

## SYSTEMATIC REVIEW

# Metabolic Benefit of Intermittent Fasting Among Type 2 Diabetes Mellitus Patients: A Systematic Review

Noraishah Mohamed Nor<sup>1,2</sup>, Nur Farhanim Mohd Fauzi<sup>1</sup>, Aflah Afandi<sup>1,2</sup>

<sup>1</sup> Department of Nutrition Sciences, Kulliyah of Allied Health Sciences, International Islamic University Malaysia, Jalan Sultan Ahmad Shah, 25200 Kuantan, Pahang, Malaysia

<sup>2</sup> Food Security And Public Health Nutrition Research Group (FOSTER)

## ABSTRACT

**Introduction:** The global economic burden is escalating due to the growing prevalence of Type 2 Diabetes Mellitus (T2DM). Maintaining T2DM remission and substantial weight loss is essential, and this review provides extensive evidence about the metabolic benefit of Intermittent Fasting (IF). **Methods:** The Preferred Reporting Items for Systematic Study and Meta-Analysis (PRISMA) procedure was utilized in this review. The search yielded 628 articles from the Scopus, ProQuest, PubMed, and Cochrane Library databases. The final 13 studies showed that IF can benefit individuals with T2DM. **Results:** Weight loss was more visible, while HbA1c and blood glucose levels could be improved. Time-restricted fasting (16 to 20 hours daily for at least five days a week) is the most suitable and feasible IF regimen for T2DM patients. **Conclusion:** IF appears to be a safe and effective strategy for improving glycemic control and promoting weight loss in patients with T2DM. However, careful monitoring of the types, quantities, and timing of food intake remains crucial to maximize its long-term benefits.

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## Corresponding Author:

Noraishah Mohamed Nor, PhD  
Email: ishah@iiu.edu.my  
Tel: +60 9 571 6400 ext. 531

## INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is a serious global health concern. It is a chronic metabolic disorder characterised by high blood sugar levels, resulting from a combination of factors such as decreased insulin production by  $\beta$ -cells of the pancreas, varying levels of insulin resistance, decreased glucose utilisation, increased hepatic glucose production, and low-grade systemic inflammation (1). In 2019, the global diabetes prevalence was estimated to be 9.3%, affecting 463 million people, and is projected to rise to 10.9% by 2045, affecting 700 million people (2). The National Health and Morbidity Survey (NHMS) revealed that the percentage of Malaysians with diabetes had risen from 11.2% to 18.3% (3). This metabolic disorder, which is often linked to obesity and a lack of physical activity, can cause long-term health problems and can be fatal.

The management of T2DM begins with lifestyle modifications and weight reduction; if this fails, medications can be prescribed. The purpose of treating

T2DM is to prevent or delay any complications and improve the quality of life (4). Even though it is an incurable disease, it can be reversed in individuals with a short duration of T2DM with sustained weight loss, calorie restriction, or bariatric surgery (5).

Intermittent Fasting (IF) has recently become a popular weight loss approach. It is a dieting strategy in which energy intake is intentionally limited over a certain period, also known as intermittent energy restriction (6). Common regimens include Alternate-Day Fasting (ADF), 5:2 Fasting Day, and Time-Restricted Feeding (TRF). For instance, ADF involves one day of reduced caloric intake (around 600 kcal for males and 500 kcal for females) and one day of unrestricted food consumption (7). Although IF is generally safe for most people, those with diabetes may be at risk of hypoglycemia and hyperglycemia due to fluctuations in blood sugar. Based on the findings of Albosta & Bakke (2021) (8), which point to IF as a practical non-pharmaceutical approach to managing T2DM, researchers have been eager to investigate it further. This is because IF seems to be a promising non-drug treatment for T2DM.

Numerous studies have shown that IF can be beneficial for people with diabetes. Employing IF can be advantageous for weight loss, decreasing fasting glucose

and insulin levels, insulin resistance, leptin levels, and boosting adiponectin levels (8–11). In some cases, patients under medical supervision have been able to stop taking insulin while following IF protocols, and this has been linked to considerable weight loss, particularly in heavier individuals and shorter time frames. However, it did not significantly affect HbA1c levels compared to those on a regular diet (10). Other reviews have revealed that short-term IF can reduce systolic blood pressure, insulin resistance, weight, LDL-cholesterol, triglycerides, and total cholesterol (9), and the result of another systematic review showed that BMI and fasting glucose levels decreased during IF periods compared to control groups (11).

Many of the existing reviews focused on the immediate advantages of intermittent fasting. To ensure healthcare professionals are able to provide informed advice to their patients with T2DM, this systematic review assesses the practical type and duration of well-tolerated intermittent fasting. The review focused on the long-term metabolic effects of IF on glycaemic control, intending to select the optimal IF regimen as a dietary intervention, ultimately improving the health and well-being of T2DM patients.

## METHODOLOGY

This systematic review followed the Preferred Reporting Items for Systematic and Meta-Analysis (PRISMA) (12) method, which included the flow diagram and checklist. Identification, screening and inclusion were all incorporated into the PRISMA method. This review was registered with PROSPERO (ID: CRD42022377296).

