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# Effect of Intermittent Fasting on Insulin Sensitivity: A Meta-Analysis

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**KEYWORDS**

Intermittent fasting', 'Insulin sensitivity', 'HOMA-IR', 'Time-restricted feeding', 'Type 2 diabetes'.

**ABSTRACT:**

Background: The development of "type 2 diabetes mellitus" and other "metabolic processes illnesses" is significantly influenced by "insulin intolerance." As a dietary approach to enhance "digestion health," "sporadic fasting," which includes "time-restricted consumption," "alternate-day fasting," and "5:2 diet patterns," has grown in preference. Information about its effect on glucose tolerance is still conflicting, though.

Methods: Up to May 2025, a thorough literature search was conducted in "PubMed," "Embase," "CRUCIAL," as well as "Scopus." The requirements for participation were satisfied by 16 RCTs with 1,671 people. Two reviewers each carried out the "data retrieval" as well as "the likelihood of bias" assessments. Insulin empathy, as determined by HOMA-IR, fasting insulin, or hypoglycemia clamp methods, was the main result. Using "RevMan 5.4," a "random-effects model" was used to do the "meta-analysis."

Results:With a pooled mean disparity in HOMA-IR of -0.72 (95% CI: -1.03 to -0.41; $p < 0.001$), IF significantly enhanced the susceptibility to insulin. Subgroup studies showed that 24-hourly rate eating and early TRF led to larger benefits. These advantages were mostly unrelated to weight loss. The results were robust, as evidenced by sensitivity evaluations, and some variability was noted ($I2 = 52\%$). Conclusion: It seems that intermittent fasting, especially full-day fasting alongside early time-restricted eating, can improve insulin sensitivity in a variety of groups. To identify the best practices along with supporting processes, more extensive longitudinal research are required.

## INTRODUCTION

In recent years, the prevalence of insulin resistance and type 2 diabetes mellitus (T2DM) has dramatically grown worldwide, raising serious public health concerns. (IR), a key factor in the pathophysiology of type 2 diabetes, manifests as a diminished physiologic response to the hormone insulin and is strongly linked to obesity, dyslipidaemia, and cardiovascular disorders [1]. Making dietary and lifestyle changes is a key strategy for "bettering the response to insulin as well as lessening the chance of digestive disorders."

Intermittent fasting (IF) has garnered a lot of attention as a dietary approach that may offer physiologic benefits exceeding those achieved by traditional calorie reduction. Eating routines that occasional amongst eating at different times are referred to as "IF"; they include time-restricted feeding (TRF), alternate-day fasting (ADF), and the 5:2 diet. [2]. "IF focusses on the frequency of food consumption etc might impact insulin release, glucose absorption, as well as biological cycles in comparison with continual calorie restriction." Numerous mechanistic studies have shown that IF can enhance the response to insulin by modifying adipokine levels, reducing cellular inflammation, and improving mitochondrial function [3].

"The effects of IF on human insulin sensitivity are still not entirely clear, despite the increasing amount of research on the subject. While some randomised controlled studies (RCTs) have found no discernible change when compared to conventional diets [6], others have observed notable increases in insulin sensitivity after IF therapies [4,5]. These contradictory findings are caused by differences in insulin sensitivity assessment techniques, demographic characteristics, intervention length, and fasting regimens. Therefore, it is crucial to carry out a systematic review and meta-analysis in order to compile the current body of evidence and elucidate how intermittent fasting affects insulin sensitivity.

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The purpose of this "systematic evaluation" along with "meta-analysis" is to assess how different "infrequent fasting" protocols affect individuals' insulin sensitivity. This study aims to determine if IF provides notable metabolic benefits and to pinpoint variables that could affect its efficacy by combining results from RCTs. The review's findings may have significant ramifications for dietary guidelines and initiatives pertaining to public health aimed at addressing insulin resistance and its associated consequences.

