World Nutrition Journal |eISSN 2580-7013

LITERATURE REVIEW

Intermittent fasting-induced improving insulin resistance in healthy obese adults: A scoping review

Nyono Dedi Prabowo[1]

1. *Nutrition Sciences Study Program, The Faculty of Health, Bhakti Wiyata Institute of Health Sciences. Jl. KH Wachid Hasyim No.65, Bandar Lor, Mojoroto, Kediri, East Java, Indonesia (64114).*

Received 25 June 2023
Accepted 28 May 2024
Published 30 August 2024

Link to DOI:
10.25220/WNJ.V08.i1.0005

Citation: Prabowo N D. Intermittent Fasting-Induced Improving Insulin Resistance in Healthy Obese Adults: A Scoping Review. World Nutrition Journal.2024 August 30,8(i1): 29-37.

Abstract

Background: Obesity is a severe global public health problem linked to chronic noncommunicable disease and increased mortality. It has harmful effects on metabolic disorders via the insulin resistance pathway. Available guidelines recommend caloric reduction via intermittent fasting for obesity management. However, the available literature is less focused on the benefits of intermittent fasting on improved insulin resistance in healthy obese adults, especially related to an accumulation of free fatty acids. Therefore, a scoping review is necessary.

Objective: This review aims to collect evidence on the benefits of intermittent fasting on improved insulin resistance in healthy obese adults.

Methods: This scoping review followed the 5-step Arksey and O'Malley framework and was submitted following PRISMA ScR. Five electronic databases were thoroughly searched. Papers are included if they are eligible. The result was a synthesis of descriptive and narrative elements.

Results: 1117 papers were collected in total. Nine randomized controlled trial studies met the review's inclusion criteria. The papers included are sourced from reputable, relevant sources. As a whole, intermittent fasting appears to benefit improved insulin resistance in healthy obese adults. Intermittent fasting has been shown to reduce insulin levels while increasing insulin sensitivity, therefore improving insulin resistance.

Conclusion: Evidence suggests that intermittent fasting can help improve insulin resistance in healthy obese adults.

Keywords: Fasting, Insulin, Insulin Resistance, Obesity

Corresponding author:
Name : Nyono Dedi Prabowo
Affiliation : Nutrition Sciences Study Program, The Faculty of Health, Bhakti Wiyata Institute of Health Sciences.
Email : nyonodediprabowo@gmail.com
https://orcid.org/0009-0005-7635-3464

Introduction

Obesity is defined as excessive fat accumulation that is measured by a body mass index (BMI) of more than 30 kg/m^2 as a result of impaired energy balance and homeostatic processes.[1-4] Obesity prevalence is increasing globally. Apart from prevention and treatment, the World Obesity Federation predicts that more than half (51%) of the global population will be obese in the coming years.[5] Although the causes of obesity are multifactorial, an excess supply of caloric intake plays an important role in developing obesity.[6]

Obesity has negative consequences that present a risk to health. It was responsible for various metabolic dysfunctions and is a single risk factor for other diseases in current investigations.[7-8] Recent studies define obesity as a disease that is caused many as 21 diseases, including metabolic disorders, and is linked to insulin resistance.[7-9] Obese individuals had a higher probability of having simple (two diseases) and complicated (≥four diseases) multimorbidity than healthy weight ones.[9] The current study explains the global cost of overweight and obesity is expected to reach $4.32 trillion per year by 2035.[5]

Considering the risk of obesity-related comorbidities and cost consequences is increasing, obesity management focuses on realistic weight loss in order to trim it.[10] Therefore, adequate therapy is required. The Obesity Medicine Association (OMA) recommends the central management of obesity through a nutritional intervention approach, especially meal arrangements.[11-12] Numerous diets have been devised to treat obesity.[13-17] The treatment is based on calorie restriction using the principle of reducing calories, and the ultimate goal is to create a negative energy balance.[18]