### Study selection

The literature search was conducted across several databases, including Scopus, ProQuest, Cochrane Library, and PubMed. Additionally, supplementary records were identified through alternative sources, such as Google Scholar, to ensure comprehensive coverage of relevant information of the topics of interest. Boolean Operators were utilised as a research strategy to identify relevant articles by inserting the appropriate keywords into the search engine. The complete search term was (“type 2 diabet\*”[Title/Abstract] OR “non-insulin dependent”[Title/Abstract] OR “diabetes mellitus” [Title/Abstract]) AND (“intermittent fasting”[Title/Abstract] OR “alternate day fasting”[Title/Abstract] OR “time-restricted fasting”[Title/Abstract] OR “periodic fasting” [Title/Abstract]).

Example of search string in the Scopus database: “Type 2 diabet\*” OR “non-insulin dependent” OR “diabetes mellitus” AND “Intermittent Fast\*” OR “Alternate day fast\*” OR “Time-restricted fast\*” OR “Periodic fast\*” AND “blood glucose control” OR “blood sugar control” OR “fasting blood glucose” OR “random blood glucose” Two independent reviewers (NFMF and NMN) first screened the articles from the selected databases by

their titles. Afterwards, the articles were further assessed according to the inclusion and exclusion criteria of the review (Table I). Subsequently, the articles were recorded, exported, and screened using Mendeley Software to eliminate duplicates. After the duplicates were removed, the remaining articles were evaluated for eligibility. Those full-text articles that did not satisfy the inclusion and exclusion criteria and did not address the research question were excluded from the study for specific reasons. Finally, the remaining full-text articles were included in the systematic review and synthesised systematically.

**Table I: Inclusion and exclusion criteria**

PICOS ELEMENTS
<p><b>Population:</b>  <i>Inclusion criteria:</i>            Female and male            Age 18 years old and above            Type 2 Diabetes Mellitus            English and Malay paper            Year: not limited</p> <p><i>Exclusion criteria:</i>            Animal studies            Review Paper            Ramadan Fasting</p>
<p><b>Intervention:</b> Intermittent fasting</p>
<p><b>Comparator:</b> None</p>
<p><b>Outcomes:</b> Blood glucose level, HbA1c</p>
<p><b>Study Design:</b>            Randomized Control Trials            Cross-sectional studies</p>

### Quality appraisal

The Quality Criteria Checklist for Primary Research (QCCPR) of the Academy of Nutrition and Dietetics (2012) was used to assess the quality of the article, including criteria for determining validity and bias (13). Ten questions were asked to evaluate the study's validity, covering topics such as the research question, sample population, sampling (bias and randomisation), intervention or exposure, measurement results, statistical analysis, and interpretation of findings. The QCCPR rates the quality of a study as positive, neutral, or negative. A high score indicates that most of the study components meet the validity requirements, while a neutral rating suggests that the study is not particularly strong. A low score, on the other hand, implies that most of the study does not meet the criteria for validity. The consensus of quality appraisal marks between the two reviewers was calculated to ensure the final total marks were more than 50% of the overall score and the included papers were high in quality (Abouzahra et al., 2020).

### Data analysis

The summary table (Table II) was derived from Cochrane and modified to suit the study's objectives. The data extracted from the included studies included author, country, and title; sources and year; purpose or problem; sample size and details; methodology or study design; duration of intervention enduring benefits of the

Table II: The summary of findings of the included studies (N=13)

Author (Year) Country	IF Regimens	IF Duration	$\Delta$ Body Weight from Baseline	$\Delta$ Blood Glu- cose level from Baseline	$\Delta$ HbA1c level from Baseline	Main Findings
Arnason et al., (2017) Canada	TRF	2 weeks	↓	↓	Not mea- sured	Individualized treatment plans for diabetes include lifestyle changes, medication, and weight loss strategies. However, many struggle to achieve or maintain these goals, leading to various drug combinations and obesity-related surgeries.
Andriessen et al., (2022) Netherlands	TRF	3 weeks	↓	↓	Not mea- sured	TRF significantly reduced overnight fasting glucose, extended normal and high glucose range periods, and consistently lower morning fasting glucose levels compared to CON.
Bhandari et al., (2022) India	TRF	4 weeks	↓	↓	-	The study found that fasting significantly improved fasting blood glucose levels, despite the insignificant effect of IF on insulin resistance due to its limited sample size.
Parr et al., (2020) Australia	TRF	4 weeks	↓	↓	↓	The study suggests that 4 weeks of TRF is feasible for T2DM patients, significantly influencing daily energy intake and preventing hypoglycaemia.
Obermayer et al., (2023) Austria	5:2	3 months	↓	Not measured	↓	The risk of hypoglycaemia during IF can be reduced by using a CGM system and reducing insulin dose on fasting days. However, it's crucial for participants and healthcare personnel to be instructed on insulin dose adjustments during IF.
Corle et al., (2018) Australia	5:2 (CON & NC)	3 months	↓	↓	↓	Any method of fasting increased the rate of hypoglycaemia in T2DM patients
Carter et al., (2016) Australia	5:2 (IER & CER)	3 months	↓	Not measured	↓	The study found significant decreases in measures over time, but not by treatment, and metformin continued to be taken even after 12 weeks of treatment.
Carter et al., (2018) Australia	5:2 (IER & CER)	12 months	↓	↓	↓	The study found that 5:2 IER is a suitable alternative to CER, with a significant decrease in insulin levels in both groups after three months of frequent follow-up visits.
Carter et al., (2019) Australia	5:2 (IER & CER)	12 months follow-up	↓	↓	↑	Total medication dose reduction was maintained over time (P = 0.004) and was not correlated to HbA1c.
Li et al., (2017) Germany	7-day modi- fied fasting	4 months	↓	↓	↓	There were no serious adverse effects in both groups.
Kahleova et al., (2014) Czech Republic	CR (A6 & B2)	5 months & 2 weeks	↓	↓	↓	The B2 regimen significantly reduced body weight, HFC, fasting plasma glucose, C-peptide, and glucagon, and improved insulin levels and sensitivity after 12 weeks of a two-meal-per-day schedule.
Sulaj et al., (2022) Germany	FMD	6 months	↓	↓	↓	After three diet cycles, 57% of FMD and 32% of M-Diet participants reduced antihyperglycemic medication, 67% after six cycles, but only 21% experienced severe hypoglycemia.
Gabel et al., (2019) United States	ADF & CR	12 months	↓	↓	Not measured	The ADF group experienced more significant reductions in fasting insulin and HOMA-IR markers compared to the control and CR groups at months 6 and 12.

