A REVIEW ON CHRONONUTRITION: The Impact of Meal Timing in Diabetes Management

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Abstract

The study of chrononutrition is the relationship between meal timing and composition and metabolic health has become important in the treatment of diabetes, especially type 2 diabetic mellitus (T2DM). This method acknowledges that our biological clocks affect how our bodies use energy, and that eating habits that are out of sync with our circadian rhythms can worsen glucose dysregulation and insulin resistance. Studies show that eating at different times of day, particularly late at night, can aggravate the effects on metabolic health and raise postprandial glycemia. Research has indicated that eating meals earlier in the day helps improve glycaemic control.This is especiallytrue when eating a balanced macronutrient distribution, which includes foods with higher protein and lower glycaemic index. Additionally, consuming foods in a certain order vegetable before carbohydrates, for example has been connected to better blood glucose responses. People with diabetes may experience improved glycaemic control and general metabolic health by coordinating their food choices with their circadian cycles. This emerging field of research highlights the need for additional research to develop practical food programs that consider chrononutrition concepts. If successful, these tactics may provide non-pharmacological ways to reduce the rising incidence of diabetes worldwide.

*Keywords**:** chrononutrition, diabetes, glycemic control, circadian rhythms, metabolic health.*

1. Introduction:

Chrononutrition, the science of aligning eating patterns with the body's circadian rhythms, has garnered increasing attention in recent years, particularly concerning its impact on metabolic health and diabetes management. Rooted in chronobiology, chrononutrition recognizes that "when" a person eats is as important as "what" they eat. This paradigm shift emphasizes the timing, frequency, and regularity of meals to enhance the body's metabolic response, thereby offering promising avenues for those managing chronic conditions like diabetes [7]. With diabetes prevalence reaching epidemic proportions worldwide, understanding how meal timing can optimize blood glucose levels and insulin sensitivity represents an innovative approach to improving long-term health outcomes. Diabetes, characterized by chronic high blood glucose levels due to impaired insulin secretion or insulin resistance, has traditionally been managed through diet, physical activity, and medication [6]. However, emerging research highlights how irregular eating patterns and late-night eating can exacerbate glucose dysregulation in individuals with diabetes, suggesting that meal timing could play a critical role in disease management [8]. This evolving field, linking circadian biology with nutritional practices, proposes that meal timing should coincide with the body's natural metabolic rhythms, potentially offering improved glycemic control and reducing diabetes complications. The basis of chrononutrition lies in the circadian clock, a biological system that regulates various physiological processes, including metabolism, appetite, and hormone secretion, on a roughly 24-hour cycle. There is evidence that the circadian rhythm affects glucose metabolism and insulin sensitivity, both of which change dramatically during the day. For example, insulin sensitivity is often higher in the morning and falls during the day, indicating that the body is better able to digest glucose in the morning [9]. Consequently, consuming larger meals earlier, in line with these natural fluctuations, can support better blood glucose regulation. This is particularly relevant for people with diabetes, where optimal glucose management is essential for preventing complications such as cardiovascular disease and neuropathy [10]. Moreover, meal timing may affect various aspects of energy balance and hunger regulation, potentially reducing overall caloric intake and promoting weight loss, both critical factors in diabetes management. Studies have shown that late-night eating can lead to impaired glucose tolerance and reduced insulin sensitivity, independent of the meal's macronutrient composition [12]. By front-loading caloric intake to earlier parts of the day, individuals may experience better blood glucose control and reduced hunger later in the day, potentially lowering the risk of overeating and weight gain, which can exacerbate diabetes symptoms. Research also indicates that intermittent fasting and time-restricted feeding, forms of chrononutrition that limit eating to specific windows, may improve glucose metabolism and insulin sensitivity in individuals with type 2 diabetes [11]. These strategies align with the body's natural rhythms and reduce the exposure to postprandial glucose spikes, offering potential therapeutic benefits. While more research is needed to establish specific guidelines, current findings support that adopting chrononutrition practices could play a significant role in optimizing diabetes management and enhancing quality of life.

In this article, we explore how chrononutrition principles can benefit people with diabetes, including the biological mechanisms that underpin this approach and practical meal-timing strategies. By aligning eating habits with the body's natural circadian rhythms, individuals may achieve improved blood glucose control, reduced insulin resistance, and a more manageable path toward overall wellness.

