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REVIEW ARTICLE

Intermittent Fasting as a Complementary Strategy to Manage Type II Diabetes and Metabolic Health: A Review

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Abstract

As an alternative or supplement to traditional pharmaceutical treatments, intermittent fasting (IF) has become a viable dietary approach for the management of type 2 diabetes mellitus (T2DM). Improved insulin sensitivity and blood glucose management are the outcomes of various IF patterns, such as time-restricted eating, alternate-day fasting and the 5:2 diet, which encourage a metabolic shift from glucose to fat utilisation. Even in patients on insulin therapy, research indicates that IF may help lower fasting blood sugar, glycated haemoglobin (HbA_1c) and insulin resistance with no risk of hypoglycaemia when appropriately monitored. Physiological benefits of IF include enhanced circadian rhythm alignment, increased autophagy, reduced oxidative stress and improved lipid metabolism. Comparisons with other dietary approaches, such as the Mediterranean, Palaeolithic, ketogenic and fasting-mimicking diets, indicate that IF offers flexibility and long-term sustainability for many individuals. However, consistent adherence and personalised strategies are essential for optimal results. Overall, IF presents a valuable complementary approach for managing T2DM and promoting better metabolic health.

Key words: Intermittent fasting; Ramadan fasting; Diabetes mellitus, type 2; Feeding; Behaviour.

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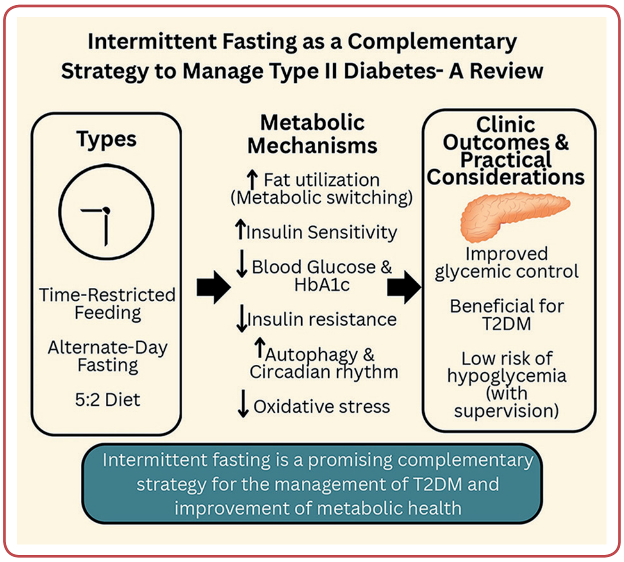

Graphical abstract

Introduction

More than 500 million adults have type 2 diabetes mellitus (T2DM), which is the most common chronic condition in the world, affecting about 90 % of all diabetes cases. The disease is a significant cause of life-threatening complications at both the microvascular and macrovascular levels, including kidney, nerve and eye diseases and cardiovascular disease, respectively. Despite pharmacological advances, many individuals fail to achieve optimal glycaemic control and global prevalence continues to rise due to sedentary lifestyles and poor dietary patterns. These challenges highlight the need for novel, sustainable,

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cost-effective dietary interventions that complement standard diabetes management.[1]

Intermittent fasting (IF) is a dietary intervention for T2DM that is becoming increasingly popular. Traditional approaches to diabetes management, including calorie restriction and carbohydrate monitoring, often prove challenging to sustain over extended periods, with many patients struggling with dietary adherence, weight regain and fluctuations in glycaemic control. Periods of low or no calorie intake alternate with regular meals during IF. The 5:2 diet, which limits intake to 500–600 calories on two non-consecutive days each week, alternate-day fasting and time-restricted eating (eg 16:8) are common strategies.[2-5] Fasting also has a long cultural and religious history such as Ramadan, Lent and Ayurvedic practices demonstrating the body's natural adaptation to feeding and fasting cycles.