Note:  $\Delta$  = change; IF (intermittent fasting); TRF (Time-Restricted Fasting); CON (consecutive day fasting); NC (non-consecutive day fasting); IER (Intermittent Energy Restriction); CER (Continuous Energy Restriction); FMD (Fasting-Mimicking Diet); ADF (Alternate-Day Fasting); CR (calories restriction); HFC (hepatic fat content)

intervention; and comments. The qualitative synthesis technique was adopted for the data abstraction.

**RESULTS**

**Overview of included studies**

A search for the term yielded 668 articles, of which 318 were from Scopus, 159 from PubMed, 63 from ProQuest, and 128 from the Cochrane Library. After eliminating duplicates, 628 articles were screened by their titles and abstracts, and 594 were deemed irrelevant and excluded. Fourteen articles that could not be retrieved were excluded, leaving only 20 for eligibility assessment. Out of the 20 full-text articles, ten were excluded from the eligibility stage as they did not meet the criteria; two articles used Ramadan fasting as the intervention, while the other eight were non-relevant. Additionally, seven records were identified through citation searching to complete the search. After assessing the seven articles for eligibility, three were included, resulting in 13 articles in this systematic review (Figure 1).

The selected studies were conducted in India (14), the Czech Republic (15), Germany (16,17), Australia (18–22), Austria (23), the Netherlands (24), the United States (25) and Canada (26). The mean age of the study population was between 18 and 77 years old, while the sample size varied from 10 to 137 subjects. These are all quantitative studies, including ten randomised control trials (n=10), pre-post studies (n=2), and an observational study (n=1). These studies met the quality appraisal

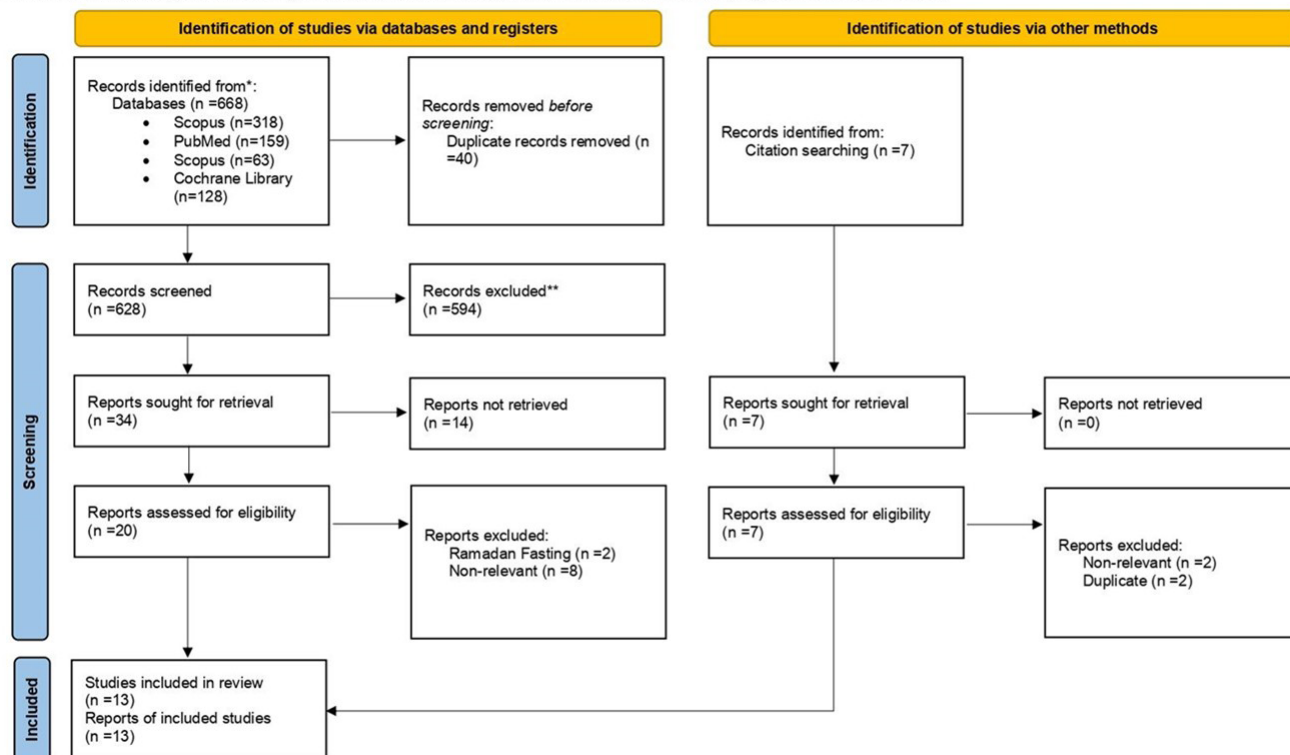
criteria, with scores ranging from neutral (18,19,26) to positive (14–17,20–23,25). The reporting of techniques, goals, and ethical approval was adequate in all studies.

