IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Role Of Intermittent Fasting On Metabolic Syndrome

[1]Prayanjani Munde, [2]Sneha Prajapati, [3]Rohit Kakad

Research Scholar

Siddhis Institute of Pharmacy Nandgaon

Abstract: This review aims to outline intermittent fasting regimens, highlight their health benefits and discover the physiological mechanisms behind to their potential effects. Evidence suggests that improved fasting regimens support weight loss and metabolic health, while reducing nighttime eating and extending fasting periods may enhance overall well-being. Metabolic syndrome (MetS) is increasingly prevalent worldwide, posing significant societal and economic challenges. Given its association with conditions like obesity, cardiovascular disease and type 2 diabetes which also exacerbate periodontal disease effective prevention and management strategies are crucial. Especially, intermittent fasting has emerged as a scientifically supported, non-pharmacological approach with potential therapeutic benefits for metabolic, inflammatory and lifestyle-related diseases. Intermittent fasting may exert its effects through the mechanisms such as circadian rhythm regulation, adipose tissue modulation, gut microbiome alterations and autophagy. Preclinical, epidemiological and clinical studies indicate its potential benefits for metabolic and inflammatory markers. However, evidence on its impact in patients with non-alcoholic fatty liver disease remains limited. Further research is needed to clarify its mechanisms and evaluate its safety and efficacy in this population. "In that also analysed how fasting and exercise, both individually and together, impact metabolic health and offer insights into potential strategies for preventing metabolic-related diseases."

Index Terms: Intermittent fasting, Fasting, Time-restricted feeding, Food timing, Gut microbiome, Circadian rhythm, Obesity, Diet, Metabolic Syndrome.

INTRODUCTION:

What is intermittent fasting?

Intermittent fasting is an eating pattern in which that involves alternating periods of minimal to no calorie intake, ranging from 12 hours to several days, followed by regular eating. This approach has gained popularity for its potential benefits on body composition and metabolic health. (1) There are several intermittent fasting regimens, including alternate day fasting, where days of complete or modified fasting are alternated with days of unrestricted eating. (2)

It activates neuroendocrine pathways, enhances cellular repair, improves glycaemic control, and regulates key metabolic pathways such as AMPK, sirtuins and mTOR. IF also decreases mitochondrial oxidative stress, inflammation, and proinflammatory markers in gingival crevicular fluid. Preclinical studies suggest its potential in managing chronic conditions like cancer, type 2 diabetes, cardiovascular diseases and neurodegenerative disorders. (3) (4)

Given the societal and economic problem of metabolic syndrome (MetS) and obesity, cost-effective therapeutic strategies are urgently needed. Lifestyle and dietary modifications remain crucial, with IF emerging as a promising non-pharmacological approach for preventing and managing chronic inflammation and sedentary lifestyle-related diseases. However, research on IF's impact on periodontal health remains limited. The current lack of studies on IF's potential benefits for periodontal disease highlights the need for further exploration. (5) (6)

This review aims to link the gap between metabolic and periodontal diseases, emphasizing IF's role in modulating chronic inflammation. It also emphasizes the importance of key metabolic regulators such as mTOR, AMPK and sirtuins in managing the metabolic stress and energy balance. By promoting IF as a complementary, cost-effective strategy, we hope to inspire future research into its integration with conventional disease management approaches for both periodontal disease and MetS. (7) (8)

Metabolic syndrome is a cluster of risk factors that increase the likelihood of developing severe health conditions like heart disease, stroke and type 2 diabetes. These risk factors include high blood pressure, elevated blood sugar, excess waist fat and abnormal cholesterol or triglyceride levels. As metabolic syndrome prevalence increases globally, it has become a significant public health concern, especially in developed countries. (9) (10)

Lifestyle modifications, such as dietary changes are effective in managing and preventing the metabolic syndrome. Intermittent fasting, which involves alternating eating and fasting periods, has gained attention for its potential benefits. Unlike traditional dieting, intermittent fasting focuses on when to eat, rather than what to eat. Intermittent fasting (IF) has gained popularity as a health trend in recent years, with several common approaches. The 16:8 method in which it involves fasting for 16 hours daily and eating within an 8-hour window. One Meal a Day (OMAD) is a more extreme form, requiring a 23-hour fast with a single meal in a 1-hour window. Alternate-day fasting comprises the fasting every other day, either completely or with minimal caloric intake. The 5:2 diet allows normal eating for five days a week while significantly reducing calories on the remaining two days. Time-restricted feeding (TRF) limits food intake to a 6-to-10-hour window during the active part of the day without altering food quality or quantity. Ramadan fasting involves refraining from food and drink from sunrise to sunset, whereas other IF methods typically permit zero-calorie beverages such as water, tea and coffee during fasting periods. (11) (12)

This eating pattern is promoted not only for weight loss but also for improving metabolic health markers such as cholesterol levels, blood sugar control and blood pressure, which are directly related to the metabolic syndrome.