2. Circadian rhythm and glucose metabolism:

Circadian rhythms, which are roughly 24-hour cycles in physiological processes, are critical for maintaining homeostasis and are intimately tied to glucose metabolism. The relationship between glucose regulation and circadian biology has drawn a lot of attention in metabolic research, emphasizing how irregularities in circadian rhythms can exacerbate metabolic diseases like diabetes and obesity. A molecular clock that is largely controlled by the hypothalamic suprachiasmatic nucleus (SCN) is responsible for the circadian rhythm, which synchronizes with environmental stimuli such as temperature and light. This clock then orchestrates peripheral clocks in various tissues, including the liver, muscle, and adipose tissue, which are directly involved in glucose metabolism. Circadian clocks affect metabolic health by regulating the expression of genes that govern insulin sensitivity, glucose synthesis, and glucose absorption. According to some studies, insulin sensitivity and glucose tolerance are higher in the morning and progressively decrease throughout the day because glucose metabolism exhibits a diurnal pattern. Because glucose is more easily stored as glycogen in the muscles and liver during times of high insulin sensitivity, this cycle aids in optimising energy consumption and storage. Insulin resistance and an increased risk of metabolic disorders can result from disruptions to this cycle, such as shift work or inconsistent sleep, which can affect glucose tolerance [13,14]. Further research has shown that insulin signalling pathways and the secretion of hormones like glucagon also exhibit circadian variation. For instance, the pancreas's β-cells, which produce insulin, are subject to circadian modulation that influences their function and the subsequent handling of postprandial glucose [15]. Moreover, animal studies reveal that misalignment of feeding times with circadian rhythms, such as eating during the typical sleeping period, results in significant impairments in glucose metabolism and increased body weight [16]. These insights underscore the importance of aligning lifestyle factors, like eating and sleeping schedules, with our innate circadian rhythms to maintain glucose homeostasis and reduce the risk of metabolic disorders.

2.1. *Circadian Regulation of Glucose Metabolism:*

Daily Rhythms in Metabolism: The circadian system orchestrates metabolic processes by alternating between active (feeding) and resting (fasting) phases. During active periods, glucose primarily derives from dietary sources, while during rest, the body relies on stored energy, particularly from liver glycogen[1,2].

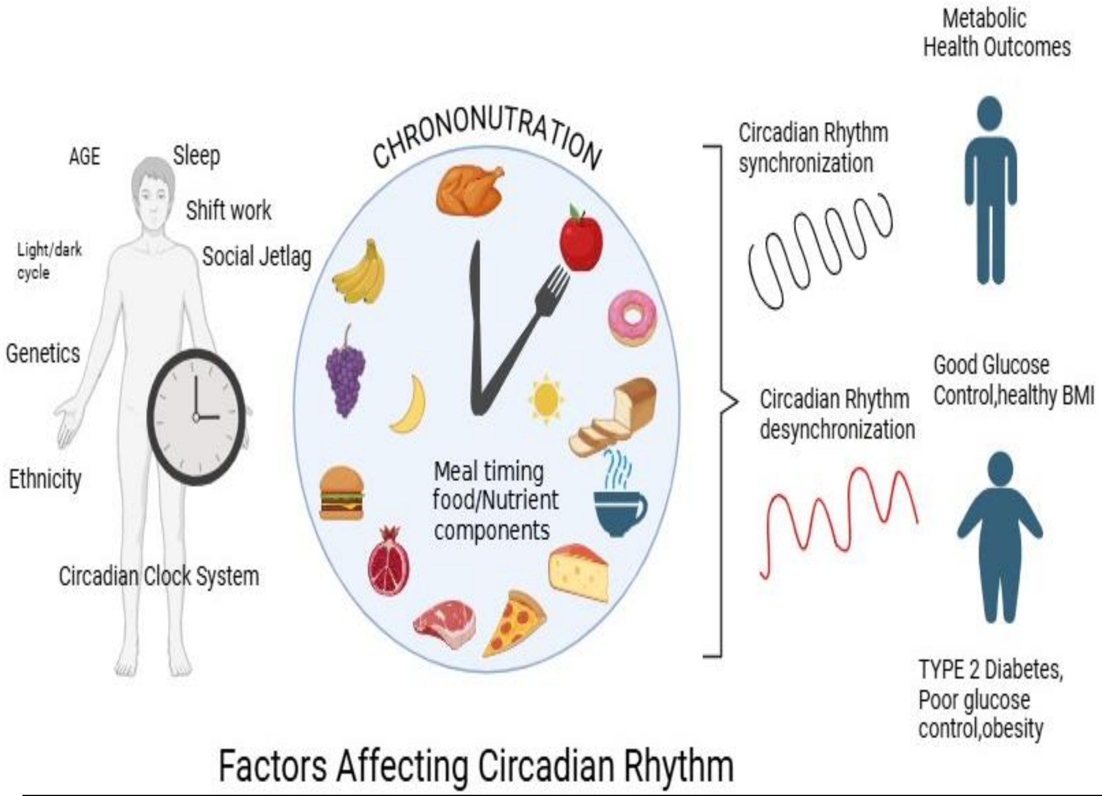

Fig. 1: A schematic representation outlining the factors affecting the circadian clock system.