The Obesity Medicine Association recommends intermittent fasting as one of ten takeaway messages in managing obesity. Obesity management with intermittent fasting is advantageous. Meta-analyses studies show that intermittent fasting therapy has beneficial outcomes for weight loss and chronic disease risk factors compared to daily calorie restriction. Intermittent fasting is characterized by recurring and periodic fasting periods, triggering adaptive changes in the body's physiological functions. Intermittent fasting modifies homeostatic, systemic, and metabolic processes, allowing the body to perform its recovery function.[19-22]

The benefits of intermittent fasting as a nutrition therapy for obesity are clear.[19,23] Nevertheless, to our knowledge, few discuss intermittent fasting on intermittent fasting on improved insulin resistance in healthy obese adults. Originally, managing obesity before moving to other diseases could significantly impact clinical results. We evaluated intermittent fasting on improving insulin resistance in healthy obese adults. As a result, this scoping review aims to investigate the function of intermittent fasting in improving insulin resistance in healthy obese adults.

Methods

Protocol design

This study was designed as a broad-scoping literature review to map pertinent evidence for intermittent fasting on improving insulin resistance in healthy obese adults. The review was carried out to summarize, map, and present evidence findings from various papers using descriptive methodologies. The 5-step Arksey and O'Malley framework was used for validation, and the results were published following PRISMA ScR (priority reporting item for systematic review and a meta-analysis extension for scoping reviews).[24]

Protocol design

We established inclusion criteria to select papers that were relevant to the review's purpose. The paper inclusion criteria were decided by publishing in English, internationally, accessible, full-text papers published after 2018, focusing on intermittent fasting to improve insulin resistance in healthy obese adults, design by randomized controlled trial (RCT), original research (protocols and review papers not permitted), the population consisted of people, the subject is overweight and obesity, and quality of evidence from reputable

journal indexed by Scopus. Exclusion criteria were set: articles with unclear results.

Information sources

We used primary papers of experimental RCTs design that met the eligibility requirement. Papers from four electronic databases, including Science Direct, Scopus, Wiley One Library, PubMed, and Google Scholar, were used to discover studies published in the last five years between January 2018 and January 2023. Five databases were chosen since they are all focused on nutrition and medical sciences and are relevant to the study's objectives.

Search strategy

A first exploratory search was conducted, which included electronic sources. The findings of this search were then utilized to build a scoping review search strategy. The database searches' keywords were as follows: "(fasting OR intermittent fasting OR time-restricted eating OR alternate day fasting) AND (obesity OR overweight) AND (insulin resistance OR insulin sensitivity) AND (RCT OR Randomized Controlled Trial)." Papers were collected, and the full text was screened for eligibility.

Result

Selection of evidence

A total of 1117 papers were identified from databases, including Science Direct 526, Scopus 73, Wiley One Library 261, PubMed 9, and Google Scholar 248 paper. In the total paper, 1117 of these, 371 items were eliminated during the initial assessment, and 113 papers were found to have a potential close match with the scoping review's emphasis. 21 paper is removed after duplicate, leaving 92 paper. Then, 58 papers are excluded by title and subject (non-human subject), leaving 37 papers eligible. Last, 18 papers are excluded by reputable evidence and subject (non-spesific evidence), leaving 19 papers suitable for analysis. Ten of them were excluded because the outcome