**The acceptable duration of fasting**

The duration of the included studies varied from 2 to 48 weeks, with the most frequent length of intervention being 12 weeks. Most of the studies were randomised controlled trials, except for Arnason (2017) for a short 2-week observational study (26), Bhandari (2021) for 4-week pre-post study (14), and Parr (2020) for 6-week pre-post study (18). The 13 studies tested various IF protocols such as 5:2 Intermittent Energy Restriction (IER), Time-Restricted Fasting (TRF), Alternate-Day Fasting (ADF), Caloric Restriction (CR), Fasting-Mimicking Diet (FMD) and 7-day Modified Fasting. However, the effects of the 5:2 and Time Restricted Feeding (TRF) diets were the most studied.

Five studies have investigated the effects of the 5:2 Intermittent Energy Restriction (IER) diet on participants. This diet involves eating normally for five days, consecutively or non-consecutively, and then reducing energy intake to 1670–2500 kJ/day (400 -600 kcal/day) for two days. The control group followed a Continuous Energy Restriction (CER) of 5000–6500 kJ/day (1200-1400 kcal/d). Other studies used a 3-day non-consecutive IF intervention, with the intervention group consuming only 25% of the advised caloric intake, with no calorie restriction for the remaining four days. This suggests that a safe calorie range of 400-600 kcal per day for fasting

PRISMA 2020 flow diagram for new systematic reviews which included searches of databases, registers and other sources



\*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).  
 \*\*If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

**Figure 1: Results of study selection using PRISMA 2020 flow diagram**

days should be observed for two to three days each week, while maintaining a regular daily intake of 1200-1400 kcal on non-fasting days.

Time-restricted fasting (TRF) involves limiting food intake to a certain window time each day, usually 16 to 20 hours of fasting. One study implemented an 8-hour time frame for eating and 16 hours of fasting (14). Only non-caloric beverages such as water, coffee, and tea were allowed during fasting, but a balanced meal was encouraged in the 8-hour eating window. Parr and colleagues (18) also conducted a TRF protocol in which meals were restricted to approximately nine hours per day on as many days as possible. Andriessen and their team (24) researched a TRF program with a maximum daily food consumption window of 10 hours. In contrast, Arnason's study (26) included a fasting window of 18-20 hours per day as well as ad libitum zero-calorie beverages. Therefore, the fasting window period of TRF may vary from 8 to 20 hours per day.

Gable and their teams performed a research study that included Alternate-Day Feeding (ADF), wherein individuals had to intake 25% of their caloric needs on "fast days" and 125% of their caloric needs on "feast days". Other investigations looked into the effectiveness of daily Caloric Restriction (CR), a Fasting-Mimicking Diet (FMD) and a 7-day Modified Fasting. Sulaj et al. (16) had their participants either adhere to the FMD or the Mediterranean diet for five days a month; afterwards, they returned to their regular diet for the duration of the cycle, which typically lasted 25 days. The FMD provided them with 4600 kJ (1100kcal/d) of energy per day (11% protein, 46% fat, and 43% carbohydrates), while days 2 through 5 offered 3000 kJ (700kcal/d) (9% protein, 44% fat, and 47% carbohydrates). Likewise, the research done by Li et al. (17) observed a 7-day Modified Fasting regimen of 300 kcal/day liquid diet with Mediterranean diet advice. Finally, the study by Kahleova et al. (15) divided the participants into groups consuming three large and three small meals daily or two large meals daily.

### **The metabolic benefit of intermittent fasting**

In terms of body weight reduction, the majority of studies have demonstrated a notable reduction ( $p < 0.05$ ) in the body weight of the participants when engaging in different types of IF (13,14,24,25,15,16,18–23), except the study conducted by Parr et al. (18) which showed insignificant reduction ( $p = 0.84$ ). This could be due to the short-term intervention of four weeks.

The results of the various IF protocols demonstrated a clear improvement in the participants' glycemic control. All fasting periods had no negative impact on the intervention or control groups. A study by Bhandari et al. (14) showed that 16 hours of IF per day for four

weeks resulted in a significant decrease in fasting blood glucose levels, with a mean reduction of 19.92 mg/dL or 1.10 mmol/L ( $p < 0.001$ ). However, there was no statistically significant change in the mean fasting serum insulin values compared to baseline readings, indicating that IF did not affect insulin resistance.