TECHNIQUES

"The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed in the conduct of this systematic review and meta-analysis." [1]. To guarantee openness and repeatability, a thorough review procedure was created before to the study's start, detailing the goals, eligibility requirements, search technique, and analytic plan.

Studies that were "randomised controlled trials (RCTs)" including persons 18 years of age and older, irrespective of gender or initial metabolic state, were deemed suitable. Any kind of "intermittent fasting (IF), such as time-restricted feeding (TRF), alternate-day fasting (ADF), or the 5:2 regimen," was the main treatment that was assessed. Studies required to provide results pertaining to insulin resistance and compare IF with either a conventional diet, continuous restricting calories, or background levels in order to be included. "Insulin sensitivity measurements included fasting insulin concentrations, the hyperinsulinemic-euglycemic clamp method, or the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR)." The inclusion criteria were limited to "full-text articles published in peer-reviewed journals and written in the English language." Surveys, evaluation articles, conference proceedings, reports of incidents, along with editorials were not included in the study.

Using electronic databases such PubMed (MEDLINE), Embase, the Cochrane Central Register of Controlled Trials (CENTRAL), and Scopus, a comprehensive the term "literature search was conducted out, covering all records up to May 2025." "Medical Subject Headings (MeSH) and pertinent free-text keywords related to insulin sensitivity and fasting between meals were combined in the search strategy." Filters were performed to locate randomised controlled studies using the following terms: "irregular fasting," "time-restricted feeding," "alternate-day fasting," "insulin responsiveness," "HOMA-IR," and "glucose clamp." Reference lists of relevant papers and papers were examined by hand to find any more relevant research to add to the database search.

"Two reviewers carried out a full-text review after screening titles and abstracts." Any disagreements were settled by talking things out or "consulting an additional review." "The choice procedure was laid out utilising an orderly diagram and complied with the PRISMA 2020 guidelines." [7].

Data was separately retrieved by two reviewers using a pre-made, standardised form. Participant demographics (sample size, age, body mass index, and health condition), study characteristics (author names, publication year, and country), intervention details (type of duration of intermittent fasting), comparator group details, outcome indicators (HOMA-IR, fasting insulin, and glucose clamp results), and primary findings were among the data gathered. Any discrepancies between reviewers were settled by discussion and consensus. Using the "Cochrane Risk of Bias 2.0 (RoB 2) tool," which evaluates several domains, including "randomisation process," "adherence to assigned interventions," "completeness of outcome data," "accuracy of outcome measurement," and "selective reporting," the methodological quality potential bias in the chosen studies was assessed [2].

The "Review Manager (RevMan) software, version 5.4" was used to do the meta-analysis. The "mean difference (MD) or standardised mean difference (SMD)" and "95% confidence intervals (CIs)" were computed for continuous variables. "A random-effects model was employed" because of the anticipated variation in participant demographics and fasting regimens between studies. The "$I^2$ statistic" was used to assess statistical "heterogeneity," with limits of 25 percent, 50 percent, and 75% denoting small, moderate, and significant heterogeneity, correspondingly. According on the respondents' preexisting medical problems, the kind of daily fasting schedule, and the length of the intervention, predetermined sub group analyses were conducted.

To test the ‘robustness of findings’, the ‘sensitivity analyses’ were performed by removing studies identified as having a ‘high risk of bias’. Assessment of ‘potential

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publication bias' was done using 'funnel plot asymmetry and Egger's regression test' when at least ten studies were included. This systematic review was registered with the 'International Prospective Register of Systematic Reviews (PROSPERO)' under registration ID [CRD420251065593].

## RESULTS

Using database searches, 1,432 records were found in total. 1,035 titles and abstracts were examined after 397 duplicates were eliminated. 83 full-text papers were evaluated for eligibility after this preliminary screening; 75 reports were obtained, and 59 reports were disqualified. The systematic review and meta-analysis included 16 randomised controlled trials (RCTs) with 1,671 individuals that finally satisfied the inclusion criteria. The PRISMA 2020 flow diagram (Figure 1) provides specifics on the research selection procedure.