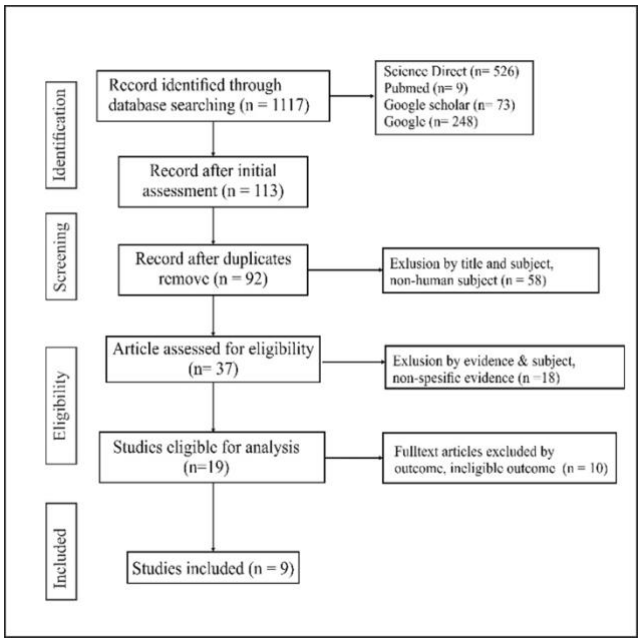

Figure 1. PRISMA flow chart.

did not match the scoping objectives. Finally, nine papers were included for a scoping review. **Figure 1** shows the PRISMA flowchart showing the search strategy used.

Characteristics of evidence

The following are the characteristics of the papers covered in this review: papers are based on research published in reputable Scopus-indexed journals. Papers is including Q1's (n = 8) and Q2's (n = 1). Papers originate from a variety of countries, including the USA (n=2), China (n=2), Iran, Portugal, South Korea, the UK, and German, respectively (n=1) are included in this scoping review (n=9). All research subjects a health, overweight or obese adults (n=9). The entire research evaluates the impact of intermittent fasting interventions. What distinguishes them is the type of intermittent fasting used. Interventions are typically classified into three types. One paper investigated alternate-day calorie restriction (ADCR). Four papers investigated time-restricted feeding/eating (TRF/TRE). Four papers investigated intermittent/continuous calorie restriction (I/CCR) or intermittent energy restriction (IER). The duration of the intervention varied from 37 days to one year. The subjects' ages varied from 18 to 75 years, with a total sample size

of 28-150. However, one paper disregards the variety of age subject requirements. BMI subject range from 23 to 50 kg/m^{2,} and one paper disregards the variety of BMI subject requirements.

Synthesis of results

The nine papers' findings support intermittent fasting's use to improve insulin resistance in healthy, obese adults. Overall, the nine papers demonstrated that after the intervention of three different types of intermittent fasting, there was a reduction in insulin resistance as measured using HOMA-IR. In other words, despite a scarcity of research, evidence suggests that intermittent fasting can aid in improving insulin resistance in healthy obese adults. **Table 1** shows the mapping, analysis, and synthesis of evidence.

Discussion

Summary of evidence

The summary of evidence is meant to summarize results following the scoping review's principal purpose. First and foremost, it should be highlighted that there aren't many papers on the use of intermittent fasting as a dietary therapy for obesity that can improve insulin resistance in healthy obese adults. The author acknowledges that the early findings of the paper may be appropriate. Exclusion techniques revealed, however, that while most papers focused RCTs on the benefits of intermittent fasting on weight reduction in obese persons, they did not focus on outcomes related to pathways linked to better insulin resistance owing to free fatty acid buildup. All of the presented investigations are only partially explained. The study's findings, on the other hand, can be woven into a crimson thread.

According to the author, there were initially 1117 documents from five electronic database sources possibly useful for study purposes. Despite hundreds of papers potentially based on the keywords we seek, the paper fails to focus on the topic, namely the effect of intermittent fasting therapies on insulin resistance in obese healthy individuals. As a result, the exclusion method used to establish eligibility excludes the paper. We are leaving only nine papers for us to cover.

Obese people are known to have a buildup of dietary fat. This buildup promotes adipose tissue expansion and increases free fatty acids in non-adipose tissue or organs, resulting in metabolic abnormalities due to impaired insulin signaling and sensitivity. This process is well-known to contribute to insulin resistance primarily.[7] Outstanding guidelines have recommended intermittent fasting as a treatment for obesity to reduce the supply of calories from dietary fat.[11] These findings may be related to the contribution of nutritional support through periodic dietary management and daily calorie restriction that modifies metabolic function.[22]