A growing body of clinical evidence suggests that IF has been shown in some studies to improve insulin sensitivity, lower glycated haemoglobin (HbA_1c) and reduce fasting blood glucose, including in certain individuals on insulin therapy, though results vary across populations and regimens.[6-8] The physiological mechanisms underlying these potential benefits including metabolic switching, AMP-activated protein kinase (AMPK) activation, circadian alignment and autophagy are discussed in detail below. Despite these promising findings, IF is not universally appropriate for all individuals with diabetes and careful medical management is advised particularly for those on insulin or other glucose-lowering drugs.[2, 6, 9, 10] This review examined the mechanisms, clinical evidence, dietary comparisons, safety and practical considerations of IF as a complementary strategy in T2DM management.[3, 4, 8, 11, 12]

Methods

A literature search was conducted across multiple scientific databases, including *PubMed, Google Scholar, ScienceDirect, Elsevier, Springer* and *Scopus*. The search was limited to publications from January 2005 to February 2025 to capture contemporary evidence while encompassing foundational studies in the field. Search terms included combinations of "intermittent fasting," "time-restricted eating," "alternate-day fasting," "5:2 diet," "type 2 diabetes," "glycaemic control," "insulin resistance" and "obesity." Studies were eligible for inclusion if they: (1) were published in English with full text available; (2) involved human subjects or, where mechanistic insights were sought, animal or *in vitro* models; (3) examined the effects of IF on glycaemic outcomes, insulin sensitivity, body weight, or related cardiometabolic parameters; and (4) were randomised controlled trials (RCTs), prospective or retrospective cohort studies, systematic reviews, or meta-analyses. Book chapters and narrative reviews were included supplementarily to provide contextual background. Studies were excluded if they: (1) did not report outcomes relevant to T2DM or obesity; (2) were published in languages other than English; (3) were conference abstracts, editorials, or opinion pieces without original data; or (4) lacked sufficient methodological detail to allow critical appraisal.

Intermittent fasting

A dietary approach known as IF alternates times of regular eating with cycles of consuming less or no calories.[13-15] This strategy encompasses a range of fasting patterns, not just one, that are all intended to produce a brief energy shortage while permitting intervals of regular nourishment. An efficient method for controlling weight, improving metabolic health and maybe prolonging life, IF has drawn a lot of attention. Time-restricted fasting (TRF) and intermittent energy restriction (IER) are the two primary categories into which the practice is generally divided.[13]

Reducing overall caloric intake on certain days or during specified times while maintaining a regular diet on other days is known as intermittent energy restriction, or IER. One example is the 5:2 diet, which limits daily caloric consumption to about 25 % of daily needs on two non-consecutive days per week. TRF, on the other hand, restricts the daily eating window to a predetermined number of hours, usually between 6 and 12 hours, without necessarily changing the total amount of calories consumed. TRF may improve metabolic efficiency and maintain hormonal balance since it closely synchronises with the body's circadian rhythm. Collectively, these fasting strategies are not only flexible and adaptable to individual lifestyles but also have demonstrated benefits for glucose regulation, insulin sensitivity, weight loss, cardiovascular health and inflammation reduction, making IF a promising tool in both clinical and general population settings.

The primary mechanism by which IER supports weight loss is through reduced overall energy intake.[16] This fasting pattern typically consists of designated fasting days followed by feeding days. An everyday IER regimen includes fasting for five days, followed by two days of normal eating, often called a twice-weekly fast.[17-19] Alternate-day fasting (ADF) is a type of IER that includes fasting every other day. People avoid calorie-dense meals and drinks on fasting days, but they are free to consume anything they want on feeding days. A variation of this approach, known as alternate-day modified fasting (ADMF), allows limited calorie intake approximately 25–30 % of daily energy requirements within a 2–4 hour eating window on fasting days, while the remaining 75 % of energy intake is restricted.[19-21]

Another type of IF is the modified fasting regimen (MFR), which permits limited calorie intake typically around 20–25 % of daily energy needs on designated fasting days.[16, 19, 22, 23] This approach is exemplified by the 5:2 diet, where individuals restrict food consumption on two non-consecutive days each week and eat normally on the remaining five days.[24]

Another fasting technique is TRF, which sets set times for eating and fasting, such as an 8-hour meal followed by a 16-hour fast, without necessarily reducing caloric intake.[25] Fasting includes religious traditions like Ramadan, during which eating is permitted only between sunset and dawn. Since this approach involves designated fasting and eating periods of approximately 12 hours each, it is considered a form of time-restricted feeding, though there are no specific calorie restrictions.[13, 14, 26, 27]

