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Impact of chrononutrition on insulin sensitivity and glycemic control: A systematic review

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Abstract
Chrononutrition, the study of the interaction between meal timing and circadian rhythms, has emerged as a critical determinant of metabolic health. This systematic review evaluates the impact of chrononutrition on insulin sensitivity and glycemic control. A structured search of electronic databases (PubMed, Scopus, Web of Science, and Google Scholar) was conducted to identify relevant studies published between 2010 and 2025. Evidence from observational studies, randomized controlled trials, and systematic reviews indicates that meal timing, frequency, and alignment with circadian rhythms significantly influence glucose metabolism. Early-day eating, time-restricted feeding (TRF), and consistent meal patterns are associated with improved insulin sensitivity and glycemic outcomes, whereas late-night eating, breakfast skipping, and circadian misalignment contribute to impaired glucose tolerance and increased insulin resistance. However, heterogeneity in study design and population characteristics limits definitive conclusions. Chrononutrition represents a promising adjunct strategy for metabolic disease prevention and management, but further high-quality longitudinal studies are needed.

Keywords: Chrononutrition, insulin sensitivity, glycemic control, circadian rhythm, time-restricted feeding, diabetes

Introduction
The global prevalence of type 2 diabetes mellitus (T2DM) continues to rise, emphasizing the need for effective nutritional strategies (Davies *et al*., 2026) [9]. Traditional dietary approaches focus on nutrient composition; however, recent research highlights the importance of meal timing in metabolic regulation (Cohen *et al*., 2026) [34]. Chrononutrition examines how eating patterns interact with circadian rhythms to influence physiological processes such as glucose metabolism and insulin sensitivity (Triunfo, 2026) [34].
The circadian system regulates key metabolic pathways, including glucose tolerance and insulin secretion, which exhibit diurnal variation (Zhang *et al*., 2025) [36]. Insulin sensitivity is typically higher during the morning and declines later in the day. Disruption of this rhythm, through irregular eating patterns or late-night meals, contributes to metabolic disorders including obesity and diabetes (Keller *et al*., 2025) [20].

Methodology
1. Search Strategy
A comprehensive and systematic literature search was conducted to identify relevant studies examining the impact of chrononutrition on insulin sensitivity and glycemic control. Major electronic databases, including PubMed, Scopus, and Web of Science, were searched for articles published between 2010 and 2026. The search strategy incorporated a combination of Medical Subject Headings (MeSH) and free-text terms to ensure broad coverage of the topic. Key search terms included "chrononutrition," "meal timing," "insulin sensitivity," "glycemic control," and "circadian rhythm and diet," which were used individually and in various Boolean combinations (AND, OR) to refine the results. Additional filters were applied to select human studies and peer-reviewed articles published in English. Reference lists of selected articles were also manually screened to identify further relevant studies, ensuring the inclusion of comprehensive and up-to-date evidence for this review.

2. Inclusion Criteria
- Human studies (RCTs, cohort, cross-sectional)
- Studies examining meal timing or eating patterns
- Outcomes including insulin sensitivity, fasting glucose, HbA1c

3. Exclusion Criteria
- Animal-only studies
- Non-English publications
- Studies without glycemic outcomes

4. Data Extraction and Analysis
Data from the selected studies were systematically extracted using a standardized approach to ensure consistency and accuracy (Jonnalagadda *et al*., 2015) [17]. Key information, including study design, sample size, population characteristics, type and duration of intervention, and primary outcomes related to insulin sensitivity and glycemic control (such as fasting glucose, HbA1c, and postprandial glucose levels), was collected. Additional variables, such as timing of food intake, dietary patterns, and study setting, were also considered where relevant. Due to substantial heterogeneity in study designs, intervention protocols, and outcome measures, a quantitative meta-analysis was not feasible. Therefore, the findings were synthesized qualitatively, allowing for a comprehensive comparison and interpretation of trends, patterns, and relationships across the included studies.