This review study found one paper with ADCR-type intermittent fasting intervention combined with exercise.[26] The second type of intermittent fasting we discovered is TRF/E.[27,28,33] And the last type is I/CCR or I/ECR.[25,29–31] Overall, the intervention of three types of intermittent fasting decreases insulin levels, enhances insulin sensitivity, and eventually improves insulin resistance. Previous systematic review studies have shown that intermittent fasting is beneficial glycemic and insulin levels control in people with type 2 diabetes and metabolic syndrome but did not focus on insulin resistance.[34] Three types of intermittent fasting (ADF, TRE, and Restriction) are known to decrease fasting glycemic levels, as well as other studies that show improved insulin sensitivity and a reduction in risk factors for chronic illness.[21,35]

Nine findings of the three types of intermittent fasting benefit insulin levels and sensitivity and insulin resistance. These findings are consistent with prior research, which found that ADF, TRF/E, and I/CCR can reduce insulin resistance.[36-37] ADCR-type intermittent fasting, although this intervention is a mix, it is not only intermittent fasting, yet it still contributes. This intervention focuses on energy conservation. Participants ingested 25% of the recommended daily calorie intake on three days of the week, alternating with 'fasting days,' and consumed ad libitum on the remaining four days ‘feed day’.[26]

Table 1. Mapping, synthesis, and analysis

Title	Country	Study type/subject	Intervention	Main findings	Reference
Effects of intermittent and continuous calorie restriction on body weight and metabolism over 50 wk: a randomized controlled trial	German	RCT/overweight/obese adult**.**	I/CCR 8 wk	Insulin concentrations and HOMA-ir were reduced in all research groups.	25
Effects of alternate day calorie restriction and exercise on cardio-metabolic risk factors in overweight and obese adults: an exploratory randomized controlled study.	South Korea	Randomized controlled study/overweight/obesity adult**.**	ADCR 50 wk	Significant insulin, glucose, and HOMA-ir reductions were observed after eight weeks of intervention.	26
Early time-restricted feeding improves insulin sensitivity, blood pressure, and oxidative stress even without weight loss in men with prediabetes.	USA	Randomized, crossover, control study/overweight/obese adult man with prediabetes.	TRF 37 d	eTRF lowers insulin levels and insulin resistance while increasing insulin sensitivity and cell responsiveness.	27.
Effects of four-hour and six-hour time-restricted feeding on weight and cardiometabolic health: a randomized controlled trial in adults with obesity.	USA	*RCT*, randomized parallel-arm trial/ adult obesity.	TRF 10 wk	TRF for 4 and 6 hours results in equal decreases in fasting insulin and insulin resistance.	28
Intermittent energy restriction is comparable to continuous energy restriction for cardiometabolic health in adults with central obesity: A randomized controlled trial; the Met-IER study.	UK	*RCT/adult with central obesity*.	I/CER 4 wk	On the whole, insulin sensitivity significantly increased and decreased insulin resistance and insulin level.	29
Effect of intermittent versus continuous calorie restriction on body weight and cardiometabolic risk markers in subjects with overweight or obesity and mild-to-moderate hypertriglyceridemia: a randomized trial.	Iran	*RCT*/overweight/obese adult.	I/CCR 8 wk	Intermittent calorie restriction improving HOMA-IR.	30
Intermittent energy restriction ameliorates adipose tissue-associated inflammation in adults with obesity: A randomized controlled trial.	Portugal	*RCT*/adult obesity.	I/CER 12 wk	Both dietary regimens improved glucose homeostasis and insulin sensitivity after 12 weeks, with a substantial drop in fasting glucose and insulin plasma concentrations and a significant rise in HOMA-β, HOMA-S, and a decrease in HOMA-IR.	31
Randomized controlled trial for time-restricted eating in overweight and obese young adults.	China	*RCT*/overweight and obese young adults.	TRE 8 wk	6-h eTRE lowered fasting insulin and insulin resistance when compared to the control.	32
Calorie Restriction with or without Time-Restricted Eating in Weight Loss.	China	*RCT*/adult obesity.	TRE 12 mth	Both time-restricted eating and calorie restriction daily were linked to lower HOMA-IR.	33

