Medical Science

To Cite:
Mandalian A, Malinowski M, Zadrożna K, Żelichowska N. Therapeutic potential of intermittent fasting regimens in type 2 diabetes mellitus: A literature review. *Medical Science* 2026; 30: e61ms3845
doi: https://doi.org/10.54905/disssi.v30i169.e61ms3845

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Peer-Review History
Received: 12 August 2025
Reviewed & Revised: 30/August/2025 to 07/March/2026
Accepted: 16 March 2026
Published: 30 March 2026

Peer-review Method
External peer-review was done through double-blind method.

Medical Science
pISSN 2321–7359; eISSN 2321–7367

DISCOVERY SCIENTIFIC SOCIETY

Therapeutic potential of intermittent fasting regimens in type 2 diabetes mellitus: A literature review

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ABSTRACT

Type 2 diabetes mellitus (T2DM) is a global medical problem. While Continuous Energy Restriction (CER) is the standard dietary intervention, it is frequently impeded by poor long-term adherence. Intermittent-Fasting (IF) and Time-Restricted Eating are subtypes of Intermittent-Fasting regimens. These interventions try to align food intake with the circadian rhythm of the pancreatic beta cells. The aim of this review is to reevaluate the effectiveness and safety of IF, with an emphasis on Time-Restricted Eating as an adjunctive therapy for T2DM. Our study will focus on reviewing the papers published between 2020 and 2025. We have mainly analyzed randomized controlled trials. We tried to emphasize the difference between IF and broader fasting protocols, with the main difference being the alignment of calorie intake with the circadian rhythm. Recent RCTs indicate that IF and TRE improve glycemic control and are responsible for weight loss. The effects are comparable to those of the Continuous Energy Restriction Diet. Time-restricted eating seems to represent a safe and effective therapeutic strategy for T2DM. It offers synergistic benefits when combined with exercise and might facilitate the reduction of pharmacological treatment. The mechanisms of time-restricted eating differ from those of CRE. According to Harris and Czaja, aligning caloric intake with the circadian rhythm promotes "beta-cell rest," which is an effect that reduces the secretory demand on beta-cells. The advantage of time-restricted eating over calorie-restricting diets lies in glycemic stability. It significantly improves "Time in Range" (TIR). Weight loss is a secondary result of unintentional calorie reduction.

Keywords: Type 2 diabetes, Time-restricted eating, Intermittent fasting, Circadian rhythm, Glycemic Control

1. INTRODUCTION

Treating Type 2 diabetes (T2DM) is often mistakenly equated with a solely pharmacological intervention. This logical fallacy leads to patients' disappointment, as without a properly adjusted diet, the treatment results will be unsatisfactory. Doctors typically recommend Continuous Energy Restriction to help patients control their weight and blood sugar. This means eating fewer calories every day. In practice, though, this is incredibly hard to do; patient adherence usually drops over time, risking weight regain and further disease progression. Because calorie counting often fails, researchers are looking for alternatives. The main issue with following a Continuous Energy Restriction diet is adhering to it. The IF diet seems

to be a more feasible approach than the Continuous Energy Restriction Diet. The IF diet focuses more on meal timing than on counting calories. The IF regimen that our paper focused on was time-restricted eating. This regimen does not require a full day of fasting, as in a 5:2 diet, where you eat ad libitum for 5 days and fast for 2 days. TRE asks us to stick to a set time window and consume all our calories within it. A popular model is a 16:8 window, which means fasting for 16 hours, including sleeping time. TRE does not require calorie counting. There is a physiological rationale behind. It seems to be more than spontaneous calorie restriction.

In a recent mechanistic paper, researchers demonstrate that modern eating patterns, characterized by high meal frequencies and nighttime consumption, lead to desynchronization of circadian clocks in the liver, adipose tissue, and pancreas. All of this contributes to insulin resistance (Harris and Czaja, 2023).

Although there are theoretical benefits, the clinical application of TRE in patients with T2DM is still a matter of debate, especially due to worries regarding the risk of hypoglycemia in insulin-treated patients. Earlier clinical guidelines published before 2023 recommended against the use of IF in patients with T2DM due to insufficient evidence (Choi et al., 2022). These recommendations and guidelines are challenged by emerging data of recent years that suggest that TRE may be both safer and more practical than CER in the T2DM population, while providing similar metabolic outcomes.