Definition of Metabolic Syndrome:

In his 1988 Banting lecture, Reaven recognized a cluster of conditions associated with the insulin resistance, which he termed "Syndrome X" or "the deadly quartet." This cluster included obesity, non-insulin-dependent diabetes mellitus, hypertension and dyslipidemia. Since then, several definitions have been proposed to better describe this combination of cardiometabolic risk factors, including the WHO definition (1998), the NCEP (National Cholesterol Education Program) definition (2003) and the IDF (International Diabetes Federation) definition (2006). (13) To resolve inconsistencies and establish a standardized diagnostic approach, major health organizations collaborated to develop the harmonized definition of metabolic syndrome (MetS), which is currently in use. (14)

Under this harmonized definition, MetS is diagnosed based on the following criteria: (15) (16)

1. Insulin resistance or prediabetes, defined by a glucose level exceeding 100 mg/dL (5.6 mmol/L) or a confirmed diagnosis of type 2 diabetes mellitus.
2. An enlarged waist circumference, with specific thresholds determined by population- and country-specific guidelines.
3. Low HDL cholesterol levels (<40 mg/dL [1.03 mmol/L] in men and <50 mg/dL [1.29 mmol/L] in women) or elevated triglycerides (≥150 mg/dL [1.69 mmol/L]), including individuals receiving treatment for dyslipidemia.
4. High blood pressure defined as a systolic reading of ≥130 mm Hg or a diastolic reading of ≥85 mm Hg, including those undergoing antihypertensive therapy.

Epidemiology of Metabolic Syndrome: (17) (18) (19)

Metabolic syndrome (MetS) results from a complex interaction of genetic and environmental factors with central obesity and visceral adipose tissue (VAT) playing a main role. VAT releases free fatty acids (FFA), promoting liver gluconeogenesis, triglyceride and VLDL production whereas impairing insulin sensitivity through lipid metabolite accumulation.

Dysregulated adipokine secretion in MetS leads to increased levels of pro-inflammatory cytokines (TNF-α, IL-6, MCP-1) and reduced adiponectin, worsening insulin resistance. Leptin resistance further disrupts energy regulation. Chronic inflammation driven by these factors contributes to muscle insulin resistance, β-cell dysfunction and increased cardiovascular risk.

Gut–adipose tissue interactions are also impaired, with decreased incretin (GLP-1, GIP) secretion and persistently high ghrelin levels, reinforcing obesity. This metabolic dysfunction, along with sympathetic nervous system and renin-angiotensin-aldosterone system activation, promotes hypertension, further compounding MetS progression.

Effects of Diet on Metabolic Syndrome: (20) (21)

The Western diet is characterized by high consumption of red and processed meats, refined grains, sweets and sugary beverages is linked to an increased risk of developing metabolic syndrome (MetS). This diet is calorie-dense and rich in saturated fatty acids (SFA), simple carbohydrates and other nutrients that promote inflammation, disrupt gut microbiota and reduce insulin sensitivity.

Research indicates that dietary patterns significantly influence MetS risk. A meta-analysis by Fabiani et al. found that the "Meat/Western" dietary pattern leads to a 19% increase in the MetS risk, while a "Healthy" dietary pattern rich in fruits, vegetables, whole grains, fish and low in processed foods correlates with a 15% decrease in the MetS risk.

Similarly, adherence to the Mediterranean diet which highlights plant-based foods, healthy fats and lean proteins has been associated with a decreased risk of MetS. A meta-analysis by Kastorini et al. showed that the Mediterranean diet is linked to a decreased risk of MetS.

The Dietary Approaches to Stop Hypertension (DASH) diet, focusing on fruits, vegetables, whole grains and lean proteins has also demonstrated benefits for MetS. Studies have shown that the DASH diet leads to reductions in blood pressure, body mass index (BMI), waist circumference and the incidence of type 2 diabetes.