Insulin Secretion Patterns: Insulin secretion is influenced by circadian rhythms, with peak levels typically occurring in alignment with feeding times. Studies indicate that insulin secretion shows a daily rhythm, peaking around midday and decreasing during the night[3]. This rhythmicity is crucial for maintaining glucose homeostasis and preventing metabolic disorders.

Role of Peripheral Clocks: Beyond the central clock in the SCN, peripheral clocks located in tissues such as the liver, pancreas, and muscle also regulate glucose metabolism. For instance, pancreatic islet cells exhibit circadian variations in insulin release, which are essential for effective glucose clearance from the bloodstream [2].

2.2 Impact of Circadian Disruption on Metabolism

Disruptions to circadian rhythms often caused by irregular sleep patterns or shift work—can lead to significant metabolic dysregulation:

Impaired Insulin Action: Circadian misalignment has been linked to decreased insulin sensitivity and impaired insulin secretion, contributing to conditions like Type 2 Diabetes Mellitus (T2DM).

Altered Glucose Tolerance: Studies show that acute disruptions can lead to increased blood glucose levels and reduced tolerance [3][5]. Genome-wide association studies have identified genetic variants associated with circadian genes that correlate with higher risks of hyperglycemia and T2DM.

2.3 Mechanisms Underlying Circadian Control

The mechanisms through which circadian rhythms influence glucose metabolism involve complex interactions between hormonal signals and metabolic pathways:

HPA Axis Regulation: The hypothalamic-pituitary-adrenal (HPA) axis plays a pivotal role in maintaining glucose homeostasis through glucocorticoid secretion, which exhibits its own circadian rhythm. This axis is influenced by the circadian clock, further linking daily cycles to metabolic control [3].

Molecular Feedback Loops: The expression of several genes involved in glucose metabolism is regulated by core clock genes like BMAL1 and CLOCK. These genes affect lipid metabolism in adipose tissues and the generation of glycogen in the liver and muscle [3].

3. Meal Timings and Glucose Metabolism:

Optimising health, especially for those with metabolic diseases like diabetes, requires an understanding of the connection between meal timing and glucose metabolism. Meal timing has been shown to have a substantial impact on insulin sensitivity, blood glucose levels, and general metabolic health.

3.1 Impact of Meal Timing on Glucose Levels:

Early Dinner Benefits: A study demonstrated that consuming dinner earlier, specifically at 18:00 instead of 21:00, resulted in improved 24-hour blood glucose levels and enhanced lipid metabolism the following day. This study highlighted a significant decrease in postprandial respiratory quotient, suggesting better metabolic efficiency with earlier meal timing [17] [18].

Breakfast Importance: Skipping breakfast has been linked to higher blood glucose concentrations and increased insulin resistance later in the day. Individuals who omit breakfast tend to experience elevated glucose levels during afternoon and evening periods, which can lead to poor glycemic control. Conversely, having a substantial breakfast can improve fasting glucose levels and insulin response throughout the day [19] [20].

Circadian Rhythms: The body's circadian rhythms play a vital role in glucose metabolism. Research shows that glucose tolerance is generally highest in the morning, with decreased sensitivity observed later in the day. This variation suggests that consuming more calories earlier in the day may enhance metabolic outcomes [20] [21].

3.2 Meal Frequency and Composition:

Regular Meal Patterns: Maintaining a consistent meal schedule with two to three balanced meals per day is recommended for optimal glucose control. Irregular eating patterns can disrupt metabolic processes, leading to challenges in regulating blood sugar levels [21] [22].

Macronutrient Timing: The composition of meals also matters. High-carbohydrate meals consumed late in the day can exacerbate glucose intolerance. In contrast, higher protein or fiber intake earlier can mitigate these effects and promote better glycemic responses [23].

3.3 Recommendations for Optimal Glucose Management:

Eat Breakfast Within 1-2 Hours of Waking: This practice helps kick-start metabolism and stabilize blood sugar levels throughout the day. Evidence suggests that breakfast consumption is linked to improved glycemic control and may help prevent fluctuations in blood sugar levels later in the day [22].

Schedule Lunch Around Midday: Eating lunch at a consistent time around midday can help stabilize glucose fluctuations throughout the day. Regular meal timing aids in the body's metabolic processes, promoting better insulin sensitivity and overall glucose management.