The aim of this review is to synthesize current evidence on the efficacy and safety of TRE as an adjunctive strategy in T2DM. Our paper evaluates the influence of TRE on glycemic control. Glycemic control will be measured, including metrics such as Time in Range (TIR), weight reduction, and the possibility of de-escalation of pharmacological treatment.

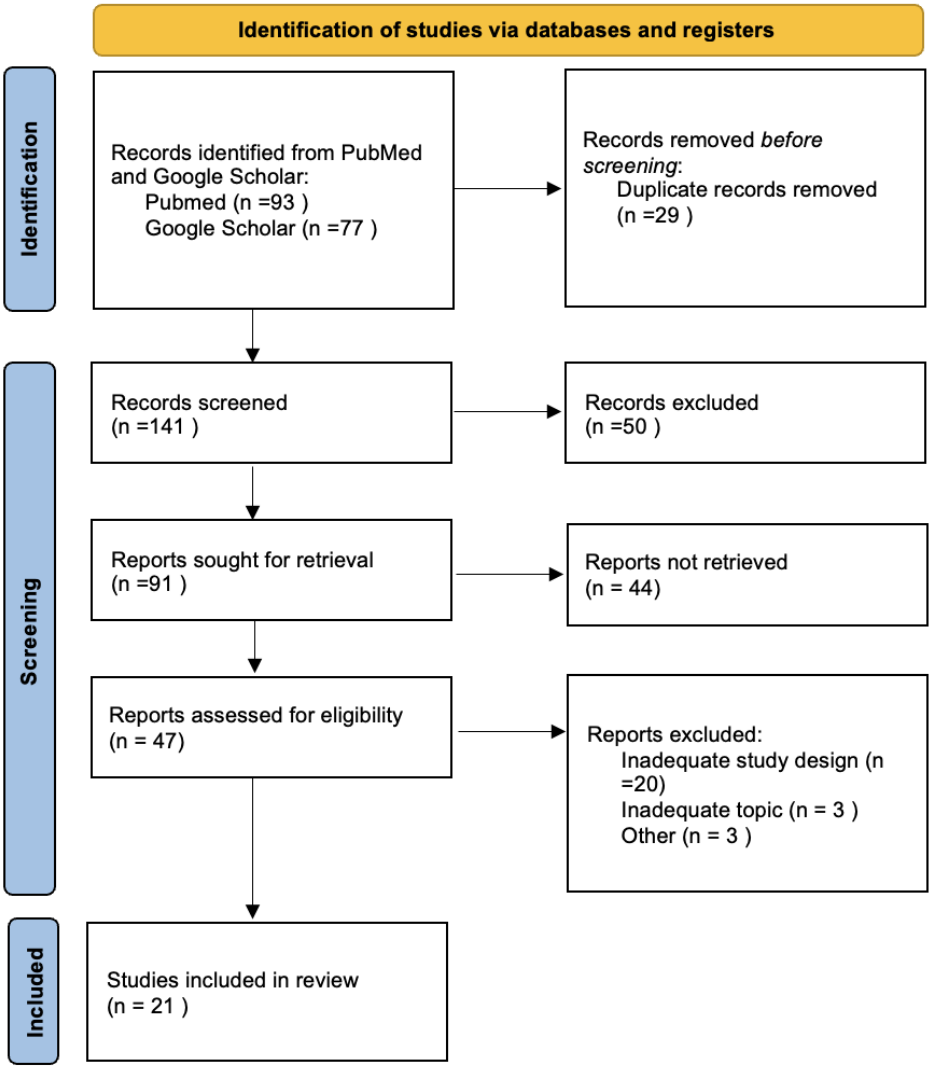

Figure 1. Prisma Flowchart.

2. REVIEW METHODS

A search was conducted in the PubMed database. Keywords included combinations of terms associated with intermittent fasting and type 2 diabetes. We searched for articles published between January 1, 2020, and January 2025. Studies were included if they involved either adults or the pediatric population with established T2DM undergoing IF protocols (including TRE) and reported on glycemic control, insulin sensitivity, safety outcomes, weight loss, or other metabolic outcomes. Data from randomized controlled trials, meta-analyses, and systematic reviews were considered and screened for relevance. The PRISMA flowchart illustrates the number of papers considered initially for this paper and the rejection process that followed (Figure 1).