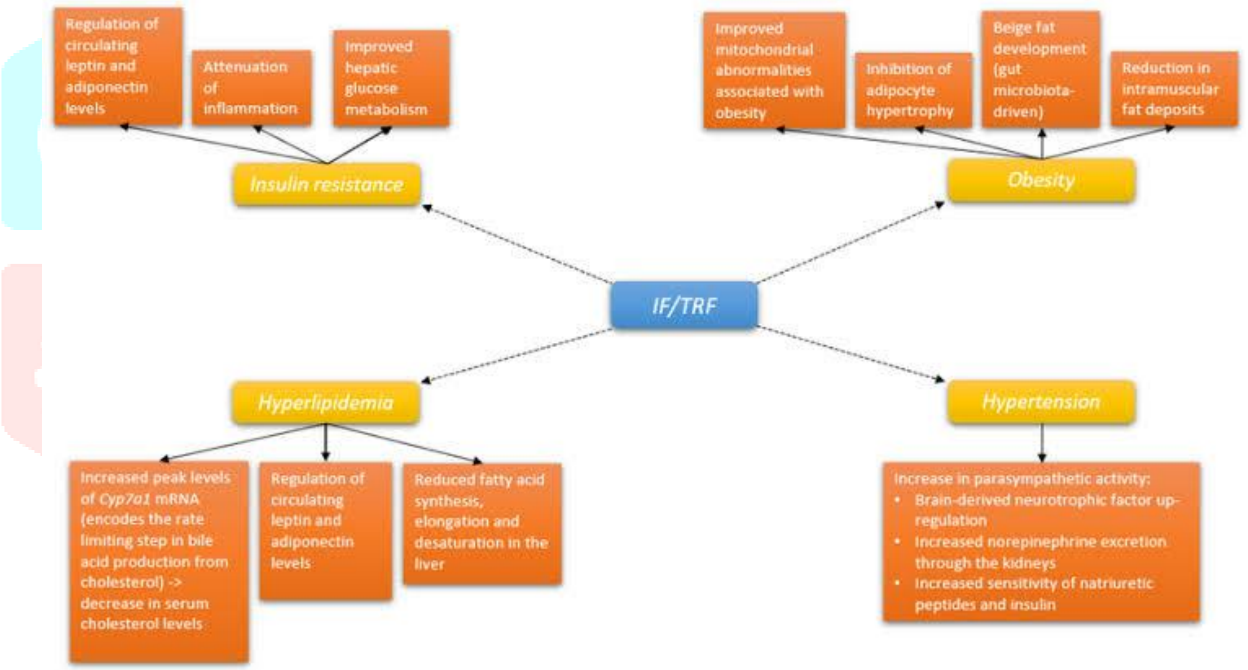

Fig 1: Pathways through which intermittent fasting/time restricted feeding may affect the constituents of metabolic syndrome. Abbreviations: IF: intermittent fasting; TRF: time-restricted feeding.

Intermittent fasting Methods:

We provide a brief background on the intermittent fasting in animal models to contextualize its application in human studies. Our review focuses on the alternate-day fasting, modified fasting regimens and time-restricted feeding. (22) A PubMed search was conducted using relevant keywords, supplemented by references from existing research and reviews.

Inclusion criteria for human studies were:

1. Randomized or nonrandomized trials
2. Adult participants
3. Outcomes related to body weight or biomarkers for diabetes, cardiovascular disease, or cancer

This is not a formal review or meta-analysis due to differences in study design, intervention methods and participant groups. Religious fasting (e.g., Ramadan) is briefly discussed separately. (23)

INTERMITTENT FASTING: HUMAN INTERVENTION TRIALS

Alternate Day Fasting: (24) (25) (26)

Alternate-day fasting involves alternating between fasting days (no calorie intake) and eating days (ad libitum consumption). Animal studies suggest it is as effective as caloric restriction in reducing insulin, glucose, cholesterol and triglycerides, with potential cancer risk benefits.

Three small human studies (8–30 participants) have examined its metabolic effects. Two reported significant weight loss with one study showing 2.5% reduction over 22 days. Improvements were observed in glucose regulation and some lipid markers, though LDL cholesterol enlarged. Inflammatory markers improved in one study.

Despite some metabolic benefits, significant hunger in fasting days raises concerns about its long-term feasibility as a public health strategy.