Physiology of IF

The physiology of IF centres on the body's transitions through key metabolic states: fed, post-absorptive, fasting and starvation.[28] During the fed state, insulin is the dominant hormone, facilitating glucose uptake as the primary energy source. As fasting progresses and liver glycogen is depleted typically around 12 hours after the last meal glucagon becomes dominant, triggering glycogenolysis and subsequently a shift toward fat metabolism, with adipose-derived triglycerides serving as the primary fuel source. This transition, termed metabolic switching, involves a shift from glucose utilisation to ketone generation and may enhance body composition, particularly in overweight individuals.[29]

At the cellular level, the metabolic changes induced by IF activate AMPK in response to elevated AMP/ADP and decreased ATP. AMPK suppresses anabolic pathways and enhances mitochondrial function and autophagy. Simultaneously, decreased glucose and amino acid availability suppresses mTOR, increasing mitochondrial biogenesis and autophagy markers.[30, 31] Fasting also increases formation of ketone bodies particularly β-hydroxybutyrate depletes liver glycogen, releases fatty acids and activates hepatic β-oxidation. Sirtuins, NAD^+-dependent deacetylases activated during fasting, further encourage autophagy and reduce oxidative stress. Together, these pathways may promote improved metabolic health and longevity.[26] IF has also been associated in some studies with increased mitochondrial efficiency and enhanced antioxidant defences (catalase, superoxide dismutase), thereby reducing reactive oxygen species (ROS) formation a mechanism potentially relevant to slowing metabolic aging and attenuating diabetic complications, though long-term human evidence remains limited.[32]

Studies suggest that the body's intrinsic circadian rhythm is a primary factor in maintaining metabolic homeostasis, influencing gluconeogenesis, glycolysis, lipid metabolism, protein synthesis and mitochondrial activity.[33-37] When eating habits and circadian timing are misaligned, metabolic disturbances including elevated insulin resistance and oxidative stress may result. Animal models, particularly using time-restricted eating (TRE), have demonstrated improvements in adipose tissue function, gut microbiome composition and liver metabolism, with small-scale human studies largely supporting these findings.[38-40] Clinically, early time-restricted eating (eTRF) has been associated with improvements in blood pressure, glucose levels, triglycerides and inflammatory markers, suggesting that circadian alignment may contribute to IF's metabolic benefits independent of caloric intake.[24]

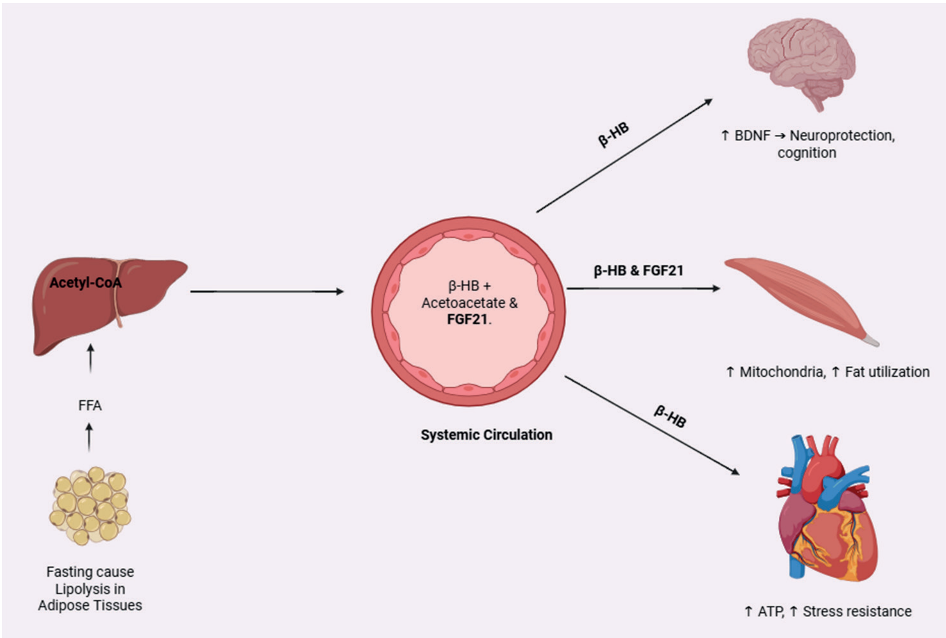

Figure 1: Metabolic adjustments to periodic fasting
BDNF: brain-derived neurotrophic factor; FGF21: Fibroblast growth factor 21; ß-HB: beta-hydroxybutyric acid; FFA: free fatty acids;