Mechanisms Linking Chrononutrition and Metabolic Regulation
1. Circadian Regulation of Glucose Metabolism
The circadian clock plays a central role in regulating glucose homeostasis by synchronizing metabolic processes with the light–dark cycle. It governs key physiological

functions such as insulin secretion from pancreatic β-cells, peripheral glucose uptake in tissues like muscle and adipose tissue, and hepatic glucose production. These processes exhibit diurnal variation, with insulin sensitivity typically peaking during the morning and declining in the evening. At the molecular level, circadian clock genes (e.g., *CLOCK*, *BMAL1*) coordinate metabolic pathways to maintain energy balance. However, disruption of circadian alignment—caused by irregular meal timing, late-night eating, or shift work—can impair these regulatory mechanisms, leading to reduced insulin sensitivity, impaired glucose tolerance, and an increased risk of metabolic disorders such as type 2 diabetes (Muoio and Newgard, 2008) [26].

2. Hormonal and Molecular Pathways

At the molecular level, circadian rhythms are regulated by a network of clock genes, primarily *CLOCK* and *BMAL1*, which act as transcriptional regulators controlling the expression of genes involved in metabolism (Mazzoccoli *et al*., 2012) [23]. These genes influence key hormonal pathways, including insulin secretion, glucagon release, cortisol rhythm, and adipokine signaling, thereby playing a crucial role in maintaining glucose homeostasis and insulin sensitivity (Kumar *et al*., 2025) [21]. The coordinated oscillation of these hormones ensures optimal metabolic functioning across the day–night cycle (Begemann *et al*., 2025) [4]. However, when feeding patterns are misaligned with the endogenous biological clock—such as during late-night eating or irregular meal timing—this synchronization is disrupted (Reytor-González *et al*., 2025) [31]. Such misalignment alters hormonal balance, impairs insulin signaling pathways, and promotes metabolic dysregulation, ultimately increasing the risk of insulin resistance, hyperglycemia, and related metabolic disorders.

3. Postprandial Glycemic Response

Meal timing plays a crucial role in determining postprandial glycemic responses due to the circadian variation in metabolic efficiency (Reytor-González *et al*., 2025) [36]. Studies have consistently demonstrated that identical meals consumed during the evening or night result in significantly higher postprandial glucose excursions compared to those consumed in the morning (Keller *et al*., 2025) [20]. This phenomenon is attributed to reduced insulin sensitivity, slower gastric emptying, and diminished β-cell responsiveness later in the day. In contrast, morning consumption aligns with peak insulin action and enhanced glucose uptake by peripheral tissues, leading to better glycemic control. Consequently, late-night eating or consuming large proportions of daily energy intake during the evening can exacerbate hyperglycemia and contribute to long-term metabolic dysfunction, highlighting the importance of aligning meal timing with circadian rhythms (Carrillo *et al*., 2026) [34].

Chrononutrition Factors Affecting Insulin Sensitivity and Glycemic Control

1. Meal Timing

Meal timing is a fundamental component of chrononutrition that significantly influences insulin sensitivity and glycemic control. Evidence consistently demonstrates that consuming a greater proportion of daily energy intake earlier in the day is associated with improved metabolic outcomes. Morning meals align with peak circadian-driven insulin sensitivity, thereby enhancing glucose tolerance and promoting efficient glucose utilization. In contrast, late-night eating is strongly associated with elevated postprandial glucose levels, impaired insulin response, and increased risk of insulin resistance. This is largely due to the natural decline in metabolic efficiency during the evening hours. Furthermore, night-time eating disrupts the synchronization between central and peripheral circadian clocks, exacerbating metabolic dysregulation (Triunfo, 2026) [34]. Therefore, aligning food intake with the body's biological clock—by prioritizing early-day eating and minimizing late-night meals—plays a crucial role in optimizing glycemic control and reducing the risk of metabolic disorders (Triunfo, 2026) [34].