Modified Fasting Regimens: (27) (28)

Modified fasting allows for 20–25% of daily energy intake on fasting days, as seen in diets like the 5:2 routine. Animal studies suggest benefits such as reduced visceral fat, improved adipokine levels, and reduced cell proliferation.

Eight human trials (10–107 overweight/obese adults) examined modified fasting over 8 weeks to 6 months. Six studies (75%) reported weight loss (3.2–8.0%). Some showed reductions in fasting insulin and lipid levels, while others found developments in inflammatory markers and mood. Side effects were minimal, though some participants experienced hunger, fatigue or irritability.

Three studies compared modified fasting to standard calorie limit, with one showing superior weight loss when combined with exercise. Overall, modified fasting and continuous calorie restriction resulted in similar weight loss (3–8% vs. 4–14%) and metabolic changes. These findings suggest that while modified fasting can aid weight loss, it does not provide significant advantages over standard calorie restriction.

Time-Restricted Feeding: (29) (30)

Animal studies suggest that time-restricted feeding (12–20 hour fasting windows) reduces body weight, cholesterol, glucose, insulin and inflammation while improving insulin sensitivity. Harmonizing feeding with circadian rhythms also appears to protect against obesity and metabolic disorders, even without calorie restriction.

In humans, only two small trials examined extended nighttime fasting. One study (29 men) found a 1.3% weight loss over two weeks with an ≥11-hour fasting window. Another 8-week study showed 4.1% weight loss when contributors ate one afternoon meal per day, along with improved glucose and cholesterol levels. Hunger was higher in the morning but did not significantly affect mood.

Although research is limited, findings suggest that aligning eating patterns with circadian rhythms may support metabolic health. (31)

RELIGIOUS FASTING: OBSERVATIONAL RESEARCH

Many religions incorporate fasting for both spiritual and physical benefits. However, published research on these fasting regimens is almost entirely observational. Therefore, we provide only an overview of these fasting regimens. (32) (33)

Ramadan Fasting:

Ramadan fasting requires abstaining from food, fluids, and smoking from dawn to sunset, with fasting durations varying by location and season. While not designed for energy restriction, it often leads to weight changes. (34)

A 2012 meta-analysis of 35 studies create significant weight loss in 62% of cases, averaging 1.24 kg, with partial regain (0.72 kg) within two weeks post-Ramadan. A 2013 meta-analysis of 30 studies reported reductions in LDL cholesterol and fasting glucose for both sexes, with HDL increases in females and weight, total cholesterol, and TG reductions in males. Some studies also noted lower inflammatory markers. (35)

While Ramadan fasting leads to the temporary weight loss and some metabolic improvements, its misalignment with circadian rhythms makes it less appropriate as a long-term weight loss strategy. (36)

Other Religious Fasts:

Religious fasting practices may have health benefits. A study of 448 hospital patients in Utah found that Latter-Day Saints who routinely fast had lower weight, fasting glucose and reduced risks of diabetes and coronary stenosis.

Seventh-day Adventists emphasize a healthy lifestyle, including plant-based diets and regular exercise, contributing to an average lifespan increase of 7.3 years. Several Adventists consume only two meals per day, with the last meal in the afternoon, leading to prolonged nighttime fasting. While this fasting pattern may have biological benefits, its direct health effects have not been studied. (37) (38)

Type of fast	Description
Complete alternate-day fasting	Involves alternating fasting days (no energy-containing foods or beverages consumed) with eating days (foods and beverages consumed ad libitum)
Modified fasting regimens	Allows consumption of 20–25% of energy needs on scheduled fasting days; the basis for the popular 5:2 diet, which involves severe energy restriction for 2 nonconsecutive days per week and ad libitum eating for the other 5 days
Time-restricted feeding	Allows ad libitum energy intake within specific time frames, inducing regular, extended fasting intervals; studies of <3 meals per day are indirect examinations of a prolonged daily or nightly fasting period
Religious fasting	Variety of fasting regimens undertaken for religious or spiritual purposes
Ramadan fasting	A fast from sunrise to sunset during the holy month of Ramadan; the most common dietary practice is to consume one large meal after sunset and one lighter meal before dawn. Thus, the feast and fast periods of Ramadan are approximately 12 hours in length
Other religious fasts	Members of the Church of Jesus Christ of Latter-Day Saints routinely abstain from food and drink for extended periods of time. Some Seventh-day Adventists consume their last of two daily meals in the afternoon, resulting in an extended nighttime fasting interval that may be biologically important