Have Dinner 2-3 Hours Before Bedtime: It is advisable to have dinner at least two to three hours before bedtime. Research indicates that early dinners are linked to improved overnight glucose profiles and a reduced risk of insulin resistance. Eating too close to bedtime can disrupt circadian rhythms and lead to higher fasting blood sugar levels the following morning. A study found that individuals who ate dinner at 6 PM had significantly lower blood sugar levels compared to those who dined at 9 PM, demonstrating the benefits of early time-restricted eating (ETRE) on glycaemic control [24].

Limit Late-Night Snacking: Avoiding food intake close to bedtime can help prevent disturbances in overnight glucose regulation. Late-night eating is associated with increased blood sugar spikes and metabolic dysfunctions. Experts recommend stopping food consumption about three hours before sleep to allow for proper digestion and minimize the risk of nocturnal glucose intolerance.

4. Meal intakes timing of ingestion: morning versus dinner:

The timing of meal intake plays a crucial role in metabolism, digestion, and overall health. Understanding the differences between morning and dinner meal timings can help optimize nutrition and well-being.

4.1 Morning Meal Timing: Breakfast

Importance of Breakfast: Breakfast is often referred to as the most important meal of the day because it breaks the overnight fast and kickstarts metabolism. Consuming breakfast within an hour of waking can enhance energy levels and stabilize blood sugar, setting a positive tone for the day ahead. Research indicates that eating breakfast early can lead to better weight management and improved metabolic health. For instance, studies have shown that those who eat breakfast within the recommended time frame are less likely to feel hungry later in the day and may have a lower body mass index (BMI) compared to those who skip breakfast or eat it later [25].

Metabolic Benefits: Research indicates that eating a high-calorie breakfast can improve insulin sensitivity and promote better weight management. For instance, studies show that individuals who consume more calories in the morning tend to have lower body mass indexes compared to those who eat larger dinners. This is likely due to the body's heightened metabolic rate in the morning, which gradually declines throughout the day. A study found that a high-calorie breakfast led to greater weight loss and reductions in waist circumference, with significant decreases in fasting glucose and insulin levels compared to a high-calorie dinner [26] [27]. Another study highlighted that a meal schedule including a high-energy breakfast improved weight loss and diabetes management in patients with obesity and type 2 diabetes, demonstrating that meal timing is crucial for metabolic health.

Recommended Timing: Experts recommend having breakfast between 6 a.m. and 10 a.m., ideally within the first hour after waking up. This timing aligns with the body's natural circadian rhythms, facilitating better digestion and nutrient absorption.

4.2 Evening Meal Timing: Dinner:

Impact of Late Dinners: Eating dinner too late, particularly close to bedtime, can disrupt digestion and interfere with sleep quality. The liver, which performs detoxification processes during sleep, may be burdened if digestion is still occurring. Late-night eating has also been linked to increased fat accumulation and poorer glucose tolerance, especially for individuals with evening chronotypes who are predisposed to weight gain when consuming calories late in the day [28].

Optimal Dinner Timing: To promote better health outcomes, it is generally advised to have dinner no later than 8 p.m., allowing at least two hours between the last meal and bedtime. This gap aids digestion and enhances sleep quality by allowing the body to focus on restorative processes rather than digestion [28].

Table no 1: Breakfast and Dinner timing chart

Aspect	**Morning (Breakfast)**	**Evening (Dinner)**
Ideal Timing	Within 1 hour of waking (6-10 a.m.)	No later than 8 p.m.
Metabolic Impact	Boosts metabolism; enhances insulin sensitivity.	Can hinder metabolism; may disrupt sleep.
Health Benefits	Stabilizes blood sugar; promotes energy.	Supports detoxification; aids digestion.
Consequences of Poor Timing	Skipping breakfast linked to obesity.	Late dinner linked to weight gain.

4. Time of Nutrient Intake and Glucose Metabolism:

Understanding the timing of nutrient intake is crucial for optimizing glucose metabolism and overall energy balance. The macronutrients carbohydrates, proteins, and fats play distinct roles in energy provision and metabolic processes.

Carbohydrates: Carbohydrates are the primary source of energy, providing 4 kcal per gram. They are broken down into glucose, which is essential for brain function and muscle activity. The body prefers glucose for immediate energy, converting excess glucose into glycogen or fat for storage. A diet should ideally consist of 45-65% carbohydrates to meet energy needs effectively [29].

Proteins: Proteins also provide 4 kcal per gram, but their primary role is not energy provision; instead, they are crucial for tissue repair and growth. During periods of low carbohydrate intake, proteins can be converted into glucose via gluconeogenesis [30].

Fats: Fats yield the most energy at 9 kcal per gram. They are metabolized more slowly compared to carbohydrates, making them a long-term energy source. However, high-fat diets can lead to increased fat storage if not balanced with carbohydrate intake [30].