ADF reduces insulin resistance by enhancing insulin sensitivity and lowering glucotoxicity from calorie intake. [36]

TRF/E type intermittent fasting positively affected insulin resistance. The intervention focused on eTRF with a daily meal schedule of 6 hours and an early dinner before 15:00, TRF 4 hours and 6 hours, the 6-hour eTRE eats ad libitum from 07:00 to 13:00, whereas the 6-hour lTRE eats ad libitum from 12:00 to 18:00, both followed by complete fasting till tomorrow, and 8 hour period adopted from 8:00 to 16:00. It is believed that this good alteration is due to glucoregulatory factors. Fasting may help manage glucose by activating the metabolic switch. The metabolic transition that happens while going from fed to fasting causes hepatocytes to produce ketone bodies, enhancing insulin sensitivity. TRE works by restricting meals briefly, promoting glycemic control, and increasing insulin sensitivity. Zhang explains mechanism effect of TRF is the circadian rhythm system. The circadian system supports improved glucose tolerance and the body's physiological response to fasting at night and morning.[27,28,32,33]

While ADCR and TRF/E help with insulin resistance, I/CCR or I/CER does the same. In the dietary intervention, the ICR group consumed 25% of daily energy needs on two non-consecutive days, while the CCR group ingested 80%, the group's weekly energy intake was reduced by 3500 kcal, the CCR group was directed to consume 70% of total energy, while the ICR group consumed 100%, and IER adopted three non-consecutive fasting days per week (very low energy diet) and a daily low-calorie diet CER. Even though the underlying mechanism is unclear, all four studies imply that changes in insulin resistance occur primarily in those in the highest tertile of HOMA-IR due to changes in plasma TG concentrations linked with insulin, which can contribute to peripheral insulin resistance. Moreover, inflammation in adipose tissue is a root cause of poor insulin signaling, and it is essential for obesity-induced insulin resistance. Given the complex interactions, the more significant drop in HOMA-IR found in the IER group may be related to the inflammatory condition.[25,29–31]

Limitations and strengths

This present review has some limitations that must be recognized. The first review's limitations only applied to papers written in English. Second, despite the fact that the five prominent databases chosen were searched and identified, it only returned the first 15 pages based on relevancy. The third limitation we are aware of is that the available sources of information are relatively restricted, with most of the studies we identified describing insulin resistance as the secondary result. Finally, despite the study's limitations, to the author's knowledge, we believe that this is the first study to examine the effect of intermittent fasting on reducing insulin resistance in overweight or obese healthy individuals. Furthermore, the papers chosen for evidence synthesis are from relevant, recognized sources indexed by Scopus, ensuring that the evidence is of high quality.

Conclusions

In conclusion, according to the findings of this scoping study, the intervention of intermittent fasting has the potential to improve insulin resistance in healthy obese adults. This scoping study is considered to be one of the stepping stones for future research. It is hoped that more comprehensive research will be carried out to provide empirical evidence future on intermittent fasting to improve insulin resistance in clinical practice in healthy obese persons. As a consequence, it is possible to avoid the development of the consequent illness.

Conflict of interest

The author states that any known financial or personal conflicts of interest did not influence the work disclosed in this study.

Acknowledgement

A government, commercial, or non-profit grant did not support this study. However, the scope of this review is supported by Sebelas Maret University as

a provider of institutional access to subscribed electronic databases.