Fig 2: Types of intermittent fasting regimens that are hypothesized to impact health outcomes

Potential Risk of (IF):

Intermittent fasting (IF) may not be right for everyone. Pregnant women should avoid it due to uncertain long-term effects. While generally safe for people with type 2 diabetes, those on glucose-lowering medication require close monitoring. Additionally, IF may cause side effects such as low energy, headaches, dizziness, mood swings, constipation, bad breath and increased focus on food. (39) (40) (41)

Intermittent Fasting and Physical Exercises for Preventing Metabolic Disorder: (42)

Physical exercise plays a key role in gut health by enhancing bowel motility, blood flow and immune function, reducing inflammation and supporting a strong intestinal barrier. Studies show that active individuals have higher levels of beneficial bacteria, such as Faecalibacterium prausnitzii and A. muciniphila, which are often decreased in those with metabolic disorders like obesity, type 2 diabetes, NAFLD and cardiovascular diseases.

Obesity: (43)

Regular physical exercise helps prevent weight gain and definitely influences gut bacteria in both obese individuals and high-fat diet-fed mice. It reduces visceral and subcutaneous fat while improving the balance of Bacteroidetes and Firmicutes, which is often disrupted in obesity. Studies show that exercise developments beneficial, butyrate-producing bacteria and key gut metabolites, supporting metabolic health. Additionally, exercise may boost Akkermansia levels and reduce harmful Proteobacteria.

CVDs: (44)

The gut microbiota contributes to cardiovascular disease by influencing factors like TMA and LPS production, bacterial migration to arterial plaques and increased blood pressure. Regular exercise on the other hand improves arterial function by boosting shear stress, lowering triglycerides and enhancing cardiac and autonomic performance. Additionally, exercise improves gut motility, which helps shed loosely bound microbes and promotes beneficial bacteria that strengthen mucosal immunity. Studies even show that transferring microbiota from exercised mice to sedentary ones results in better heart function, likely due to exercise-induced changes in gut microbial diversity and the release of protective metabolites.

T2D: (45)

Research shows that exercise reduces type 2 diabetes risk by improving insulin sensitivity and glucose tolerance. It also modulates the gut microbiota, where interventions like interval and moderate-intensity workouts lower inflammatory markers (e.g., TNF-α and LPS), increase the beneficial Bacteroidetes/Firmicutes ratio and reduce levels of bacteria such as Clostridium and Blautia. Moreover, exercise intensity plays a role moderate exercise tends to decrease certain bacterial groups, while higher-intensity exercise boosts different butyrate-producing microbes that support the gut barrier integrity and overall metabolic.

NAFLD: (46)
NAFLD is marked by excess triglyceride buildup in liver cells, largely due to fatty acid esterification. Its development is linked to insulin resistance, oxidative stress, inflammation and other factors. In insulin-resistant adipose tissue increased lipolysis elevates free fatty acids in the blood, which are then absorbed by the liver. Notably, physical exercise improves liver health by enhancing lipid metabolism, boosting insulin sensitivity and reducing inflammation. For instance, a trial in diabetic obese patients with NAFLD showed that both high-intensity interval and moderate-intensity continuous exercise effectively lowered triglyceride and visceral fat levels.

Modulation Effects of Combining IF and Physical Exercises on Metabolic Syndrome:
Intermittent fasting (IF) and physical exercise are effective strategies for preventing metabolic disorders with their combination yielding superior benefits. Studies indicate that IF and exercise enhance insulin metabolism, increase AMPK activity and GLUT4 protein and improve glycemic tolerance. Research demonstrations that combining alternate-day fasting (ADF) with aerobic exercise reduces intrahepatic triglycerides in obese individuals with NAFLD. Additionally, IF with exercise significantly improves lipid profiles, reduces fat mass, increases fat-free mass and enhances functional capacities, particularly in obese women. Animal studies further support these findings, demonstrating reduced fat accumulation and lower LDL levels. (47) (48)