Time-Restricted Eating: Time-restricted eating (TRE), which limits caloric intake to a specific time window each day, has been shown to improve metabolic health. A study involving 7,619 participants found that earlier meal start times were associated with lower fasting glucose levels and reduced insulin resistance. Specifically, every hour delay in meal commencement correlated with approximately 0.6% higher fasting glucose and a 3% increase in insulin resistance [31].

Circadian Rhythms: The body's circadian rhythms significantly affect glucose metabolism. Humans typically exhibit peak glucose tolerance in the morning, which declines throughout the day. Consuming meals that align with these natural rhythms can optimize metabolic processes, while mistimed eatingsuch as late-night mealscan lead to desynchronization of internal clocks, increasing the risk for obesity and type 2 diabetes [32].

Nutrient Composition and Sequence: The order in which nutrients are consumed during a meal also influences glucose levels. Consuming non-carbohydrate macronutrients (like proteins and fats) before carbohydrates can reduce postprandial blood glucose spikes by delaying gastric emptying and enhancing insulin response. This suggests that not only when we eat but also how we structure our meals can have profound effects on glucose metabolism [33] [34].

4.1 Physiological Mechanisms:

Insulin Regulation: After eating, insulin is secreted to facilitate glucose uptake into cells. The effectiveness of this process is influenced by meal timing; for instance, insulin sensitivity tends to be higher in the morning compared to later in the day. This variation underscores the importance of aligning meal times with periods of heightened metabolic activity [35].

Gluconeogenesis and Glycogenolysis: During fasting periods, such as overnight sleep, the liver performs gluconeogenesis to maintain blood glucose levels. Conversely, after meals, glycogen stored in the liver is mobilized to regulate blood sugar levels. The timing of food intake can thus impact these metabolic pathways [36].

5. Timing Fat and Protein Foods to Lower Glycaemic Response of Carbohydrate Meals:

The timing and composition of meals play a crucial role in managing blood glucose levels, particularly for individuals with diabetes or those at risk of developing it. Recent studies have shown that co-ingesting fat and protein with carbohydrate-rich foods can significantly lower the glycaemic response, which is the rise in blood glucose following a meal.

Protein's Role: Incorporating protein into carbohydrate meals has been shown to reduce postprandial glucose levels. A study found that adding protein to carbohydrate meals resulted in a lower incremental area under the curve (iAUC) for blood glucose compared to meals containing carbohydrates alone. This effect is particularly notable when protein is consumed before carbohydrates, as it enhances insulin secretion and improves glucose metabolism [37] [38] [39]. For instance, a high-protein diet has been demonstrated to lower blood glucose postprandially in individuals with type 2 diabetes, leading to improved overall glucose control

Fat's Influence: Dietary fat, particularly when consumed prior to carbohydrate intake, can also attenuate the glycaemic response. For instance, olive oil consumed half an hour before a starchy meal significantly reduced postprandial glucose levels in type 2 diabetics. The delayed gastric emptying caused by fat slows the absorption of glucose into the bloodstream, leading to a more gradual increase in blood sugar levels [40].

Timing and Sequence of Food Intake: The order in which foods are consumed can further optimize glycaemic control. Consuming vegetables first, followed by protein sources like meat, and then carbohydrates such as rice has been shown to lower blood glucose spikes. This sequence allows for the fiber and nutrients from vegetables to slow down carbohydrate digestion [38] [39].

6. Timing the consumption of food components for glycaemic control:

Effective management of glycaemia is influenced by not only the types of foods consumed but also their timing within meals. Research highlights several strategies that can optimize glycaemic responses, particularly for individuals with diabetes.

Food Order: The sequence in which foods are consumed can significantly impact blood glucose levels. Studies indicate that consuming vegetables or low-glycaemic index (GI) foods before high-carbohydrate items can lead to lower postprandial glucose peaks. For instance, eating kiwifruit (KF) prior to wheaten biscuits (WB) resulted in reduced glycaemic responses compared to simultaneous consumption [41] [42]. This suggests that the order of food intake is crucial for managing blood sugar levels effectively.

Temporal Separation: Introducing a time gap between different food components can also be beneficial. Consuming KF 30 minutes before WB was found to optimize satiety while minimizing glycaemic spikes, suggesting that a separation of about 30 minutes between carbohydrate-rich and other food items could enhance glycaemic control [41] [43].

Meal Splitting:Dividing carbohydrate intake into smaller portions spread throughout the meal may help moderate glycaemic responses. For example, a carbohydrate-rich entrée followed by a lower carbohydrate main course could reduce peak glucose levels [44]. This approach supports the idea that meal frequency and timing play significant roles in controlling postprandial glucose excursions, especially in diabetic patients [45].