Beyond glycaemic and metabolic effects, fasting has been shown in animal and preliminary human studies to raise levels of brain-derived neurotrophic factor (BDNF), promoting synaptic plasticity and neural resilience factors increasingly relevant to diabetes-associated cognitive decline.[41] Collectively, these physiological adaptations integrating circadian biology, hormonal regulation, mitochondrial health and autophagy provide the mechanistic basis for IF's therapeutic potential in metabolic disorders, including T2DM (Figure 1).[42]

T2DM, insulin resistance and IF

People who are obese have a three to four times higher chance of getting diabetes than people who are normal weight and T2DM.[43] Impaired insulin secretion from pancreatic β-cells and decreased responsiveness of insulin-sensitive tissues are hallmarks of its pathogenesis, which frequently necessitates exogenous insulin therapy.[44] A number of theories have been put up to explain how insulin resistance develops, but one that is generally accepted links excessive body fat to long-term inflammation, which in turn fuels insulin resistance.[2] IF can help counteract this by reducing calorie intake, promoting weight loss and improving metabolic efficiency, thereby decreasing obesity-related insulin resistance. Another proposed mechanism suggests that the calorie reduction associated with IF leads to sustained decreases in insulin secretion and increased activation of AMPK, both of which enhance glucose regulation and insulin sensitivity.[2, 14]

The impact of IF on insulin sensitivity has been the subject of numerous clinical investigations in the literature. Studies assessing alternate-day fasting are among them.[45, 46] The 5:2 approach of IF[47-50] and ADMF protocols.[51-56] While not all studies reported these outcomes, overall, these show increases in insulin sensitivity and decreases in dyslipidaemia. Sutton et al conducted intriguing research examining how IF affected insulin sensitivity. This five-week randomised crossover study investigated the effects of eTRF in males with pre-diabetes under isocaloric conditions. Despite no significant changes in fasting glucose or glucose tolerance, eTRF was associated with meaningful reductions in fasting and postprandial insulin levels and improved insulin sensitivity and β-cell function, suggesting potential metabolic benefits independent of weight loss.[57, 58]

Many clinical investigations have shown similar results, suggesting that IF improves insulin sensitivity and decreases plasma insulin more efficiently than it does fasting glucose levels.[59-61] According to the Expert Panel Update of the 2002 Consensus Guidelines,[62] IF therapy led to considerable weight loss in both diabetes and non-diabetic groups, according to a large-scale trial with 741 individuals (completed n = 697). On average, people without diabetes dropped −4.31 ± 2.41 kg, whereas those with T2DM lost −5.29 ± 2.56 kg.[63] These findings suggest that IF, particularly eTRF, may offer potential benefits for metabolic health, insulin efficiency, β-cell function and weight management.

Comparisons to other regimens

Comparing IF with other dietary approaches reveals distinct metabolic effects and adherence challenges and is essential for positioning IF appropriately within evidence-based T2DM management. Caloric restriction (CR) involves reducing total caloric intake without resulting in malnutrition.[64] Numerous studies have demonstrated that CR can produce weight loss and may improve insulin sensitivity, mitochondrial function and cardiovascular risk factors in overweight individuals.[34, 65] However, investigations conducted over the past few decades have consistently demonstrated that most people cannot sustain CR for long periods, making long-term adherence challenging.[14] While IF and CR share similar short-term metabolic benefits, IF's flexible protocols may offer greater practicality. Further long-term randomised controlled trials are nonetheless needed to confirm IF's sustained superiority or equivalence.[66-69]

The Mediterranean diet, characterised by vegetables, legumes, fruits, whole grains, nuts, olive oil, moderate fish and dairy and limited red meat has accumulated the most consistent long-term evidence for cardiovascular and overall metabolic health benefits among the dietary approaches reviewed.[70] It remains the benchmark dietary approach for sustained cardiometabolic risk reduction. In a 12-month randomised controlled trial involving 250 overweight adults assigned to the Palaeolithic diet, IF, or Mediterranean diet, systolic blood pressure reduction was greatest in the Mediterranean diet group.[70] Christian Orthodox fasting, which closely mirrors the Mediterranean dietary pattern, has also been associated with favourable changes in adiponectin levels and may offer comparable metabolic benefits.[71-77]

The Palaeolithic diet attempts to improve health outcomes by excluding grains, legumes and dairy products.[78] A meta-analysis of 58 clinical trials involving 4,635 adults investigated its effects on chronic disease prevention, though results sometimes conflicted with its theoretical benefits. In comparative trials, the Palaeolithic diet was chosen least often by participants, suggesting lower acceptability relative to IF or the Mediterranean diet.[70] Evidence specifically in T2DM populations remains limited.