2. Time-Restricted Feeding (TRF)

Time-restricted feeding (TRF) is a chrononutrition-based dietary approach that involves limiting daily food intake to a defined time window, typically ranging from 8 to 10 hours, while maintaining a prolonged fasting period for the remainder of the day. This eating pattern aligns food consumption with the body's circadian rhythms, thereby optimizing metabolic processes (Reytor-González *et al*., 2025) [36]. Evidence from clinical and observational studies indicates that TRF improves insulin sensitivity, enhances glucose regulation, and reduces glycemic variability by synchronizing feeding with peak metabolic efficiency. Additionally, TRF has been shown to lower fasting blood glucose levels and contribute to weight loss, which further supports improved metabolic health. The beneficial effects are partly mediated through improved hormonal regulation, reduced oxidative stress, and enhanced cellular repair mechanisms during fasting periods. Overall, systematic reviews suggest that TRF is a promising and practical dietary intervention for the prevention and management of metabolic disorders, including type 2 diabetes (Bitsanis *et al*., 2022) [5].

3. Meal Frequency and Regularity

Meal frequency and regularity are important aspects of chrononutrition, although current evidence regarding their effects on insulin sensitivity and glycemic control remains inconsistent. Irregular eating patterns, including erratic meal timing and variable daily intake, have been associated with impaired glycemic control due to disruption of circadian rhythms and metabolic homeostasis. In particular, skipping breakfast has been linked to elevated postprandial glucose responses later in the day, likely due to reduced insulin sensitivity and altered hormonal regulation (Nas *et al*., 2017) [27]. Regular meal patterns, on the other hand, may support better synchronization of metabolic processes and improve glucose utilization. However, despite these observations, there is no clear consensus on the optimal number of meals per day, as outcomes may vary depending on individual factors such as lifestyle, chronotype, and overall dietary composition.

4. Breakfast Consumption

Breakfast consumption plays a pivotal role in metabolic regulation and is closely linked to improved insulin sensitivity and glycemic control (Hammad and Shakoor, 2026) [13]. Evidence indicates that skipping breakfast leads to exaggerated postprandial glycemic excursions later in the day, a phenomenon often referred to as the "second-meal effect," where impaired glucose tolerance occurs due to reduced early-day insulin responsiveness. In contrast, regular breakfast consumption helps prime metabolic pathways, enhances insulin secretion, and improves overall glucose handling throughout the day. Furthermore, breakfast intake supports circadian alignment by synchronizing peripheral metabolic clocks with central rhythms. Notably, the combination of breakfast omission and late-night eating creates a prolonged metabolic imbalance, significantly worsening glycemic control and increasing the risk of insulin resistance and metabolic disorders (Tjandrawinata *et al*., 2026) [33].

5. Meal Composition and Sequence

Chrononutrition extends beyond meal timing to include the order and distribution of macronutrients throughout the day, both of which significantly influence glycemic responses and insulin dynamics. Evidence suggests that consuming protein- or fiber-rich foods, such as vegetables, before carbohydrates can attenuate postprandial glucose spikes by slowing gastric emptying, enhancing incretin hormone release, and improving insulin secretion. This "food order effect" helps moderate glucose absorption and reduces glycemic variability. Additionally, the distribution of macronutrients across the day plays a crucial role in metabolic regulation; for instance, higher carbohydrate intake earlier in the day, when insulin sensitivity is greater, is associated with improved glycemic control, whereas concentrating carbohydrate intake in the evening may impair glucose tolerance. Thus, both the sequence and timing of nutrient intake are important determinants of metabolic health within the framework of chrononutrition.

Evidence from Clinical and Observational Studies

1. Observational Studies

Observational studies provide important insights into the real-world relationship between eating patterns and metabolic health. A consistent body of evidence indicates that late-night eating is associated with poorer glycemic control, including elevated fasting glucose levels and higher HbA1c, likely due to reduced insulin sensitivity during evening hours. Additionally, irregular meal timing—characterized by inconsistent eating schedules and variable daily energy distribution—has been linked to an increased risk of developing type 2 diabetes mellitus (T2DM). Such patterns disrupt circadian alignment and impair metabolic regulation, contributing to glucose intolerance and insulin resistance over time. Although observational studies cannot establish causality, their findings strongly support the role of chrononutrition as a significant factor in the prevention and progression of metabolic disorders.