7. Meal Frequency and Circadian Patterns:

Regular Meal Patterns: Evidence suggests that maintaining a consistent meal schedule, including breakfast and multiple smaller meals, is associated with better glycaemic control in individuals with type 1 diabetes. Skipping breakfast was linked to higher daily blood glucose levels and poorer overall control [46] [47].

Circadian Influence: The timing of meals relative to the body's circadian rhythms can also affect glucose metabolism. Consuming larger meals earlier in the day rather than in the evening has been shown to produce lower postprandial glucose levels, likely due to greater insulin sensitivity in the morning [48].

7.1 Glycaemic Index and Load:

Low-GI Foods: Incorporating low-GI foods throughout the day can help maintain stable blood sugar levels. A diet rich in low-GI carbohydrates has been associated with reduced postprandial blood glucose levels over 24 hours [49].

Glycaemic Load Management: Reducing the overall glycaemic load by selecting foods with lower carbohydrate content or higher fiber can further assist in controlling blood sugar spikes after meals [48].

8. CONCLUSION:

Research on the effects of meal time on metabolic health, or chrononutrition, has become a key component of diabetes management, especially Type 2 diabetes (T2D). Aligning eating habits with the body's circadian rhythms has a significant influence, according to recent studies. The timing of food intake may be just as important as the nutritional content itself, as key data show that late-night eating is associated with worse glycaemic management regardless of meal composition.

- Glycaemic control and insulin sensitivity are generally improved in people who eat their larger meals earlier in the day. There is evidence to support this, since diets that emphasise breakfast can dramatically lower post-prandial glucose levels when compared to diets that eat larger meals later.
- Time-restricted feeding and other chrono-nutrition techniques have been linked to better metabolic results, such as lower fasting blood glucose levels and a lack of need for diabetes medication.

Conflict of Interest:

The authors have no conflict of interest.

REFERENCES:

1. Poggiogalle, E., Jamshed, H., & Peterson, C. M. (2018). Circadian regulation of glucose, lipid, and energy metabolism in humans. *Metabolism*, *84*, 11-27. doi: 10.1016/j.metabol.2017.11.017
2. Kalsbeek, A., La Fleur, S., & Fliers, E. (2014). Circadian control of glucose metabolism. *Molecular metabolism*, *3*(4), 372-383.doi: 10.1016/j.molmet.2014.03.002
3. Hong Thuan Tran, Takeru Kondo, Amal Ashry et al. (2024). Effect of circadian clock disruption on type 2 diabetes. Chronobiology, Volume 15. https://doi.org/10.3389/fphys.2024.1435848
4. Ch, R., Rey, G., Ray, S. *et al.* (2021) Rhythmic glucose metabolism regulates the redox circadian clockwork in human red blood cells. *Nat Commun* **12**, 377. https://doi.org/10.1038/s41467-020-20479-4
5. Amirali Hariri, Mina Mirian, Ali Zarrabi et al. (2023) The circadian rhythm: an influential soundtrack in the diabetes story. Clinical Diabetes. Volume 14. https://doi.org/10.3389/fendo.2023.1156757
6. American Diabetes Association. (2022). *Standards of Medical Care in Diabetes—2022*. Diabetes Care, 45(Supplement 1), S1-S264. https://doi.org/10.2337/dc22-SINT
7. Gabel, K., Marcell, J., Cienfuegos, S., Kalam, F., &Varady, K. A. (2021). Time-restricted eating for the prevention and management of metabolic diseases. *Endocrine Reviews, 42*(3), 405-441. https://doi.org/10.1210/endrev/bnab001
8. Hutchison, A. T., Regmi, P., Manoogian, E. N., Fleischer, J. G., Wittert, G. A., Panda, S., & Heilbronn, L. K. (2022). Time-restricted eating improves glucose metabolism in men at risk for type 2 diabetes: A randomized crossover trial. *Obesity, 30*(3), 675-684. https://doi.org/10.1002/oby.23365
9. Qian, J., Scheer, F. A., & Hu, K. (2016). Effects of meal timing and fasting on the circadian regulation of glycemic control in humans. *Proceedings of the National Academy of Sciences, 113*(10), E1300-E1305. https://doi.org/10.1073/pnas.1511758113
10. Schroder, E. A., Harfmann, B. D., Zhang, X., England, J. H., Hodge, B. A., Wen, Y., &Esser, K. A. (2017). Intrinsic muscle clock is necessary for musculoskeletal health. *The Journal of Physiology, 595*(6), 1691-1707. https://doi.org/10.1113/JP273511
11. Stenvers, D. J., Scheer, F. A. J. L., Schrauwen, P., La Fleur, S. E., &Kalsbeek, A. (2019). Circadian clocks and insulin resistance. *Nature Reviews Endocrinology, 15*(2), 75-89. https://doi.org/10.1038/s41574-018-0122-1
12. Zhu, Y., & Luo, W. (2020). The effects of meal timing on blood glucose and insulin: Implications for shift workers and night eaters. *Nutrients, 12*(6), 1909. https://doi.org/10.3390/nu12061909
13. Panda, S. (2016). *Circadian physiology of metabolism*. Science, 354(6315), 1008-1015.
14. Bass, J., & Takahashi, J. S. (2010). *Circadian integration of metabolism and energetics*. Science, 330(6009), 1349-1354.
15. Qian, J., & Scheer, F. A. (2016). *Circadian system and glucose metabolism: Implications for physiology and disease*. Trends in Endocrinology & Metabolism, 27(5), 282-293.
16. Salgado-Delgado, R., et al. (2013). *Disruption of circadian rhythms: A crucial factor in metabolic disorders*. International Journal of Endocrinology, 2013.
17. Nakamura, K., Tajiri, E., Hatamoto, Y., Ando, T., Shimoda, S., & Yoshimura, E. (2021). Eating dinner early improves 24-h blood glucose levels and boosts lipid metabolism after breakfast the next day: a randomized cross-over trial. *Nutrients*, *13*(7), 2424.
18. Morgan, L. M., Shi, J. W., Hampton, S. M., & Frost, G. (2012). Effect of meal timing and glycaemic index on glucose control and insulin secretion in healthy volunteers. *British Journal of Nutrition*, *108*(7), 1286-1291.
19. Ahola, A. J., Mutter, S., Forsblom, C., Harjutsalo, V., &Groop, P. H. (2019). Meal timing, meal frequency, and breakfast skipping in adult individuals with type 1 diabetes–associations with glycaemic control. *Scientific reports*, *9*(1), 20063.
20. Alkhulaifi, F., &Darkoh, C. (2022). Meal timing, meal frequency and metabolic syndrome. *Nutrients*, *14*(9), 1719.
21. Bertelsen, J., Christiansen, C., Thomsen, C., Poulsen, P. L., Vestergaard, S., Steinov, A., ... & Hermansen, K. (1993). Effect of meal frequency on blood glucose, insulin, and free fatty acids in NIDDM subjects. *Diabetes care*, *16*(1), 4-7.
22. Gómez-Ruiz, R. P., Cabello-Hernández, A. I., Gómez-Pérez, F. J., & Gómez-Sámano, M. Á. (2024). Meal frequency strategies for the management of type 2 diabetes subjects: A systematic review. *Plos one*, *19*(2), e0298531.
23. Morgan, L. M., Shi, J. W., Hampton, S. M., & Frost, G. (2012). Effect of meal timing and glycaemic index on glucose control and insulin secretion in healthy volunteers. *British Journal of Nutrition*, *108*(7), 1286-1291.
24. Nakamura, K., Tajiri, E., Hatamoto, Y., Ando, T., Shimoda, S., & Yoshimura, E. (2021). Eating dinner early improves 24-h blood glucose levels and boosts lipid metabolism after breakfast the next day: a randomized cross-over trial. *Nutrients*, *13*(7), 2424.
25. Lopez-Minguez, J., Gómez-Abellán, P., &Garaulet, M. (2019). Timing of breakfast, lunch, and dinner. Effects on obesity and metabolic risk. *Nutrients*, *11*(11), 2624.
26. Jakubowicz, D., Barnea, M., Wainstein, J., &Froy, O. (2013). High caloric intake at breakfast vs. dinner differentially influences weight loss of overweight and obese women. *Obesity*, *21*(12), 2504-2512.
27. Jakubowicz, D., Wainstein, J., Tsameret, S., & Landau, Z. (2021). Role of high energy breakfast "big breakfast diet" in clock gene regulation of postprandial hyperglycemia and weight loss in type 2 diabetes. *Nutrients*, *13*(5), 1558.
28. Gu, C., Brereton, N., Schweitzer, A., Cotter, M., Duan, D., Børsheim, E., ... & Jun, J. C. (2020). Metabolic effects of late dinner in healthy volunteers—a randomized crossover clinical trial. *The Journal of Clinical Endocrinology & Metabolism*, *105*(8), 2789-2802.
29. Nakrani, M. N., Wineland, R. H., & Anjum, F. (2020). Physiology, glucose metabolism.
30. Remesar, X., &Alemany, M. (2020). Dietary energy partition: The central role of glucose. *International journal of molecular sciences*, *21*(20), 7729.