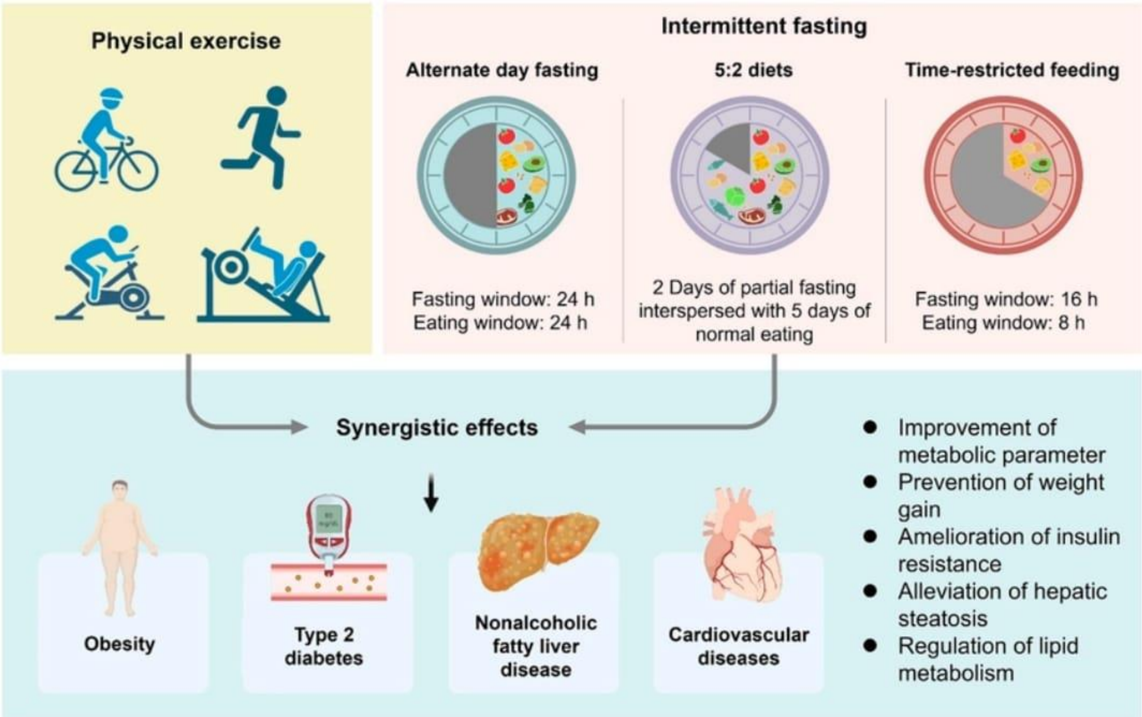

Fig 3: Combining physical exercise and IF for preventing metabolic disorders.

CONCLUSION:

Even a single fasting interval in humans (e.g., overnight) can reduce basal concentrations of many metabolic biomarkers associated with chronic disease such as insulin and glucose. For example, patients are required to fast for 8–12 hours before blood draws to achieve steady-state fasting levels for many metabolic substrates and hormones. An important clinical and scientific question is whether adopting a regular, intermittent fasting regimen is a feasible and sustainable population-based strategy for promoting metabolic health. Further, properly powered, controlled clinical research is needed to test whether intermittent fasting regimens can complement or replace energy restriction and if so, whether they can facilitate long-term metabolic improvements and body weight management. The Summary Points are supported by the current evidence. Additionally, intermittent fasting regimens attempt to translate the positive effects of fasting regimens in rodents and other mammals into practical eating patterns for reducing the risk of chronic disease in humans.

In the Future Issues section, we suggest issues that should be addressed in research investigating intermittent fasting and metabolic health.

This overview suggests that intermittent fasting regimens may be a promising approach to losing weight and improving metabolic health for people who can safely tolerate intervals of not eating or eating very little, for certain hours of the day, night or days of the week. If proven to be efficacious, these eating regimens may offer promising nonpharmacological approaches to improving health at the population level with multiple public health benefits.

REFERENCE:

1. Albosta MJB. "Intermittent fasting: is there a role in the treatment of diabetes? A review of the literature and guide for primary care physicians.". (2021).

2. Anton SD MKDWea. Flipping the metabolic switch: understanding and applying the health benefits of fasting. Obesity (SilverSpring). 2018; 26(2): 254–68.

3. Zubrzycki A CKKKZWA. The role of low-caloriediets and intermittent fasting in the treatment of obesity and type-2diabetes. J Physiol Pharmacol.. 2018; 69(5): 10.26402.