Kahleova (15) found that, despite similar caloric intake between the two groups (taking small and frequent six meals per day vs taking two meals per day), the group taking two meals per day experienced a greater reduction in fasting plasma glucose ( $p = 0.004$ ;  $-0.78$  mmol/l; 95% CI  $-0.89, -0.68$  mmol/l vs  $-0.47$  mmol/l; 95% CI  $-0.57, -0.36$  mmol/l). Additionally, both groups experienced similar reductions in HbA1c. Furthermore, Obermayer (23) discovered that participants who used the non-consecutive method of IF experienced a significant decrease in HbA1c levels after 12 weeks, with a decrease of  $7.3 \pm 12.0$  mmol/mol compared to an increase of  $0.1 \pm 6.1$  mmol/mol in the control group ( $p = 0.012$ ). Additionally, the IF group also experienced improved insulin levels and insulin sensitivity.

Corley (19) found that the average change in fasting blood glucose was 19.8 mg/dL and 23.4 mg/dL in the non-consecutive and consecutive day fasting, respectively. In contrast, the average change in HbA1c level was  $-0.7\%$  and  $-0.6\%$ , respectively. Additionally, Gabel et al. (25) observed that ADF and CR groups had significantly lower fasting blood glucose levels. Moreover, TRF used 6-8 hours of fasting (23) or 10-20 hours of fasting (26), which were seen to reduce fasting blood sugar significantly.

In 2016 and 2018, Carter et al. conducted a study using the same intervention method, comprising intermittent energy restriction (IER) and continuous energy restriction (CER) for 12 weeks (21,22). Results indicated a significant reduction in HbA1c levels ( $-0.5 \pm 0.9\%$ ;  $p < 0.001$ ) and ( $-0.4\%$   $p < 0.001$ ) respectively. However, the follow-up session in 2019 (20) revealed an increase in HbA1c levels by 1% and 0.4% ( $p = 0.32$ ). Sulaj et al. (16) reported that after 6 months of following a fasting-mimicking diet (FMD), there was a decrease in both the fasting blood glucose and HbA1c levels ( $p < 0.05$ ). However, these glycemic parameters increased again at the 3-month follow-up. Parr (18) and Li (17) found an insignificant reduction in HbA1c and fasting blood glucose levels.

Studies generally showed no significant hypoglycemic episodes during the intervention period since the insulin and medication doses were adjusted accordingly. Corley et al., (19) found that the 5:2 diet regimens, was an exception, as hypoglycemia increased even with the reduction of medication doses. Across the studies, medication intake was reduced by 40-57% during the

intervention period.

## DISCUSSION

Intermittent fasting (IF) can induce a metabolic shift that positively alters body composition by reducing fat mass. This metabolic shift occurs from lipid synthesis and fat storage to the mobilisation of fat in the form of ketones. Ketones are then transported to muscle cells and neurons, where they are metabolised to acetyl coenzyme and generate adenosine triphosphate (ATP). It typically occurs within 12 to 36 hours of fasting when the glycogen in the hepatocytes becomes depleted (27). When the body does not have enough glucose for energy, lipolysis in adipose tissue will be accelerated. This process increases free fatty acid levels, increasing the synthesis of fatty acid-derived ketones in the body as a preferred fuel source (28).

Intermittent fasting (IF) is beneficial in reducing adiposity and insulin resistance during the transition of fuel sources or metabolic reprogramming(29). Therefore, it is evident that all IF regimens can improve glycemic control in patients with type 2 diabetes mellitus (T2DM). This is supported by the results of 13 studies included in this systematic review, where all studies reported clinically significant reductions in body weight and glycemic control among participants, except for the study conducted by Carter et al. (20). According to Zhang et al., (2022), the IF helps to induce more weight loss among T2DM patients compared to continuous calorie restrictions (30). In usual practice, the calorie restriction was reduced by 20-30% of the requirement aiming for calorie deficit conditions. The practice has proven beneficial for patients' metabolic health (31). The process behind the calorie restriction is to improve energy utilisation at the mitochondrial level by inhibiting the anabolic mechanism. Additionally, IF triggers the production of pancreatic  $\beta$ -cells and improves pancreatic islet function, where the fasting/eating window may interact with circadian rhythms, improving blood glucose while restoring the body to normal functioning (32). One study conducted in the Netherlands, found that combining fasting in diabetic treatment helps reduce the Metformin dosage and HbA1c results (33). The effect of fasting on the body physiology positively affects metabolic functions in T2DM patients practising IF, including the ability to reduce weight, glucose-lowering drug dosage, HbA1c, and blood glucose.

The safety of IF has been established under physician observation, as patients initially may experience moderate constipation and dizziness during the first few days of fasting, and these side effects typically go away by the second week (19,32,33). After two weeks to a month, most people no longer experience the early hunger and irritability as their bodies and brains get used to the new routine (33,34). In customising the best IF intervention for each patient, the patients are

advised to gradually increase the duration and regularity of fasting over several months and discuss with a dietitian the feasibility and obstacles of the IF regime recommendations (35).