3. RESULTS & DISCUSSION

3.1. Hypothetical Pathophysiological Mechanisms: Beta-Cells and Circadian Rhythm

According to Harris and Czaja (2023), the key difference between a CRE and a TRE is TRE's ability to induce what they call a beta-cell rest process. Harris and Czaja (2023), note that contemporary eating patterns disturb peripheral clocks in the pancreas and liver. TRE would realign calorie intake with the body's active phase. This could lead to optimized metabolic flexibility. This process lowered demand on the beta cells. This theory of "circadian alignment" is supported by Parrotta et al., (2025). In their paper, they note that fasting intervals induce autophagy and reduce oxidative stress in beta cells. This diminishes stress on the ER and preserves beta cell mass and function (Brown and Matveyenko, 2025), which is critical because loss of beta cell mass is a critical prognostic factor for the progression of T2DM; the decline in mass of beta cells is what leads to insulin therapy.

3.2. Impact on Glycemic Control and Weight Loss

Recent randomized controlled trials have provided evidence for the efficacy of various intermittent fasting regimens, including TRE. Recent evidence suggests that specific fasting protocols can be highly competitive with standard drug therapies. In a recent randomized controlled trial, the TRE intervention presented promising results. Implementation of TRE alongside a pharmacological intervention led to greater reductions in HbA1c and weight loss than either Metformin or Empagliflozin in monotherapy. The reduction in HbA1c was substantial, being -1,9%, and the reduction in weight was -9,7kg on average (Guo et al., 2024). A different RCT that focused on insulin-dependent patients and implemented a 3-day intermittent fasting schedule resulted in a -0.73% drop in HbA1c and a -4.8kg weight reduction. These results are meaningful enough to allow for downward adjustments in their insulin doses.

The evidence indicates that the effectiveness of time-restricted eating is similar to that of standard calorie-restricted diets. In a recent RCT that lasted for 3 months, participants followed a 16:8, 14:10, and a normal control diet. The group following a controlled diet was the control group. The weight change from baseline was most substantial in the 16:8 group. The weight change in the 16:8 group was -4.02% compared to -0.55% in the control group. Metabolic outcomes were significantly improved from baseline in both IF groups (Sukkriang and Buranapin, 2024).

Another point concerns the research by Parr et al., (2024), which found that a window of 9 hours for eating led to reductions in HbA1c comparable to those from standard dietary advice over 6 months. Additionally, the observation of Trico et al., (2024) showed a similar decrease in HbA1c in the group focusing on early carbohydrate consumption and the group following the Mediterranean diet. No additional metabolic benefit was found from restricting early carbohydrates compared with a Mediterranean diet with the same number of calories. This shows that the impact on patients' health is similar across these different methods of eating, dieting, and nutrition. Therefore, the option between these strategies may depend on the ability to follow the rules of the diet.

Meta-analyses by Nam et al., (2025) found that TRE specifically increases Time in Range (TIR) by 10.51% and reduces fasting glucose. Their work also showed that TRE stresses its role in stabilizing daily changes rather than just lowering average glycemia. Alternate Day Fasting (ADF) showed a slight advantage over Continuous Energy Restriction (CER) for weight loss, and daily TRE performed similarly to CER, according to a Meta-analysis by Semnani-Azad et al., (2025). These results show that periodic IF, such as 5:2, may drive weight loss and HbA1c reduction through caloric deficits sufficient to produce these effects. TRE primarily benefits glycemic stability. Weight loss during TRE would be a derivative of spontaneous and unintentional calorie restriction.

According to Bravo-Garcia et al., (2025) combining TRE with other habit modifications may improve treatment results. They conducted a randomized crossover trial examining the acute effects of combining an 8-hour TRE window (10:00–18:00) with post-meal exercise in patients with T2DM. TRE alone did not substantially change the 14-hour glucose area under the curve (AUC) when compared to a 12-hour eating window. However, implementing a post-meal exercise (15-minute walk, 2000 steps) had a potent effect on lowering insulin 14-h AUC.

