has emerged as a promising and rapidly advancing field that underscores the importance of aligning dietary intake with the body's intrinsic circadian rhythms to optimise metabolic health and reduce the growing burden of chronic diseases. Increasing scientific evidence suggests that the timing of food consumption is not merely a behavioural choice but a critical determinant of physiological function. Synchronising meal timing with endogenous biological cycles has been shown to enhance insulin sensitivity, improve glucose regulation and support lipid metabolism, thereby contributing to better cardiovascular and overall metabolic health. A growing body of observational and interventional research consistently demonstrates that individuals who consume meals earlier in the day and maintain regular eating patterns experience improved metabolic outcomes compared to those with irregular or late-night eating habits. Chrononutrition strategies such as eTRF, reduced late-night caloric intake and consistent meal scheduling have been associated with improved weight management, reduced adiposity and a lower risk of developing obesity, type 2 diabetes and cardiovascular diseases. These findings highlight the potential of meal timing as a modifiable lifestyle factor that can be incorporated into preventive and therapeutic approaches for metabolic disorders.

Despite these promising findings, several gaps remain that warrant further investigation. Future research should focus on large-scale, long-term randomised controlled trials to establish causality and determine optimal meal timing strategies across diverse populations. In particular, there is a need to better understand the underlying molecular and physiological mechanisms through which chrononutrition exerts its effects. This includes exploring the roles of hormonal regulation (such as insulin, cortisol and melatonin), mitochondrial function, oxidative stress and the expression of circadian clock genes. Furthermore, advancing the field of chrononutrition will require a shift toward more personalised approaches. Individual variability in factors such as age, sex, chronotype (morningness-eveningness preference), genetic predisposition and lifestyle behaviours may influence how individuals respond to specific meal timing interventions. Integrating chrononutrition with precision nutrition frameworks could enable the development of tailored dietary strategies that maximise individual health benefits.

From a broader perspective, the principles of chrononutrition have significant implications for public health and clinical practice. Incorporating meal timing recommendations into dietary guidelines, chronic disease management protocols and preventive healthcare strategies could enhance their effectiveness. Additionally, workplace and corporate wellness programs may benefit from promoting structured meal timing and reducing shift-related circadian disruption. Public health campaigns that raise awareness about the importance of when we eat, in addition to what we eat, could play a vital role in addressing the global rise in metabolic disorders.

## Conclusion

In conclusion, chrononutrition represents a paradigm shift in nutritional science, moving beyond traditional dietary composition to include the temporal dimension of eating behaviour. With continued interdisciplinary research and growing clinical interest, chrononutrition holds substantial potential to become an integral component of precision nutrition and personalised medicine. Ultimately, it offers a novel and practical approach to improving metabolic health and combating lifestyle-related diseases on a global scale.

## Ethics

This study was a secondary analysis based on the currently existing data and did not directly involve with human participants or experimental animals. Therefore, the ethics approval was not required in this paper.

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## Conflicts of interest

The authors declare that there is no conflict of interest.

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## Data access

The data that support the findings of this study are available from the corresponding author upon reasonable individual request.

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