The duration of IF has been shown to impact metabolic outcomes, particularly fasting blood sugar. Studies have demonstrated a significant reduction in HbA1c and fasting blood glucose when IF is practised for 12 months. A study done by Ekberg et al. (2024) reported that in the first six months, the 5:2 fasting successfully improved body weight, insulin sensitivity (HOMA-IR) and insulin secretion (C-peptide and IGF1BP) in T2DM patients, and the 12-month follow-up persistent positive effects were observed minimally (36). Additionally, the FMD using meal replacement products successfully improved the metabolic outcomes of the T2DM patients and reduced the glucose-lowering medicine eight times more than the control group; despite decreased drug use, a higher drop in HbA1c levels was found in the FMD group compared to the control group (33). Also, a study using 5:2 fasting with meal replacement products found a significant reduction in HbA1c levels in the experimental group compared to a control group taking Metformin and Empagliflozin (37).

Kahleova et al. (2014) reported that when assessed on T2DM participants, the 2-meals per day regimen improved better compared to 6-meals per day. The fasting between meals may be even more critical than the types of macronutrient intake. Although the diet had high fat content, the timing of meals increased insulin sensitivity and decreased body weight in one experimental study (Sherman et al., 2012). The critical factor is how the meals are distributed, whereas eating meals later in the day also reduces weight reduction success. The success of weight reduction was not attributed to differences in calorie intake, macronutrient distribution, or energy expenditure, but it was more related to the circadian system, the continuous synchronisation of a person's physiological processes with their environment. A study by Teong et al. (2024) concluded that early time-restricted eating (TRE) (0800 to 1600 hours) improved glucose tolerance by increasing insulin sensitivity among the participants.

All 13 studies found that glycemic control and body weight improved with intermittent fasting (IF) interventions, regardless of the type and duration of the intervention. However, it is important to note that while participants were able to maintain their weight reduction during the follow-up period, their blood glucose levels showed a slight increase from the baseline. Additionally, the HbA1c levels of patients with stable HbA1c (<7%, 53 mmol/mol) increased by 0.3% (3.3 mmol/mol) annually, according to a 10-year retrospective study (38). The decline in beta cell function over time contributes to reduced treatment efficacy, as shown in the UK Prospective Diabetes Study (38). Similarly, in the Look Ahead Study, participants regained about 25%

of their lost weight between years 1 and 2 (39). Other follow-up studies on intermittent fasting using an FMD also showed similar outcomes, with HbA1c and weight increasing at the 6-month check-up (16). These findings suggest that without ongoing intervention and dietetic support, regression of glycemic control and weight gain is likely, regardless of the type of treatment.

### Recommendations and Limitations

Intermittent fasting (IF) may not be appropriate for all people, particularly those with complications. Although IF has demonstrated promising benefits in the majority of metabolic illnesses, it also has many negative aspects. Hypoglycemia, dizziness, and weakness are commonly reported adverse effects (16-18). However, all IF regimens positively impact health; nevertheless, no data supports the alleged harmful effects of IF regimens. As a result, it is recommended that future research look into the long-term consequences and sustainability of TRF with meal replacement on metabolic benefit, which can be done as a longitudinal study. Furthermore, a fasting person's food intake, meal pattern and timing should be documented and studied.

The current review has limitations by including low-sample-size cross-sectional studies, which may limit the potential of the conclusions to be generalised to a broader population of T2DM patients. However, the combination of the selected studies were sufficient to conclude this topic based on quality appraisal results. Furthermore, the variation in the intervention groups includes adults who take blood sugar-lowering medication and those who do not. The medicine may target the same metabolic pathways, which may interfere with the outcome of IF. This can be overcome by performing a meta-analysis in the future investigation.

### CONCLUSION

Based on current information, intermittent fasting appears to be a safe and effective method for reducing weight and improving glycaemic control in patients with T2DM. While HbA1c levels initially decrease with IF, they would gradually increase over time due to declining beta cell function. Thus, continuous monitoring by healthcare providers of the patient's food intake and eating patterns is crucial. Choosing a fasting regimen that suits the patient's needs is necessary; according to this review, time-restricted feeding (TRF) is the most practical method for T2DM patients, with 6 to 20 hours of fasting daily. In order to maximise the benefits of fasting, it should be scheduled to coincide with the circadian rhythm, which runs from sunset to early in the morning.