A recent study provides evidence for the long-term effects of an intermittent fasting diet as the sustainability of its metabolic benefits remains a matter of debate. The metabolic benefits, such as reduction in HbA1c, HOMA-IR (an index of insulin resistance), and body weight, observed after the 6-month intervention were often maintained at the 12-month post-intervention follow-up. This suggests that IF might produce lasting metabolic benefits and that adherence post-intervention is significant (Ekberg et al., 2024). An overview of the key findings from the RCTs is shown in Table 1.

Table 1. Key findings of RCTs with emphasis on impact on glycemic control and weight loss

Author (Year)	Study population	Intervention Protocol	Key Findings
Guo et al., (2024)	Adulsts with T2DM	5:2 Diet (Meal replacement) vs. Metformin vs. Empagliflozin	The 5:2 diet resulted in superior HbA1c reduction (-1.9%) compared to pharmacological treatments (-1.6% and -1.5%) and significant weight loss (-9.7 kg).
Obermayer et al., (2023)	Insulin-treated T2DM patients	Intermittent Fasting (3 days/week) with 20% basal insulin reduction	Significant reduction in HbA1c (-0.73%) and body weight (-4.8 kg) without severe hypoglycemic events; enabled insulin dose reduction.
Sukkriang & Buranapin (2024)	Obese patients with T2DM	TRE 16:8 vs. TRE 14:10 (3 days/week)	Both protocols significantly reduced HbA1c. The 16:8 group achieved greater weight loss (-4.02%) compared to the 14:10 group (-3.15%).
Parr et al., (2024)	Adults with T2DM	9-hour TRE window vs. Standard Dietetic Advice	TRE resulted in HbA1c reductions comparable to standard care over 6 months; benefits were linked to weight loss rather than timing alone.
Hegedus et al., (2024)	Adolescents with T2DM	Late TRE (12:00–20:00)	High adherence (6.2 days/week) and spontaneous caloric reduction (-271 kcal/day); demonstrated feasibility of later eating windows.
Bravo-Garcia et al., (2025)	Adults with T2DM	8-hour TRE + Post-meal exercise	Combination of TRE and exercise significantly reduced insulin levels, suggesting a synergistic effect on insulin sensitivity.

3.3. Effects on Lipid Metabolism and Cardiovascular Risk

Glycemia is not the only metabolic parameter affected by TRE. In the INTERFAST-2 trial, Pammer et al., (2024) found that TRE did not improve HDL cholesterol more than a standard diet. According to Pammer et al., (2024) it did, however, increase serum levels of apolipoprotein M [ApoM]. ApoM is a marker linked to insulin sensitivity and lipid metabolism. Kirkham et al., (2022) reviewed that TRE consistently reduces blood pressure and may improve lipid profiles; these changes are proportional to the weight that was lost, so there is no indication that these changes are a result of TRE's additional metabolic benefits. A systematic review by Silva et al., (2023) indicated that the metabolic effects of TRE were heavily dependent on the patient's initial health status. Patients who were obese before starting an intervention have noticed major metabolic benefits. The metabolic benefits were visible in adiposity and lipid homeostasis.

Systolic blood pressure was statistically significantly reduced. The improvements for patients with T2DM were less pronounced but substantial in their major metabolic dysfunctions.

Timing and Feasibility

A recent RCT compared two fasting regimens- a 14:10 IF protocol with a 16:8 IF protocol. Both protocols reduced weight and HbA1c compared with controls. The protocol with a shorter eating window induced greater weight loss (-4,02% vs -3.15%). This indicates that following a narrower eating window corresponds with clinical benefits. A weight loss of -3.15% is still substantial compared with the control group (-0.55%) (Sukkriang and Buranapin, 2024). This suggests that patients do not need to stick to a narrower window to benefit from TRE. This significantly improves the feasibility of TRE.

Regarding the timing of the eating window, Hegedus et al., (2024) conducted a "Late TRE" protocol (12:00–20:00) in adolescents with T2DM. This feasibility trial reported high adherence (6.2 days/week) and a spontaneous caloric reduction of -271 kcal/day. This supports the theory that shifting the window to later hours is a viable option for populations that struggle with early restricted feeding.