Open Access

References

1. Jin X, Qiu T, Li L, Yu R, Chen X, Li C, et al. Pathophysiology of obesity and its associated diseases. Acta Pharm Sin B [Internet]. 2023; Available from: https://www.sciencedirect.com/science/article/pii/S2211383523000126
2. Klein S, Gastaldelli A, Yki-Järvinen H, Scherer PE. Why does obesity cause diabetes? Cell Metab [Internet]. 2022;34(1):11–20. Available from: https://www.sciencedirect.com/science/article/pii/S1550413121006318
3. Dhurandhar N V. What is obesity? Int J Obes [Internet]. 2022;46(6):1081–2. Available from: https://doi.org/10.1038/s41366-022-01088-1
4. Löffler MC, Betz MJ, Blondin DP, Augustin R, Sharma AK, Tseng YH, et al. Challenges in tackling energy expenditure as obesity therapy: From preclinical models to clinical application. Mol Metab [Internet]. 2021;51:101237. Available from: https://www.sciencedirect.com/science/article/pii/S221287782100082X
5. Mahase E. Global cost of overweight and obesity will hit $4.32tn a year by 2035, report warns. BMJ [Internet]. 2023;380. Available from: https://www.bmj.com/content/380/bmj.p523
6. Hall KD, Farooqi IS, Friedman JM, Klein S, Loos RJF, Mangelsdorf DJ, et al. The energy balance model of obesity: beyond calories in, calories out. Am J Clin Nutr [Internet]. 2022;115(5):1243–54. Available from: https://doi.org/10.1093/ajcn/nqac031
7. Tong Y, Xu S, Huang L, Chen C. Obesity and insulin resistance: Pathophysiology and treatment. Drug Discov Today [Internet]. 2022;27(3):822–30. Available from: https://www.sciencedirect.com/science/article/pii/S1359644621004797
8. Luli M, Yeo G, Farrell E, Ogden J, Parretti H, Frew E, et al. The implications of defining obesity as a disease: a report from the Association for the Study of Obesity 2021 annual conference. eClinicalMedicine [Internet]. 2023;58:101962. Available from: https://www.sciencedirect.com/science/article/pii/S2589537023001396
9. Kivimäki M, Strandberg T, Pentti J, Nyberg ST, Frank P, Jokela M, et al. Body-mass index and risk of obesity-related complex multimorbidity: an observational multicohort study. Lancet Diabetes Endocrinol [Internet]. 2022;10(4):253–63. Available from: https://www.sciencedirect.com/science/article/pii/S221385872200033X
10. Yumuk V, Tsigos C, Fried M, Schindler K, Busetto L, Micic D, et al. European Guidelines for Obesity Management in Adults. Obes Facts [Internet]. 2015;8(6):402–24. Available from: https://doi.org/10.1159/000442721
11. Fitch A, Alexander L, Brown CF, Bays HE. Comprehensive care for patients with obesity: An obesity medicine association position statement. Obes Pillars [Internet]. 2023;100070. Available from: https://www.sciencedirect.com/science/article/pii/S2667368123000165
12. Davis R, Rogers M, Coates AM, Leung GKW, Bonham MP. The Impact of Meal Timing on Risk of Weight Gain and Development of Obesity: a Review of the Current Evidence and Opportunities for Dietary Intervention. Curr Diab Rep [Internet]. 2022;22(4):147–55. Available from: https://doi.org/10.1007/s11892-022-01457-0
13. Markovic TP, Proietto J, Dixon JB, Rigas G, Deed G, Hamdorf JM, et al. The Australian Obesity Management Algorithm: A simple tool to guide the management of obesity in primary care. Obes Res Clin Pract [Internet]. 2022;16(5):353–63. Available from: https://www.sciencedirect.com/science/article/pii/S1871403X22000709
14. Popp C, Hu L, Wang C, Curran M, Li H, Kharmats A, et al. A Randomized Clinical Trial to Compare a Precision Nutrition Intervention Targeting a Reduction in Postprandial Glycemic Response to Meals With a Low-Fat Diet for Weight Loss. Curr Dev Nutr [Internet]. 2022;6:1122. Available from: https://www.sciencedirect.com/science/article/pii/S2475299123210768