The ketogenic diet, characterised by very high fat and very low carbohydrate content, induces ketone body production and shifts energy metabolism from carbohydrates to lipids metabolic effects that partially overlap with those of fasting. In comparison to balanced low-calorie diets, it may produce more rapid initial weight loss.[79, 80] However, concerns regarding long-term sustainability, cardiovascular effects and the risk of hypoglycaemia in medicated T2DM patients limit its broad applicability and further research is required.

Periodic fasting typically water-only or very-low-calorie diets for two or more consecutive days has been associated in some studies with metabolic health benefits including improved insulin sensitivity and lipid metabolism, but carries risks of malnutrition, hypoglycaemia and hypotension when conducted outside of specialised clinical settings.[81-85] To avoid these adverse effects, a plant-based fasting-mimicking diet (FMD) has been developed, providing approximately 35–55 % of recommended daily caloric intake cyclically over 4–7 days every few weeks to months. Evidence from mouse models and a randomised clinical trial supports beneficial effects of repeated FMD cycles on aging biomarkers and metabolic disease risk factors; however, data in pharmacologically managed T2DM populations remain limited.[81-85]

Ramadan intermittent fasting (RIF), which involves complete abstinence from food and drink from dawn to sunset, has grown as a research topic, though its metabolic effects remain debated. Studies suggest modest weight loss[86] reported an average reduction of 1.2 kg without significant changes in body composition.[86, 87] Glycaemic outcomes in individuals with T2DM require particularly careful medication management during Ramadan, given the altered meal timing and risk of hypoglycaemia.

Feasibility of IF in modern lifestyle

Fasting can be challenging and its practicality in modern lifestyles is sometimes questioned. However, IF is considered more adaptable than other restrictive diets, such as ketogenic, vegan, or daily calorie-restricted plans, due to its multiple flexible protocols.[14] Additionally, IF aligns with the body's natural circadian rhythm, making it a more physiologically compatible approach. Tinsley et al[40, 88] examined the effects of time-restricted eating on lifestyle-related diseases in working adults and found that this pattern improved quality of life and was feasible to maintain.[89] Similarly, Wegman et al[90] evaluated the feasibility of IF in humans, with survey results suggested that participants successfully adhered to the fasting regimen.[91] Randomised trials and reviews showed that IF can be safe when implemented with structured medication adjustment, frequent glucose monitoring and patient education to reduce hypoglycaemia risk. Protocols typically include pre-emptive dose reductions of hypoglycaemiainducing agents and close followup, underlining that IF should be initiated and supervised by healthcare professionals rather than used as an unsupervised weightloss strategy. The American Diabetes Association (ADA) does not yet specifically endorse IF as a standard therapy, IF and timerestricted eating are conceptually aligned with ADA guidance on flexible, personcentred nutritional approaches, attention to meal timing/chrono nutrition and integration with pharmacologic treatment and diabetes technology.[5, 9, 92-95]

Discussion

Fasting-based dietary interventions are now emerging as possible treatment options for the prevention of diverse maladies, such as metabolic disorders, cardiovascular ailments, cancers, neurodegenerative disorders and obesity.[86] Long-term research must be undertaken to endorse the sustainability of interventions that promote health and deal with compliance, including randomised controlled trials with more than 1 year of follow-up. Whereas animal trials and, to a limited extent, clinical trials may limit feeding patterns, setting a time frame to consume food may be exceptionally difficult for humans. In the long run, among the dietary approaches reviewed, the Mediterranean diet currently has the most consistent evidence for long-term sustained improvements in cardiovascular risk factors, though comparisons across regimens are limited by heterogeneous study designs. In conjunction with each weight-reduction diet-subject redundancy, these aspects make selecting a given plan dependent on the patient to whom it will be applied. Not forgetting the torturous adherence to the chronic dietary program, such as IF and TRE, focus discussion on formulating high-efficacy intervention programs with short intervention periods to achieve successful long-term results.[96-101]