Safety and Clinical Guidelines

In 2022, the Korean Diabetes Association recommended against the use of IF in the T2DM population. Questions have been brought up regarding the risk of hypoglycemia (Choi et al., 2022). RCT by Obermayer et al., (2023) challenges this recommendation. In their trial, the authors provide safety data for insulin-treated patients on a TRE diet. In their trial, no severe hypoglycemia occurred, and significant HbA1c reductions (-7.3mmol/mol) were achieved over 12 weeks. A reduction greater than 10% in insulin dose was also achieved. They concluded that IF is a safe dietary option for insulin-treated people with T2DM.

A systematic review concluded that patients undergoing the TRE regimen may lower the dose of oral antihyperglycemic medication. Across 13 reviewed studies, 4 reported a successful reduction in medication during the intervention (van den Burg et al., 2023). The argument continues over whether TRE impacts sleep quality. An RCT from 2024 found that an 8-hour window TRE (12.00-20.00) did not alter either sleep duration or quality. It has also not exacerbated pre-existing insomnia compared to the comparison group (Pavlou et al., 2024).

The crucial discussion in the current literature is whether results in weight loss, decrease in HbA1c, glucose AUC, and HOMA-IR are a result of a spontaneous calorie restriction that would accompany TRE or a result of an extra benefit of TRE that is the induction of the beta-cell rest. A study by Parr et al. suggests that when control groups actually adhere to calorie counting, the extra effect of TRE is negligible.

This supports the hypothesis, implying that TRE is primarily a behavioral tool to facilitate energy deficit without the need to count calories. On the other hand, the meta-analysis by Nam et al., identifying considerable improvements in Time in Range (TIR), and the finding by Bravo-Garcia et al. regarding synergistic insulin-lowering effects of exercise, suggest metabolic benefits beyond those from weight loss. The authors claim that these results are an effect of the restoration of the peripheral circadian clocks.

As we noted above, the 2022 consensus by the Korean Diabetes Association recommended against Intermittent Fasting in T2DM. Their concerns were due to hypoglycemia and a lack of evidence (Choi et al., 2022). In contrast, an RCT demonstrated that TRE is safe even in insulin-treated patients if medication doses are adjusted, for example, a 20% reduction in basal insulin on fasting days (Guo et al., 2024). Researchers claim that TRE shouldn't be contraindicated but rather treated as a dietary strategy that requires supervision of a professional.

However, it is worth noting that TRE has its limitations. Liu et al. found that the metabolic benefits of TRE are most powerful in the short term (<3 months) and disappear after discontinuation (Liu et al., 2025). Fortunately, researchers found that post- intervention adherence is high (Ekberg et al., 2024).

4. CONCLUSION

The evidence gathered in this paper points to the conclusion that IF, with an emphasis on the TRE regimen, is a viable dietary intervention in patients with T2DM. Regardless of where the benefits of TRE stem from, it is a diet that produces significant weight loss and, according to high-quality trials, does not result in hypoglycemic events if appropriate changes in drug administration are made. 2022 guidelines against IF in T2DM recommending against IF in T2DM need to be re-evaluated. The concerns regarding a TRE diet were due to hypoglycemia. High-quality RCTs did not note hypoglycemic events when adjustments in insulin doses were made.

Future clinical practice should focus on adjusting medication doses and personalizing the eating window in order to achieve the best clinical outcomes.

Acknowledgments
We would like to express my sincere gratitude to all those who supported me throughout the course of this work.

Authors' Contributions
Andrzej Mandalian: Conceptualisation, methodology, formal analysis, investigation
Andrzej Mandalian: Methodology, writing – original draft
Maciej Malinowski: Formal analysis, writing – review & editing
Natalia Żelichowska: Resources, data curation, writing – review & editing
Katazyna Zadrożna: Resources, data curation
Katarzyna Zadrożna: Visualisation
All authors have read and agreed with the final, published version of the manuscript.

Informed consent
Not applicable.

Ethical approval
Not applicable. This article does not contain any studies with human participants or animals performed by any of the authors.

Funding
This research did not receive any external funding like specific grant from funding agencies in the public, commercial, or nonprofit sectors.

Conflict of interest
The authors declare that they have no conflicts of interest, competing financial interests or personal relationships that could have influenced the work reported in this paper.

Data and materials availability
All data associated with this study will be available based on a reasonable request to the corresponding author.

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