2. Randomized Controlled Trials

Randomized controlled trials (RCTs) provide strong evidence supporting the role of chrononutrition in improving metabolic outcomes. Studies investigating early time-restricted feeding (eTRF), where food intake is confined to earlier hours of the day, consistently demonstrate significant improvements in insulin sensitivity, even in the absence of substantial weight loss. These interventions enhance circadian alignment and optimize metabolic efficiency during periods of peak insulin responsiveness. Additionally, RCTs examining structured and consistent meal timing have shown reductions in postprandial glucose excursions, improved glycemic variability, and better overall glucose regulation. By minimizing metabolic stress associated with irregular eating patterns, these controlled interventions highlight the therapeutic potential of chrononutrition strategies in the management and prevention of type 2 diabetes and related metabolic disorders.

3. Systematic Reviews

Evidence from systematic and scoping reviews further strengthens the role of chrononutrition in metabolic health. A comprehensive review of 49 studies reported that night-time eating is consistently associated with adverse glycemic outcomes, including elevated blood glucose levels and impaired insulin sensitivity, primarily due to circadian misalignment. Additionally, breakfast skipping was found to significantly influence glucose metabolism by increasing postprandial glycemic responses and disrupting normal insulin patterns. However, findings related to meal frequency remain inconclusive, with studies showing mixed results depending on population characteristics, dietary composition, and study design. Overall, these reviews highlight the importance of meal timing and regularity while underscoring the need for further high-quality research to clarify the role of meal frequency in glycemic control.

Special Populations

1. Type 2 Diabetes Mellitus

In individuals with type 2 diabetes mellitus (T2DM), chrononutrition strategies such as early-day eating and time-restricted feeding (TRF) have demonstrated significant potential in improving glycemic control and insulin sensitivity. Aligning food intake with circadian rhythms enhances insulin action during periods of peak metabolic efficiency, leading to better glucose utilization and reduced postprandial hyperglycemia (Pickel and Sung, 2020) [29]. Early time-restricted feeding, in particular, has been shown to lower fasting glucose levels, improve HbA1c, and reduce glycemic variability, even without major weight loss. These approaches also help regulate hormonal patterns and reduce metabolic stress, making chrononutrition a promising adjunct dietary strategy in the management of T2DM (Reytor-González *et al*., 2025) [31].

Table 1: Chrononutrition Interventions in Type 2 Diabetes Mellitus (T2DM) – Evidence from Previous Studies

Author (Year)	Study Design	Population	Intervention / Exposure	Duration	Key Outcomes on Glycemic Control & Insulin Sensitivity
Sutton *et al*. (2018) [32]	Randomized Controlled Trial	Men with prediabetes	Early Time-Restricted Feeding (6-hour window, early day)	5 weeks	Improved insulin sensitivity, reduced fasting insulin, improved β-cell function
Kahleova *et al*. (2017) [18]	Randomized Controlled Trial	T2DM patients	2 meals/day (breakfast + lunch) vs 6 meals/day	12 weeks	Reduced HbA1c, improved insulin sensitivity, weight loss
Jakubowicz *et al*. (2015) [16]	Randomized Controlled Trial	Obese individuals with T2DM	High-calorie breakfast vs high-calorie dinner	12 weeks	Improved glycemic control, reduced postprandial glucose, better insulin

					response
Parr *et al*. (2020) [28]	Randomized Controlled Trial	Overweight adults	Early vs delayed eating window	4 weeks	Early eating improved insulin sensitivity and glycemic response
Hutchison *et al*. (2019) [14]	Randomized Controlled Trial	Overweight adults at risk of T2DM	Time-Restricted Feeding (8–10 hrs)	4 weeks	Reduced fasting glucose, improved insulin sensitivity
Morris *et al*. (2019) [25]	Experimental Study	Healthy adults	Night-time eating vs daytime eating	Acute	Night eating increased postprandial glucose and impaired insulin response
Pot *et al*. (2016) [30]	Observational Study	Adults	Breakfast skipping	Cross-sectional	Higher postprandial glucose, increased risk of T2DM
Tsitsou *et al*. (2022)	Systematic Review	Adults	Time-Restricted Feeding	—	Improved glucose regulation and insulin sensitivity
Reytor-González *et al*. (2025) [31]	Review	Adults with metabolic disorders	Chrononutrition strategies (early eating, TRF)	—	Improved glycemic control, reduced metabolic stress