Comparing dietary approaches, such as IF, CR, the Mediterranean and Palaeolithic diets, ketogenic diets, periodic fasting and religious fasting practices, reveals distinct metabolic effects and differing challenges with adherence for each regimen. Calorie restriction and IF are sometimes viewed together, attributing to their seemingly similar benefits of weight loss and improvement of metabolic markers. Long-term adherence to calorie restriction is often challenging, while IF provides greater flexibility and can yield comparable metabolic benefits. However, further long-term randomised controlled trials are needed to confirm its sustainability and effectiveness.[66-69] The Mediterranean diet has accumulated considerable evidence supporting its association with cardiovascular health and overall health maintenance, though individual responses and adherence vary. This diet emphasises whole foods, healthy fats and moderate consumption of animal products, promoting long-term health through sustainable lifestyle habits. Similarly, Christian Orthodox Fasting possesses some characteristics common with the Mediterranean diet and holds promise for metabolic health. Very fashionable diets, such as the Paleo and ketogenic diets, may be effective in promoting weight loss and metabolic flexibility. Yet, they may lack long-term compliance due to their restricted nature. Among them, the ketogenic diet mimics several aspects of fasting by inducing ketone production and switching the body's energy metabolism; however, the very apprehensions regarding its sustainability in the long run and its effects on cardiovascular health call for more research. On the one hand, we have significant metabolic benefits from periodic fasting or adopting a water-only fast. On the other hand, they yield safety and practicality challenges. Therapeutic fasting in a hospital setting has controlled benefits, while fasting-mimicking diet

(FMD) has emerged as a solution that has efficacy with safety: the regular fasting episodes without the extreme calorie deprivation.[16, 17, 86, 102]

Religious fasting regimes have much more insight into their cultural and spiritual dimensions than their physiological ones. Research on RIF has shown slight weight loss effectiveness; however, the metabolic effects have yet to be reported. Beneficial changes in adiponectin levels appear to be influenced by OF, which may contribute to improved metabolic health.[103-105]

Some of the significant challenges involved in evaluating the different dietary interventions are compliance and sustainability. Fasting and calorie restriction can induce health benefits in the short run, but compliance with the dietary pattern is necessary to achieve health benefits in the long run. IF trials in T2DM report outcomes over 3–24 months; although shortterm improvements in HbA_1c, weight and insulin dose are consistent, longer followup shows that metabolic benefits often wane after discontinuation and robust data beyond two years are scarce.[94, 95] The Mediterranean diet may be seen as the exception because it is a practical and well-researched dietary plan with sustained cardiovascular and metabolic health benefits. Ultimately, any dietary scheme should consider personal preference, health status and lifestyle factors to provide sustained compliance with a plan for enhanced well-being.[106-109]

Conclusion

This review suggests that IF may serve as a flexible, physiologically grounded adjunct to standard care for T2DM across various protocols (time-restricted eating, alternate-day/5:2 patterns and fasting-mimicking cycles). Evidence from a number of studies indicates that IF may help reduce fasting glucose, HbA_1c, insulin resistance, body weight and cardiometabolic risk when implemented under medical supervision, though results appear heterogeneous and are likely dependent on population characteristics and the specific regimen employed. Mechanistically, IF has been proposed to leverage circadian alignment and "metabolic switching" (AMPK activation, mTOR down-regulation, enhanced autophagy and mitochondrial function), which may contribute to improvements in glycaemic control, although the clinical relevance of these pathways requires further investigation. While comparison with other dietary approaches suggests the Mediterranean pattern may have stronger long-term adherence data, IF could offer practical flexibility in certain populations; by contrast, more restrictive strategies may face sustainability or safety challenges outside controlled settings. IF is not universally appropriate particularly for patients on insulin or sulfonylureas, in whom hypoglycaemia risk warrants careful consideration and would require individualised protocols, patient education and thorough medication review. Key priorities for future research include the development of standardised regimens, trials with outcomes beyond 12 months, rigorous safety evaluation in medicated T2DM populations and assessment of real-world adherence. On balance, IF may be best considered a patient-centred, complementary strategy within evidence-based medical nutrition therapy, rather than a definitive intervention, pending more robust and consistent long-term evidence.

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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