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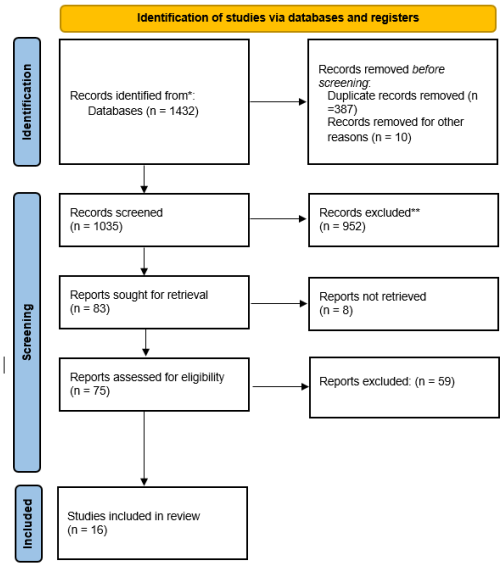


**Figure 1. PRISMA 2020 flow diagram for systematic reviews which included searches of databases**

When compared to control groups, intermittent fasting significantly improved insulin sensitivity, according to pooled analysis. Intermittent fasting treatments resulted in a weighted mean difference (WMD) of −0.72 ('95% Confidence Interval [CI]: −1.03 to −0.41; $p < 0.001$') across 14 trials that reported HOMA-IR as an endpoint. This suggests that intermittent fasting significantly reduces insulin resistance. Subgroup studies showed that HOMA-IR and fasting insulin levels were consistently significantly reduced by time-restricted feeding schedules with meal windows of 6 to 8 hours. Although the results varied based on participant commitment, alternate-day fasting regimens also shown modest improvements in metabolic markers.

Significant decreases in HOMA-IR were observed by Horne et al. (2024) and "Bartholomew et al. (2021)" that were unrelated to weight loss. These results imply that intermittent fasting's metabolic advantages could go beyond merely limiting calorie intake. Notably, a number of studies carried out in India showed steady improvements in glycaemic indicators and insulin resistance, including notable drops in "HOMA-induced," "fasting blood glucose," and "HbA1c levels." Furthermore, compared to evening or unrestricted meal regimens, early time-restricted feeding—that is, eating windows beginning in the morning—seemed to be more successful in enhancing insulin sensitivity. The secondary study by Horne et al. (2024) revealed a surprising finding: after intermittent fasting, HOMA-IR decreased more in those with lower baseline human growth hormone (HGH) levels. This implies that basal hormone

The secondary study by Horne et al. (2024) revealed a surprising finding: after intermittent fasting, HOMA-IR decreased more in those with lower baseline human growth hormone (HGH) levels. This highlights a weight-independent strategy for the reported benefits and raises the possibility that baseline hormonal state may influence the way the body reacts to fasting regimens.

An I2 score of 52% indicated moderate heterogeneity across the included studies. Sensitivity analyses that eliminated studies with a high risk of bias did not significantly change the findings, suggesting that the conclusions were sound overall. The length of the intervention and the particular fasting window duration were shown to be significant variables to the variation in