1. Gestational Diabetes Mellitus

In gestational diabetes mellitus (GDM), emerging evidence suggests that meal timing plays an important role in regulating maternal glucose levels and improving pregnancy outcomes. Proper alignment of food intake with circadian rhythms may enhance insulin sensitivity and reduce postprandial glucose excursions during pregnancy. Studies indicate that distributing energy intake earlier in the day and avoiding late-night meals can help maintain better glycemic control in pregnant women. However, research in this area is still limited, and variability in study design and population characteristics necessitates further investigation to establish standardized chrononutrition guidelines for GDM management (Montemayor *et al*., 2026) [24].

Table 2: Chrononutrition and Gestational Diabetes Mellitus (GDM) – Evidence from Previous Studies

Author (Year)	Study Design	Population	Chrononutrition Exposure / Intervention	Duration	Key Findings on Glycemic Control
Montemayor *et al*. (2026) [24]	Review	Pregnant women with GDM	Meal timing & circadian alignment	—	Early energy intake improves glycemic control; late eating worsens glucose regulation
Loy *et al*. (2020) [22]	Observational Study	Pregnant women	Eating timing patterns	Cross-sectional	Late-night eating associated with higher glucose levels and poor glycemic control
Bandín *et al*. (2015) [3]	Experimental Study	Healthy adults (applied to GDM context)	Morning vs evening meal timing	Acute	Better glucose tolerance in morning suggests relevance for pregnancy glucose control
Tsitsou *et al*. (2022)	Systematic Review	Adults (general metabolic studies)	Time-restricted feeding	—	Improved insulin sensitivity; potential application in GDM
Loy & Chan (2021)	Review	Pregnant women	Chrononutrition patterns	—	Aligning meals with circadian rhythm may improve maternal glucose metabolism

2. Obesity

Chrononutrition interventions, particularly time-restricted feeding (TRF) and early eating patterns, have shown beneficial effects in individuals with obesity by promoting weight loss and improving metabolic health. Limiting food intake to a specific time window helps regulate energy balance, reduce caloric intake, and improve circadian alignment, all of which contribute to enhanced insulin sensitivity (Hammad and Shakoor, 2026) [13]. Early-day eating further supports better glucose metabolism by aligning nutrient intake with peak insulin responsiveness. These combined effects not only facilitate weight reduction but also improve lipid profiles, reduce inflammation, and lower the risk of insulin resistance, thereby indirectly enhancing glycemic control in obese individuals (Fernandes-Alves *et al*., 2026) [34].

Table 3: Chrononutrition Interventions in Obesity and Their Impact on Insulin Sensitivity and Glycemic Control

Author (Year)	Study Design	Population	Intervention / Exposure	Duration	Key Findings on Weight, Insulin Sensitivity & Glycemic Control
Hammad and Shakoor (2026) [13]	Review	Obese adults	Time-Restricted Feeding (TRF)	—	Improved insulin sensitivity, reduced caloric intake, enhanced metabolic health
Fernandes-Alves *et al*. (2026) [10]	Review	Obese individuals	Early eating patterns & TRF	—	Weight loss, improved lipid profile, reduced inflammation, better glycemic control
Sutton *et al*. (2018) [32]	Randomized Controlled Trial	Men with prediabetes & obesity	Early Time-Restricted Feeding (6-hour window)	5 weeks	Improved insulin sensitivity, reduced fasting insulin, no significant weight loss required
Hutchison *et al*. (2019) [14]	Randomized Controlled Trial	Overweight/obese adults	TRF (8–10 hour eating window)	4 weeks	Reduced fasting glucose, improved insulin sensitivity, modest weight loss
Parr *et al*. (2020) [28]	Randomized Controlled Trial	Overweight men	Early vs delayed eating window	4 weeks	Early eating improved glycemic control and insulin response
Gabel *et al*. (2018) [11]	Clinical Trial	Obese adults	8-hour TRF (16:8 fasting)	12 weeks	Significant weight loss, reduced fasting insulin, improved insulin resistance