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### REFERENCES

1. Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB, et al. Pathophysiology of type 2 diabetes mellitus. *Int J Mol Sci.* 2020;21(17):1–34. doi: 10.3390/ijms21176275.
2. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. *Diabetes Res Clin Pract.* 2019;157:107843. doi: <https://doi.org/10.1016/j.diabres.2019.107843>
3. Institute for Public Health. National Health and Morbidity Survey (NHMS) 2019: Non-communicable diseases, healthcare demand, and health literacy—Key Findings Published. Vol. 1. Shah Alam; 2020. doi: 10.18356/be4d1601-en.
4. Davies MJ, Aroda VR, Collins BS, Gabbay RA, Green J, Maruthur NM, et al. Management of Hyperglycemia in Type 2 Diabetes, 2022. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care.* 2022;45(11):2753–86. doi: 10.2337/dci22-0034.
5. MOH. Malaysia Clinical Practice Guidelines Management Of Type 2 Diabetes Mellitus Quick Reference Guide for Healthcare Professionals [Internet]. Clinical Practice Guidelines, Management of Type 2 Diabetes Mellitus. 2020. Available from: [https://www.moh.gov.my/moh/resources/Penerbitan/CPG/Endocrine/QR\\_T2DM\\_6th\\_Edition\\_QR\\_Guide\\_Digital.pdf](https://www.moh.gov.my/moh/resources/Penerbitan/CPG/Endocrine/QR_T2DM_6th_Edition_QR_Guide_Digital.pdf)
6. Antoni R, Johnston K, Collins A, Robertson MD. The Effects of Intermittent Energy Restriction on Indices of Cardiometabolic Health. *Res Endocrinol.* 2014;2014:1–24. doi: 10.5171/2014.459119.
7. Trepanowski JF, Kroeger CM, Barnosky A, Klempel MC, Bhutani S, Hoddy KK, et al. Effect of Alternate-Day Fasting on Weight Loss, Weight Maintenance, and Cardioprotection Among Metabolically Healthy Obese Adults: A Randomized Clinical Trial. *JAMA Intern Med.* 2017;7(177):930–8. doi: 10.1001/jamainternmed.2017.0936.Effect.
8. Albosta M, Bakke J. Intermittent fasting: is there a role in the treatment of diabetes? A review of the literature and guide for primary care physicians. *Clin Diabetes Endocrinol.* 2021;7(1):1–12. doi: 10.1186/s40842-020-00116-1.
9. Abeyasekera KN. Benefits of Intermittent Fasting: A Systematic Review of Randomized Clinical Trials. *Physician Assist Stud | Student Artic [Internet].* 2020; Available from: <https://scholar.dominican.edu/physician-assistant-studies-student-articles/12>

10. Borgundvaag E, Mak J, Kramer CK. Metabolic Impact of Intermittent Fasting in Patients with Type 2 Diabetes Mellitus: A Systematic Review and Meta-analysis of Interventional Studies. *J Clin Endocrinol Metab.* 2021;106(3):902–11. doi: 10.1210/clinem/dgaa926.
11. Cho Y, Hong N, Kim KW, Cho SJ, Lee M, Lee YH, et al. The effectiveness of intermittent fasting to reduce body mass index and glucose metabolism: A systematic review and meta-analysis. *J Clin Med.* 2019;8(10). doi: 10.3390/jcm8101645.
12. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ.* 2021;372. doi: 10.1136/bmj.n71.
13. American Dietetic Association. ADA Quality Criteria Checklist: Primary Research [Internet]. 2012. p. 1–6. Available from: <http://www.adaevidencelibrary.com/topic.cfm?cat=1317>
14. Bhandari V, Dureja S, Bachhel R, Gupta M, Sidhu R. Effect of intermittent fasting on various health parameters in obese type 2 diabetics: A pilot study. *Natl J Physiol Pharm Pharmacol.* 2021;12(0):1. doi: 10.5455/njppp.2022.12.08281202120082021.
15. Kahleova H, Belinova L, Malinska H, Oliyarnyk O, Trnovska J, Skop V, et al. Eating two larger meals a day (breakfast and lunch) is more effective than six smaller meals in a reduced-energy regimen for patients with type 2 diabetes: A randomised crossover study. *Diabetologia.* 2014;57(8):1552–60. doi: 10.1007/s00125-014-3253-5.
16. Sulaj A, Kopf S, von Rauchhaupt E, Kliemank E, Brune M, Kender Z, et al. Six-Month Periodic Fasting in Patients With Type 2 Diabetes and Diabetic Nephropathy: A Proof-of-Concept Study. *J Clin Endocrinol Metab.* 2022;107(8):2167–81. doi: 10.1210/clinem/dgac197.
17. Li C, Sadraie B, Steckhan N, Kessler C, Stange R, Jeitler M, et al. Effects of A One-week Fasting Therapy in Patients with Type-2 Diabetes Mellitus and Metabolic Syndrome – A Randomized Controlled Explorative Study. *Exp Clin Endocrinol Diabetes.* 2017;125(9):618–24.
18. Parr EB, Devlin BL, Lim KHC, Moresi LNZ, Geils C, Brennan L, et al. Time-restricted eating as a nutrition strategy for individuals with type 2 diabetes: A feasibility study. *Nutrients.* 2020;12(11):1–22. doi: 10.3390/nu12113228.
19. Corley BT, Carroll RW, Hall RM, Weatherall M, Parry-Strong A, Krebs JD. Intermittent fasting in Type 2 diabetes mellitus and the risk of hypoglycaemia: a randomized controlled trial. *Diabet Med.* 2018;35(5):588–94. doi: 10.1111/dme.13595.
20. Carter S, Clifton PM, Keogh JB. The effect of intermittent compared with continuous energy restriction on glycaemic control in patients with type 2 diabetes: 24-month follow-up of a randomised noninferiority trial. *Diabetes Res Clin Pract* [Internet]. 2019;151:11–9. doi: <https://doi.org/10.1016/j.diabres.2019.03.022>
21. Carter S, Clifton PM, Keogh JB. Effect of Intermittent Compared With Continuous Energy Restricted Diet on Glycemic Control in Patients With Type 2 Diabetes: A Randomized Noninferiority Trial. *JAMA Netw open.* 2018;1(3):e180756. doi: 10.1001/jamanetworkopen.2018.0756.
22. Carter S, Clifton PM, Keogh JB. The effects of intermittent compared to continuous energy restriction on glycaemic control in type 2 diabetes; a pragmatic pilot trial. *Diabetes Res Clin Pract.* 2016;122:106–12. doi: 10.1016/j.diabres.2016.10.010.
23. Obermayer A, Tripolt NJ, Pferschy PN, Kojzar H, Aziz F, Muller A, et al. Efficacy and Safety of Intermittent Fasting in People With Insulin-Treated Type 2 Diabetes (INTERFAST-2)—A Randomized Controlled Trial. *Diabetes Care.* 2023;46(2):463–8. doi: 10.2337/dc22-1622.
24. Andriessen C, Fealy CE, Veelen A, van Beek SMM, Roumans KHM, Connell NJ, et al. Three weeks of time-restricted eating improves glucose homeostasis in adults with type 2 diabetes but does not improve insulin sensitivity: a randomised crossover trial. *Diabetologia.* 2022;65(10):1710–20. doi: 10.1007/s00125-022-05752-z.
25. Gabel K, M. CK, Trepanowski JF, Hoddy KK, Cienfuegos S, Kalam F, et al. Differential effects of alternate day fasting versus daily calorie restriction on insulin resistance. *Obes (Silver Spring).* 2019;27(9):1443–50. doi: 10.1002/oby.22564. Differential.
26. Arnason TG, Bowen MW, Mansell KD. Effects of intermittent fasting on health markers in those with type 2 diabetes: A pilot study. *World J Diabetes.* 2017;8(4):154. doi: 10.4239/wjd.v8.i4.154.
27. Antoni R, Johnston KL, Collins AL, Robertson MD. Intermittent v. continuous energy restriction: Differential effects on postprandial glucose and lipid metabolism following matched weight loss in overweight/obese participants. *Br J Nutr.* 2018;119(5):507–16. doi: 10.1017/S0007114517003890.
28. Zang BY, He LX, Xue L. Intermittent Fasting: Potential Bridge of Obesity and Diabetes to Health? *Nutrients.* 2022;14(5):1–21. doi: 10.3390/nu14050981.
29. Vasim I, Majeed CN, DeBoer MD. Intermittent Fasting and Metabolic Health. *Nutrients.* 2022;14(3):1–15. doi: 10.3390/nu14030631.
30. Zhang Q, Zhang C, Wang H, Ma Z, Liu D, Guan X, et al. Intermittent Fasting versus Continuous Calorie Restriction: Which Is Better for Weight Loss? *Nutrients.* 2022;14(9):1–19. doi: 10.3390/nu14091781.
31. Msane S, Khathi A, Sosibo A. Therapeutic Potential of Various Intermittent Fasting Regimens