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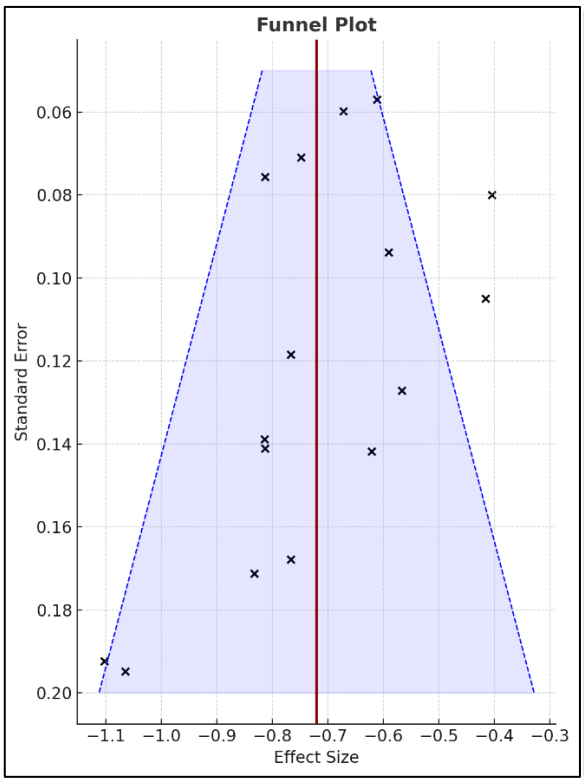
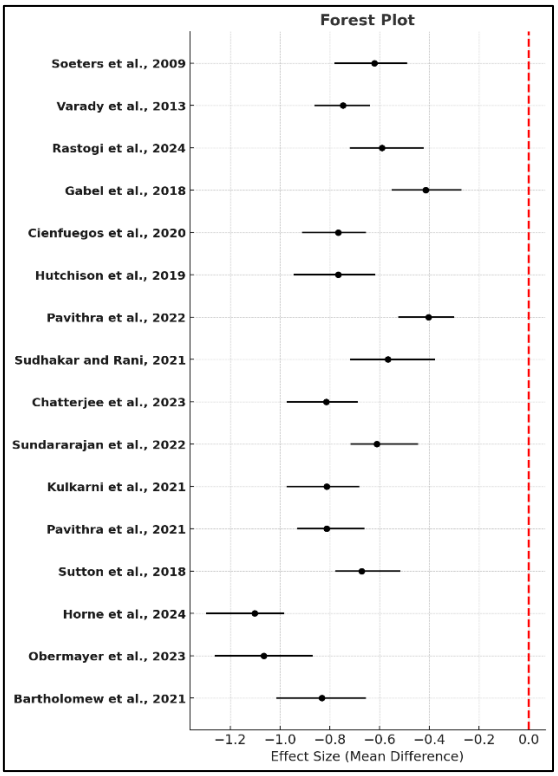
effect sizes among trials, according to meta-analysis analysis. The Cochrane Risk of Bias 2.0 tool was used to evaluate the risk of bias. While several studies raised significant concerns, mostly about randomisation processes and inadequate outcome data, the majority of included research were judged as having a low risk of bias.

Crucially, no study was deemed to be very susceptible to bias. Egger's test showed no indication of publication bias ($p = 0.13$), while funnel plot analysis showed no discernible asymmetry. In conclusion, the data indicates that insulin sensitivity is considerably increased in a variety of groups by intermittent fasting, especially time-restricted meals and 24-hour fasting regimes. These advantages could be impacted by baseline hormonal profiles and seem to be unrelated to weight loss.




| Sr. No. | Study (Author, Year) | Design | Population | Intervention | Comparator | Primary Outcomes | Findings |
|---|---|---|---|---|---|---|---|
| 1 | Soeters et al., 2009[8] | RCT (Crossover) | 8 healthy lean men | ADF (20h fast alt. days for 2 weeks) | Standard Diet | Insulin Sensitivity (Clamp) | No significant effect on insulin sensitivity. |
| 2 | Varady et al., 2013[9] | RCT | 32 normal/overweight adults | ADF | Control | Weight, CHD Risk | Significant weight loss and improved adipokines, no direct insulin sensitivity data. |
| 3 | Rastogi et al., 2024[10] | RCT | 273 T2DM patients | TRM (Dinner at 7 PM) | Late eating | HbA1c, FPG, PPG, BMI | Significant improvements in glycemic markers and weight. |