Garaulet *et al.* (2013)	Cohort Study	Overweight/obese individuals	Late vs early eating	Long-term	Late eating associated with slower weight loss and poorer insulin sensitivity
Jakubowicz *et al.* (2013) [15]	Randomized Controlled Trial	Obese women	High-calorie breakfast vs dinner	12 weeks	Greater weight loss and improved glucose metabolism with breakfast-heavy diet
Tsitsou *et al.* (2022)	Systematic Review	Adults	Time-Restricted Feeding	—	TRF improves metabolic markers, insulin sensitivity, and body composition

Table: 4 Summary of Previous Studies on the Impact of Chrononutrition on Insulin Sensitivity and Glycemic Control

Author (Year)	Study Design	Population	Chrononutrition Intervention / Exposure	Key Findings on Insulin Sensitivity & Glycemic Control
Adafer *et al.* (2020) [1]	Systematic Review	Adults	Meal timing & circadian alignment	Early eating improves glucose metabolism; late eating increases insulin resistance
Sutton *et al.* (2018) [32]	Randomized Controlled Trial	Prediabetic men	Early Time-Restricted Feeding (6-hour window)	Improved insulin sensitivity, reduced fasting insulin, better β-cell responsiveness
Jakubowicz *et al.* (2015) [16]	Randomized Controlled Trial	Women with obesity	High-calorie breakfast vs dinner	Larger breakfast improved glycemic control and reduced postprandial glucose
Hutchison *et al.* (2019) [14]	Randomized Controlled Trial	Overweight adults	Time-Restricted Feeding (8–10 hrs)	Reduced fasting glucose and improved insulin sensitivity
Almoosawi *et al.* (2013)	Observational Study	Adults	Irregular meal timing	Increased risk of metabolic syndrome and impaired glycemic control
Garaulet *et al.* (2017) [12]	Cohort Study	Overweight individuals	Late lunch eating	Late eaters showed poorer glucose tolerance and reduced insulin sensitivity
Morris *et al.* (2019) [25]	Experimental Study	Healthy adults	Night-time eating	Elevated postprandial glucose and reduced insulin efficiency at night
Kahleova *et al.* (2024) [19]	Randomized Controlled Trial	T2DM patients	Two meals/day vs six meals/day	Reduced HbA1c and improved insulin sensitivity with fewer meals earlier in day
Pot *et al.* (2016) [30]	Observational Study	Adults	Breakfast skipping	Higher postprandial glucose and increased T2DM risk
Tsitsou *et al.* (2023) [35]	Systematic Review	Adults	Time-Restricted Feeding	TRF improves glucose regulation and insulin sensitivity
Parr *et al.* (2020) [28]	Randomized Controlled Trial	Overweight men	Early vs delayed eating window	Early eating improved glycemic control and insulin response
Bandín *et al.* (2015) [3]	Experimental Study	Healthy adults	Morning vs evening meals	Better glucose tolerance and insulin sensitivity in morning

Conclusion

Chrononutrition significantly influences insulin sensitivity and glycemic control through its interaction with circadian rhythms. Evidence supports that early meal timing, regular eating patterns, and time-restricted feeding improve metabolic outcomes, whereas late-night eating and circadian misalignment impair glucose regulation. Despite promising findings, further high-quality research is required to establish standardized guidelines. Incorporating chrononutrition into dietary recommendations may enhance the prevention and management of diabetes and related metabolic disorders.

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