4. Parveen SaYAA. "Impact of Intermittent Fasting on Metabolic Syndrome and Periodontal Disease—A Suggested Preventive Strategy to Reduce the Public Health Burden. International journal of environmental research and public health. 2022;: 14536.

5. Longo VD, Mattson MP. Fasting: Molecular Mechanisms and Clinical Applications. Cell Metab. 2014; 19: 181–192.

6. Grajower MM, Horne BD. Clinical Management of Intermittent Fasting in Patients with Diabetes Mellitus. Nutrients. 2019; 11: 873.

7. Varady KA, Bhutani S, Church EC, Klempel. M.C. Short-Term Modified Alternate-Day Fasting: A Novel Dietary Strategy for Weight Loss and Cardioprotection in Obese Adults. Am. J. Clin. Nutr. 2009; 90: 1138–1143.

8. Templeman I, Thompson D, Gonzalez J, Walhin JP, Reeves S, Rogers PJ, et al. Intermittent Fasting, Energy Balance and Associated Health Outcomes in Adults: Study Protocol for a Randomised Controlled Trial. 2018;: 86.

9. Herzig S, Shaw RJA. Guardian of Metabolism and Mitochondrial Homeostasis. Nat. Rev. Mol. Cell Biol. 2018;: Nat. Rev. Mol. Cell Biol.

10. Kane AE, Sinclair DA. Sirtuins and NAD+ in the Development and Treatment of Metabolic and Cardiovascular Diseases. Circ. Res. 2018; 123: 868–885.

11. De Cabo R, Mattson MP. Effects of Intermittent Fasting on Health, Aging, and Disease. N. Engl. J. Med. 2019; 381: 2541–2551.

12. Almabruk BA,ea. The Role of Intermittent Fasting on Metabolic Syndrome: A Systematic Review and Meta-Analysis. Cureus. 2024.

13. Vrdoljak Jea. Can fasting curb the metabolic syndrome epidemic?". Nutrients 14.3. 2022;: 456.

14. Nilsson PM, Tuomilehto J, Rydén L. The metabolic syndrome—What is it and how should it be managed? Eur. J. Prev. Cardiol. 2019; 26: 33–46.

15. Reaven GM. Banting lecture 1988. Role of insulin resistance in human disease. Diabetes. 1988; 37: 1595–1607.

16. Popa S, Mo¸ta M, Popa A, Mo¸ta E, Serafinceanu C, Guja C, et al. Prevalence of overweight/obesity, abdominal obesity and metabolic syndrome and atypical cardiometabolic phenotypes in the adult Romanian population. PREDATORR study. J. Endocrinol. Investig. 2016; 39: 1045–1053.

17. Moore JX, Chaudhary N, Akinyemiju T. Metabolic Syndrome Prevalence by Race/Ethnicity and Sex in the United States, National Health and Nutrition Examination Survey,. Prev. Chronic Dis. 2017. 1988–2012.; 14: E24.

18. National Health and Nutrition Examination Survey. Available online: https://www.cdc.gov/nchs/data/factsheets/factsheet_nhanes.pdf. .

19. Fabiani R, Naldini G, Chiavarini M. Dietary Patterns and Metabolic Syndrome in Adult Subjects: A Systematic Review and Meta-Analysis. Nutrients. 2019; 11: 2056.

20. Zinöcker MK, Lindseth IA. The Western Diet-Microbiome-Host Interaction and Its Role in Metabolic Disease. Nutrients. 2018; 10: 365.

21. Julibert A, Bibiloni MDM, Tur JA. Dietary fat intake and metabolic syndrome in adults: A systematic review. Nutr. Metab. Cardiovasc. Dis. 2019; 29: 887–905.

22. Patterson RE,ea. Intermittent fasting and human metabolic health. Journal of the Academy of Nutrition and Dietetics. 2015;: 1203.

23. Varady KA HM. Alternate-day fasting and chronic disease prevention: a review of human and animal trials. Am J Clin Nutr. 2007; 86: 7–13.

24. Halberg N HMSNea. Effect of intermittent fasting and refeeding on insulin action in healthy men. J Appl Physiol.. 2005; 99: 2128–2136.

25. Heilbronn LK SSMCASRE. Alternate-day fasting in nonobese subjects: effects on body weight, body composition, and energy metabolism. Am J Clin Nutr.. 2005; 81: 69–73.