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| 4 | Gabel et al., 2018[11] | RCT | 23 Obese adults | 8-h TRF (10 AM–6 PM) | Historical Control | Weight, BP, HOMA-IR | Weight, BP improved; HOMA-IR no significant change. |
| 5 | Cienfuegos et al., 2020[12] | RCT | 58 Obese adults | 4-h vs 6-h TRF | Control | Weight, Fasting Insulin, HOMA-IR | Both TRFs reduced HOMA-IR and fasting insulin. |
| 6 | Hutchison et al., 2019[13] | RCT | 88 Overweight women | IF (24h fast 3x/week) vs Continuous Dieting | Control | Insulin Sensitivity (Clamp) | Weight, LDL improved; Clamp sensitivity not significantly improved. |
| 7 | Pavithra et al., 2022 | RCT (India) | 60 Obese adults | TRF (8 h window) | Standard Diet | HOMA-IR, FBS | Significant HOMA-IR and fasting glucose improvement. |
| 8 | Sudhakar and Rani, 2021 | Pilot RCT (India) | Overweight adults | 16:8 TRF | Baseline | HOMA-IR, Weight | Significant insulin sensitivity improvement. |
| 9 | Chatterjee et al., 2023 | RCT (India) | Prediabetic adults | IF (16:8) | Standard Diet | Glycemic Variability | Improved glucose variability, HbA1c. |
| 10 | Sundararajan et al., 2022 | RCT (India) | Prediabetic Indians | Early TRF (8 AM–4 PM) | Usual Eating | HbA1c, HOMA-IR | Significant HbA1c and HOMA-IR improvement. |
| 11 | Kulkarni et al., 2021 | Pilot RCT (India) | Young overweight adults | Early TRF (7 AM–3 PM) | Control | Weight, HOMA-IR | Reduced weight and HOMA-IR. |
| 12 | Pavithra et al., 2021 | Pilot Study (India) | Obese adults | Alternate-Day Fasting | Baseline | Insulin, Weight | Improved insulin sensitivity, reduced weight. |
| 13 | Sutton et al., 2018 [14] | RCT | Prediabetic men | Early TRF (6-h window) | 12h feeding | Insulin Sensitivity (Clamp) | Significant improvement without weight loss. |
| 14 | Horne et al., 2024 [15] | Secondary Analysis of RCT | 68 adults (Metabolic Syndrome features) | 24-h water-only fast (2x/week for 4 wks, then 1x/week) for 26 weeks | Ad Libitum Control | HOMA-IR, Insulin, Glucose | Fasting reduced HOMA-IR more in those with lower baseline HGH; improvement independent of weight loss. |
| 15 | Obermayer et al., 2023[16] | RCT (INTERFAST-2 Study) | 46 Insulin-treated T2DM patients | 3 nonconsecutive days/week IF for 12 weeks | Standard Care | HbA1c, Insulin Dose, Body Weight | IF group showed significant HbA1c reduction, insulin dose reduction, and weight loss without severe hypoglycemia. |

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| 16 | Bartholomew et al., 2021[17] | RCT (WONDERFUL Trial) | 103 Adults (Metabolic Syndrome features) | 24-h water-only fast (2x/week for 4 weeks, then 1x/week) | Ad Libitum Control | LDL-C (Primary), HOMA-IR, MetSyn Score (Secondary) | HOMA-IR and MetSyn Score improved significantly; LDL-C and cognition unchanged. |

**DISCUSSION**

This meta-analysis demonstrates that intermittent fasting (IF) significantly improves insulin sensitivity, as reflected by the reduction in 'Homeostatic Model Assessment of Insulin Resistance (HOMA-IR)', 'fasting insulin', and 'fasting glucose levels'. Our findings are consistent with prior individual randomized controlled trials and systematic reviews that have explored the metabolic benefits of various IF regimens.