31. Ludwig, D. S., Apovian, C. M., Aronne, L. J., Astrup, A., Cantley, L. C., Ebbeling, C. B., ... & Friedman, M. I. (2022). Competing paradigms of obesity pathogenesis: energy balance versus carbohydrate-insulin models. *European journal of clinical nutrition*, *76*(9), 1209-1221.
32. Long, T. Diabetes Type 2: Nothing Sweet About It.
33. Kubota, S., Liu, Y., Iizuka, K., Kuwata, H., Seino, Y., & Yabe, D. (2020). A review of recent findings on meal sequence: An attractive dietary approach to prevention and management of type 2 diabetes. *Nutrients*, *12*(9), 2502.
34. Nesti, L., Mengozzi, A., &Tricò, D. (2019). Impact of nutrient type and sequence on glucose tolerance: physiological insights and therapeutic implications. *Frontiers in Endocrinology*, *10*, 144.
35. Versteeg, R. I., Ackermans, M. T., Nederveen, A. J., Fliers, E., Serlie, M. J., & La Fleur, S. E. (2018). Meal timing effects on insulin sensitivity and intrahepatic triglycerides during weight loss. *International Journal of Obesity*, *42*(2), 156-162.
36. Versteeg, R. I., Ackermans, M. T., Nederveen, A. J., Fliers, E., Serlie, M. J., & La Fleur, S. E. (2018). Meal timing effects on insulin sensitivity and intrahepatic triglycerides during weight loss. *International Journal of Obesity*, *42*(2), 156-162.
37. Gannon, M. C., Nuttall, F. Q., Saeed, A., Jordan, K., & Hoover, H. (2003). An increase in dietary protein improves the blood glucose response in persons with type 2 diabetes. *The American journal of clinical nutrition*, *78*(4), 734-741.
38. Beaudry, K. M., & Devries, M. C. (2019). Nutritional strategies to combat type 2 diabetes in aging adults: the importance of protein. *Frontiers in Nutrition*, *6*, 465683.
39. Nuttall, F. Q., & Gannon, M. C. (2013). Dietary protein and the blood glucose concentration. *Diabetes*, *62*(5), 1371.
40. Dugardin, C., Fleury, L., Touche, V., Ahdach, F., Lesage, J., Tenenbaum, M., ... &Cudennec, B. (2022). An exploratory study of the role of dietary proteins in the regulation of intestinal glucose absorption. *Frontiers in Nutrition*, *8*, 769773.
41. Mishra, S., McLaughlin, A., &Monro, J. (2023). Food order and timing effects on glycaemic and satiety responses to partial fruit-for-cereal carbohydrate exchange: A randomized cross-over human intervention study. *Nutrients*, *15*(14), 3269.
42. Morgan, L. M., Shi, J. W., Hampton, S. M., & Frost, G. (2012). Effect of meal timing and glycaemic index on glucose control and insulin secretion in healthy volunteers. *British Journal of Nutrition*, *108*(7), 1286-1291.
43. Sivakumar, E., Saranya, V., & Swaminathan, P. (2023). Correlation of meal timing and interval with glycemic control in patients with Type 2 diabetes. *National Journal of Physiology, Pharmacy and Pharmacology*, *13*(4), 895-898.
44. Henry, C. J., Kaur, B., & Quek, R. Y. C. (2020). Chrononutrition in the management of diabetes. *Nutrition & diabetes*, *10*(1), 6.
45. Ahola, A. J., Mutter, S., Forsblom, C., Harjutsalo, V., &Groop, P. H. (2019). Meal timing, meal frequency, and breakfast skipping in adult individuals with type 1 diabetes–associations with glycaemic control. *Scientific reports*, *9*(1), 20063.
46. Kalsbeek, A., La Fleur, S., & Fliers, E. (2014). Circadian control of glucose metabolism. *Molecular metabolism*, *3*(4), 372-383.
47. Hariri, A., Mirian, M., Zarrabi, A., Kohandel, M., Amini-Pozveh, M., Aref, A. R., ... & Sivakumar, P. M. (2023). The circadian rhythm: an influential soundtrack in the diabetes story. *Frontiers in Endocrinology*, *14*, 1156757.
48. Mason, I. C., Qian, J., Adler, G. K., & Scheer, F. A. (2020). Impact of circadian disruption on glucose metabolism: implications for type 2 diabetes. *Diabetologia*, *63*(3), 462-472.
49. Van Cauter, E., Polonsky, K. S., &Scheen, A. J. (1997). Roles of circadian rhythmicity and sleep in human glucose regulation. *Endocrine reviews*, *18*(5), 716-738.