- in Alleviating Type 2 Diabetes Mellitus and Prediabetes: A Narrative Review. *Nutrients*. 2024;16(16). doi: 10.3390/nu16162692.
32. Wei F, Gong L, Lu S, Zhou Y, Liu L, Duan Z, et al. Circadian transcriptional pathway atlas highlights a proteasome switch in intermittent fasting. *Cell Rep*. 2022;41(4). doi: 10.1016/j.celrep.2022.111547.
  33. van den Burg EL, Schoonakker MP, van Peet PG, van den Akker-van Marle EM, Lamb HJ, Longo VD, et al. Integration of a fasting-mimicking diet programme in primary care for type 2 diabetes reduces the need for medication and improves glycaemic control: a 12-month randomised controlled trial. *Diabetologia* [Internet]. 2024;67(7):1245–59. doi: 10.1007/s00125-024-06137-0.
  34. de Cabo R, Mattson MP. Effects of Intermittent Fasting on Health, Aging, and Disease. *N Engl J Med*. 2019;381(26):2541–51. doi: 10.1056/nejmra1905136.
  35. Xiaoyu W, Yuxin X, Li L. The effects of different intermittent fasting regimens in people with type 2 diabetes: a network meta-analysis. *Front Nutr*. 2024;11(January). doi: 10.3389/fnut.2024.1325894.
  36. Ekberg NR, Hellberg A, Sundqvist ML, Hirschberg AL, Catrina S-B, Brismar K. The 5:2 Diet Affects Markers of Insulin Secretion and Sensitivity in Subjects with and without Type 2 Diabetes—A Non-Randomized Controlled Trial. *Int J Mol Sci*. 2024;25(17):9731. doi: 10.3390/ijms25179731.
  37. Guo L, Xi Y, Jin W, Yuan H, Qin G, Chen S, et al. A 5:2 Intermittent Fasting Meal Replacement Diet and Glycemic Control for Adults with Diabetes: The EARLY Randomized Clinical Trial. *JAMA Netw Open*. 2024;7(6):e2416786. doi: 10.1001/jamanetworkopen.2024.16786.
  38. Ohde S, Deshpande GA, Yokomichi H, Takahashi O, Fukui T, Yamagata Z. HbA1c monitoring interval in patients on treatment for stable type 2 diabetes. A ten-year retrospective, open cohort study. *Diabetes Res Clin Pract*. 2018;135:166–71. doi: 10.1016/j.diabres.2017.11.013.
  39. Look AHEAD Research Group, “Long Term Effects of a Lifestyle Intervention on Weight and Cardiovascular Risk Factors in Individuals with Type 2 Diabetes: Four Year Results of the Look AHEAD Trial,” *Arch Intern Med*, vol. September, no. 17, pp. 1566–1575, 2010, doi: 10.1016/S0140-6736(09)61457-4.10-year.