26. Horne BD MJLDea. Randomized cross-over trial of short-term water-only fasting: Metabolic and cardiovascular consequences. Nutr Metab Cardiovasc Dis. 201`3; 23: 1050–1057.

27. Varady KA RDMHBGBTMHM. Modified alternate-day fasting regimens reduce cell proliferation rates to a similar extent as daily calorie restriction in mice. FASEB J. 2008; 22: 2090–2096.

28. Varady KA RDHM. Dose effects of modified alternate-day fasting regimens on in vivo cell proliferation and plasma insulin-like growth factor-1 in mice. J Appl Physiol. 2007; 103: 547–551.

29. Varady KA RDLYMHBHM. Varady KA, Roohk DJ, Loe YC, McEvoy-Hein BK, Hellerstein MK. J Lipid Res. 2007; 48: 2212–2219.

30. Williams KV MMKDWR. The effect of short periods of caloric restriction on weight loss and glycemic control in type 2 diabetes.. Diabetes Care. 1998; 21: 2–8.

31. Johnson JB SWCRea. Alternate day calorie restriction improves clinical findings and reduces markers of oxidative stress and inflammation in overweight adults with moderate asthma. Free Radic Biol Med. 2007; 42: 665–674.

32. Varady KA BSCEKM. Short-term modified alternate-day fasting: a novel dietary strategy for weight loss and cardioprotection in obese adults. Am J Clin Nutr. 2009; 90: 1138–1143.

33. Harvie MN PMMMea. The effects of intermittent or continuous energy restriction on weight loss and metabolic disease risk markers: a randomized trial in young overweight women. Int J Obes Suppl.. 2011; 35: 714–727.

34. Bhutani S KMKCTJVK. Alternate day fasting and endurance exercise combine to reduce body weight and favorably alter plasma lipids in obese humans.. Obesity.. 2013; 2: 1370–1379.

35. Eshghinia S MF. The effects of modified alternate-day fasting diet on weight loss and CAD risk factors in overweight and obese women. J Diabetes Metab Disord. 2013; 12: 4.

36. Harvie MN WCPMea. The effect of intermittent energy and carbohydrate restriction v. daily energy restriction on weight loss and metabolic disease risk markers in overweight women. Br J Nutr.. 2013; 110: 1534–1547.

37. Stote KS BDSKea. A controlled trial of reduced meal frequency without caloric restriction in healthy, normal-weight, middle-aged adults. Am J Clin Nutr.. 2007; 85: 981–988.

38. Zhang Lea. Intermittent fasting and physical exercise for preventing metabolic disorders through interaction with gut microbiota: a review. Nutrients. 2023;: 2277.

39. Lavallee CM,ea. The role of intermittent fasting in the management of nonalcoholic fatty liver disease: a narrative review. Nutrients. 2022;: 4655.

40. 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.. 2021; 179: 109003.

41. 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: Diabetologia.

42. Zhang Lea. Intermittent fasting and physical exercise for preventing metabolic disorders through interaction with gut microbiota: a review. Nutrients. 2023;: 2277.

43. obesity. Epwgaatgmiammohfdi. Exercise prevents weight gain and alters the gut microbiota in a mouse model of high fat diet-induced obesity.. PLoS ONE. 2014; 9: e92193.

44. Allen JM, Mailing LJ, Niemiro GM, Moore R, Cook MD, White BA, et al. Exercise alters gut microbiota composition and function in lean and obese humans. Med. Sci. Sports Exerc. 2018; 50: 747–757.

45. Motiani KK, Collado MC, Eskelinen JJ, Virtanen KA, Loyttyniemi E, Salminen S, et al. Exercise training modulates gut microbiota profile and improves endotoxemia. Med. Sci. Sports Exerc.. 2020; 52: 94–104.

46. Tuovinen E, Keto J, Nikkila J, Matto J, Lahteenmaki K. Cytokine response of human mononuclear cells induced by intestinal Clostridium species.. Anaerobe. 2013; 19: 70–76.

47. Leung C, Rivera L, Furness JB, Angus PW. The role of the gut microbiota in NAFLD. Nat. Rev. Gastroenterol.. Hepatol.. 2016; 13: 412–425.

48. Lanter BB, Sauer K, Davies DG. Bacteria present in carotid arterial plaques are found as biofilm deposits which may contributeto enhanced risk of plaque rupture. MBio. 2014; 5: e01206-14.