15. Aronica L, Rigdon J, Offringa LC, Stefanick ML, Gardner CD. Examining differences between overweight women and men in 12-month weight loss study comparing healthy low-carbohydrate vs. low-fat diets. Int J Obes [Internet]. 2021;45(1):225–34. Available from: https://doi.org/10.1038/s41366-020-00708-y
16. Al Aamri KS, Alrawahi AH, Al Busaidi N, Al Githi MS, Al Jabri K, Al Balushi F, et al. The effect of low-carbohydrate ketogenic diet in the management of obesity compared with low caloric, low-fat diet. Clin Nutr ESPEN [Internet]. 2022;49:522–8. Available from: https://www.sciencedirect.com/science/article/pii/S2405457722001590
17. Verde L, Barrea L, Docimo A, Savastano S, Colao A, Muscogiuri G. Chronotype as a predictor of weight loss and body composition improvements in women with overweight or obesity undergoing a very low-calorie ketogenic diet (VLCKD). Clin Nutr [Internet]. 2023;42(7):1106–14. Available from: https://www.sciencedirect.com/science/article/pii/S0261561423001565
18. Westerterp-Plantenga MS. Challenging energy balance - during sensitivity to food reward and modulatory factors implying a risk for overweight - during body weight management including dietary restraint and medium-high protein diets. Physiol Behav [Internet]. 2020;221:112879. Available from: https://www.sciencedirect.com/science/article/pii/S0031938420301967
19. Alexander L, Christensen SM, Richardson L, Ingersoll AB, Burridge K, Golden A, et al. Nutrition and physical activity: An Obesity Medicine Association (OMA) Clinical Practice Statement 2022. Obes Pillars. 2022 Mar 1;1:100005.
20. Patikorn C, Roubal K, Veettil SK, Chandran V, Pham T, Lee YY, et al. Intermittent Fasting and Obesity-Related Health Outcomes: An Umbrella Review of Meta-analyses of Randomized Clinical Trials. JAMA Netw Open [Internet]. 2021;4(12):e2139558–e2139558. Available from: https://doi.org/10.1001/jamanetworkopen.2021.39558
21. Ezzati A, Rosenkranz SK, Phelan J, Logan C. The Effects of Isocaloric Intermittent Fasting vs Daily Caloric Restriction on Weight Loss and Metabolic Risk Factors for Noncommunicable Chronic Diseases: A Systematic Review of Randomized Controlled or Comparative Trials. J Acad Nutr Diet [Internet]. 2023;123(2):318-329.e1. Available from: https://www.sciencedirect.com/science/article/pii/S2212267222009923
22. Tang D, Tang Q, Huang W, Zhang Y, Tian Y, Fu X. Fasting: From Physiology to Pathology. Adv Sci [Internet]. 2023;10(9):2204487. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1002/advs.202204487
23. Gu L, Fu R, Hong J, Ni H, Yu K, Lou H. Effects of Intermittent Fasting in Human Compared to a Non-intervention Diet and Caloric Restriction: A Meta-Analysis of Randomized Controlled Trials. Vol. 9, Frontiers in nutrition. Switzerland; 2022. p. 871682.
24. Westphaln KK, Regoeczi W, Masotya M, Vazquez-Westphaln B, Lounsbury K, McDavid L, et al. From Arksey and O'Malley and Beyond: Customizations to enhance a team-based, mixed approach to scoping review methodology. MethodsX [Internet]. 2021;8:101375. Available from: https://www.sciencedirect.com/science/article/pii/S2215016121001680
25. Schübel R, Nattenmüller J, Sookthai D, Nonnenmacher T, Graf ME, Riedl L, et al. Effects of intermittent and continuous calorie restriction on body weight and metabolism over 50 wk: a randomized controlled trial. Am J Clin Nutr [Internet]. 2018;108(5):933–45. Available from: https://www.sciencedirect.com/science/article/pii/S000291652203026X
26. Oh M, Kim S, An KY, Min J, Yang HI, Lee J, et al. Effects of alternate day calorie restriction and exercise on cardio-metabolic risk factors in overweight and obese adults: an exploratory randomized controlled study. BMC Public Health [Internet]. 2018;18(1):1124. Available from: https://doi.org/10.1186/s12889-018-6009-1
27. Sutton EF, Beyl R, Early KS, Cefalu WT, Ravussin E, Peterson CM. Early Time-Restricted Feeding Improves Insulin Sensitivity, Blood Pressure, and Oxidative Stress Even without Weight Loss in Men with Prediabetes. Cell Metab. 2018 Jun;27(6):1212-1221.e3.
28. Cienfuegos S, Gabel K, Kalam F, Ezpeleta M, Wiseman E, Pavlou V, et al. Effects of 4- and 6-h Time-Restricted Feeding on Weight and Cardiometabolic Health: A Randomized Controlled Trial in Adults with Obesity. Cell Metab. 2020 Sep;32(3):366-378.e3.
29. Pinto AM, Bordoli C, Buckner LP, Kim C, Kaplan PC, Del Arenal IM, et al. Intermittent energy restriction is comparable to continuous energy restriction for cardiometabolic health in adults with central obesity: A randomized controlled trial; the Met-IER study. Clin Nutr [Internet]. 2020;39(6):1753–63. Available from:

https://www.sciencedirect.com/science/article/pii/S0261561419302961
30. Maroofi M, Nasrollahzadeh J. Effect of intermittent versus continuous calorie restriction on body weight and cardiometabolic risk markers in subjects with overweight or obesity and mild-to-moderate hypertriglyceridemia: a randomized trial. Lipids Health Dis [Internet]. 2020;19(1):216. Available from: https://doi.org/10.1186/s12944-020-01399-0
31. Castela I, Rodrigues C, Ismael S, Barreiros-Mota I, Morais J, Araújo JR, et al. Intermittent energy restriction ameliorates adipose tissue-associated inflammation in adults with obesity: A randomised controlled trial. Clin Nutr [Internet]. 2022;41(8):1660–6. Available from: https://www.sciencedirect.com/science/article/pii/S0261561422002126
32. Zhang L min, Liu Z, Wang J qi, Li R qiang, Ren J yi, Gao X, et al. Randomized controlled trial for time-restricted eating in overweight and obese young adults. iScience [Internet]. 2022;25(9):104870. Available from: https://www.sciencedirect.com/science/article/pii/S2589004222011427
33. Liu D, Huang Y, Huang C, Yang S, Wei X, Zhang P, et al. Calorie Restriction with or without Time-Restricted Eating in Weight Loss. N Engl J Med [Internet]. 2022;386(16):1495–504. Available from: https://doi.org/10.1056/NEJMoa2114833
34. Wang X, Li Q, Liu Y, Jiang H, Chen W. Intermittent fasting versus continuous energy-restricted diet for patients with type 2 diabetes mellitus and metabolic syndrome for glycemic control: A systematic review and meta-analysis of randomized controlled trials. Diabetes Res Clin Pract [Internet]. 2021;179:109003. Available from: https://www.sciencedirect.com/science/article/pii/S0168822721003624
35. Silverii GA, Cresci B, Benvenuti F, Santagiuliana F, Rotella F, Mannucci E. Effectiveness of intermittent fasting for weight loss in individuals with obesity: A meta-analysis of randomized controlled trials. Nutr Metab Cardiovasc Dis [Internet]. 2023; Available from: https://www.sciencedirect.com/science/article/pii/S0939475323001862
36. Ingersen A, Helset HR, Calov M, Chabanova E, Harreskov EG, Jensen C, et al. Metabolic effects of alternate-day fasting in males with obesity with or without type 2 diabetes. Front Physiol [Internet]. 2022;13. Available from: https://www.frontiersin.org/articles/10.3389/fphys.2022.1061063
37. Che T, Yan C, Tian D, Zhang X, Liu X, Wu Z. Time-restricted feeding improves blood glucose and insulin sensitivity in overweight patients with type 2 diabetes: a randomised controlled trial. Nutr Metab (Lond) [Internet]. 2021;18(1):88. Available from: https://doi.org/10.1186/s12986-021-00613-9