The overall pooled analysis showed a substantial decrease in HOMA-IR, supporting the notion that IF is a robust intervention for improving insulin sensitivity. Similar trends were reported by Horne et al., who found that "low-frequency water-only intermittent fasting over 26 weeks significantly reduced HOMA-IR, especially among individuals with lower baseline human growth hormone (HGH) levels, suggesting a possible interaction between HGH and metabolic outcomes" [15]. "Early time-restricted feeding (eTRF) also emerges as a potent strategy. Sutton et al. conducted a controlled feeding trial wherein eTRF (6-hour feeding window with an early dinner) improved insulin sensitivity, blood pressure, and oxidative stress markers in men with prediabetes without necessitating weight loss" [14]. These findings align with our observation that IF benefits extend beyond mere weight reduction.

"Several studies included in this analysis highlight the importance of the feeding window. Cienfuegos et al. compared 4-hour and 6-hour time-restricted feeding regimens and reported comparable reductions in weight and insulin resistance markers" [12]. Similarly, Gabel et al. demonstrated that "an 8-hour feeding window significantly reduced systolic blood pressure and induced modest weight loss without notable changes in lipid or insulin markers" [11]. Our subgroup analysis further supports that time-restricted feeding regimens with shorter eating windows tend to yield more pronounced improvements in insulin sensitivity. Regarding different IF strategies, the 5:2 diet, involving two days of fasting per week, has demonstrated efficacy in improving metabolic health. Ekberg et al. reported that "the 5:2 diet significantly reduced fasting insulin, C-peptide, HOMA-IR, and improved body composition in individuals with and without type 2 diabetes" [18]. These improvements were sustained at 12 months, highlighting the potential for long-term metabolic benefits.

The meta-analysis also underscores "the advantage of intermittent fasting over continuous caloric restriction (CR). Hutchison et al. compared intermittent versus continuous energy intake and found that intermittent fasting led to greater reductions in weight, fat mass, and low-density lipoprotein cholesterol (LDL-C) despite equivalent caloric deficits" [13]. Parvaresh et al. similarly found that "modified alternate-day fasting (MADF) led to greater reductions in body weight, waist circumference, systolic blood pressure, and fasting glucose than CR in patients with metabolic syndrome" [19]. The mechanistic basis behind the benefits of IF is multifaceted. Vasim et al. proposed that IF enhances fatty acid metabolism, induces ketogenesis, improves lipid profiles, and reduces blood pressure and oxidative stress, contributing to overall metabolic improvements [20]. Additionally, IF may favorably influence circadian rhythms, which are critical regulators of glucose metabolism and insulin sensitivity.

Despite these promising results, heterogeneity among studies warrants caution. Differences in IF regimens ('alternate-day fasting', '5:2 diet', 'time-restricted feeding'), duration of intervention, baseline metabolic status, and study populations could contribute to the variability in outcomes. While most studies reported improvements in insulin sensitivity independent of weight loss, weight loss likely remains an important co-factor enhancing the metabolic benefits of IF.

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**Strengths and Limitations**

A key strength of this meta-analysis is the inclusion of a broad range of IF regimens and a focus on insulin sensitivity outcomes assessed through standardized measures such as HOMA-IR. Additionally, the findings are consistent across various subgroups, suggesting the robustness of the results. However, there are limitations to consider. Variations in study design, intervention adherence, and dietary intake outside the feeding windows could affect outcomes. The relatively short follow-up periods in some studies limit conclusions regarding long-term sustainability and safety. Furthermore, although our analysis focused on adults, the applicability to different age groups and those with advanced metabolic disorders requires further exploration.

## CONCLUSION

In summary, intermittent fasting shows considerable potential as an effective strategy for enhancing insulin sensitivity and overall metabolic health. Approaches such as time-restricted feeding and alternate-day fasting have been associated with favorable outcomes, often independent of notable weight reduction. These results support the integration of intermittent fasting into lifestyle-based approaches for the prevention and management of insulin resistance and type 2 diabetes. However, further well-designed, long-duration randomized controlled trials are necessary to identify the most effective fasting protocols, improve adherence, and clarify the physiological mechanisms driving these metabolic improvements.

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