



The Impact of Intermittent Fasting on Metabolic Health and Chronic Disease Prevention: A Comprehensive Review

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ABSTRACT: Intermittent fasting has gained attention as a dietary approach focusing on the timing of eating rather than the specific foods being consumed. Unlike the traditional calorie restriction, intermittent fasting involves alternating periods of fasting and eating. Several prevalent forms of IF exist, each with unique fasting durations and eating windows. For instance, the 16/8 method restricts food intake to an 8-hour window each day, followed by 16 hours of fasting. The 5:2 diet involves eating regular meals for five days a week and significantly reducing calorie intake to 500-600 calories on the remaining two non-consecutive days. Another popular method, Eat-Stop-Eat, includes one or two 24-hour fasts per week without calorie restriction on non-fasting days. The rising interest in IF is due to its potential health benefits, such as weight loss, chronic disease prevention, and improved metabolic health. IF may reduce the risk of obesity, diabetes, cardiovascular disease, and certain cancers. The increasing interest in IF is largely due to its potential health benefits, including the prevention of multiple chronic diseases, weight reduction, and improvements in metabolic health markers. A growing body of scientific evidence suggests that IF may positively impact metabolic health, potentially reducing the risk of obesity, diabetes, cardiovascular disease, and certain types of cancer. Intermittent fasting can enhance weight management and health improvement, but further research is needed to understand its long-term effects on people, optimal protocols, and potential risks. This will help guide informed decisions on the safe way and effective use.

KEYWORDS: Intermittent fasting, weight management, metabolic health, chronic disease prevention

INTRODUCTION

Intermittent fasting (IF) has garnered substantial attention as a novel dietary approach that entails alternating periods of fasting and consuming. IF, in contrast to conventional calorie restriction, emphasises the timing of food consumption rather than the specific foods consumed (1). There are numerous prevalent varieties of intermittent fasting, each with its own unique fasting durations and eating windows. For example, the 16/8 method entails restricting food intake to an 8-hour window each day and abstaining for 16 hours(2). The 5:2 diet is another prevalent method, which entails consuming standard meals on five days per week and significantly reducing calorie consumption to 500-600 calories on the other two non-consecutive days(3). Eat-Stop-Eat, an additional intermittent fasting approach, entails one or two 24-hour fasts per week, with no calorie restriction on the remaining days(4).

The increasing interest in IF can be attributed to its potential to provide a diverse range of health benefits, such as the prevention of chronic diseases, reduced weight, and enhanced metabolic health markers(5). A burgeoning body of scientific evidence indicates that IF may have significant impacts on metabolic health, potentially reducing the risk of obesity, diabetes, cardiovascular disease, and certain types of cancer(6).

The objective of this exhaustive review is to conduct a critical analysis of the current state of scientific evidence regarding the potential of intermittent fasting to prevent chronic diseases and its impact on metabolic health. The review will assess the impact of various IF protocols on critical metabolic health indicators, including inflammation, glucose regulation, insulin sensitivity, and lipid profiles. Furthermore, it will evaluate the potential mechanisms by which IF may affect metabolic health and the risk of chronic diseases, such as modifications in gene expression, cellular repair processes, and intestinal microbiome composition.

Additionally, this review will examine the most recent evidence regarding the use of IF to prevent and manage specific chronic diseases, such as cancer, cardiovascular disease, type 2 diabetes, and obesity. Lastly, it will identify voids in the current body of knowledge and emphasise areas for future research to gain a more comprehensive understanding of the long-term effects and sustainability of IF as a lifestyle-modifying intervention.



Intermittent Fasting and Cardiovascular Health

One diet that shows great promise to help cardiovascular health is intermittent fasting. IF can apparently significantly affect many important cardiovascular risk markers, including blood pressure, resting heart rate, cholesterol levels, triglycerides, glucose, and insulin, according to an increasing body of research. Remarkably, these changes show up in a somewhat short two to four week period of IF program implementation (7,8). The metabolic changes experienced during fasting periods—such as enhanced fat oxidation, greater insulin sensitivity, and lower inflammation—are assumed to provide the basis for these favourable benefits (9).

Particularly notable is how IF affects blood pressure. By an astounding 4.16 mmHg and diastolic blood pressure by 2.92 mmHg, a thorough systematic review and meta-analysis by Cho et al. (2019) demonstrated that IF dramatically lowered systolic blood pressure by comparison to control groups (10). A study by Sutton et al. (2018), which showed early time-restricted feeding, a type of IF, not only improved blood pressure but also decreased oxidative stress and hunger in men with prediabetes(11).

Apart from its influence on blood pressure, IF has shown amazing ability in enhancing lipid profiles. If IF could lower total cholesterol by a significant 10-21% and triglycerides by an amazing 14-42% in humans (12), a review by Santos and Macedo (2018) highlighted The higher lipolysis and fat oxidation experienced during fasting periods is believed to be mediator of these changes in lipid profiles (13).

It is important to understand, nevertheless, that if the eating plan is not long-term, the advantages of IF on cardiovascular health could be fleeting. According to certain research, the changes in cardiovascular risk variables could fade several weeks after the IF program is stopped (14). This emphasises the need of long-term commitment to IF as a lifestyle change in order to preserve its cardioprotective properties.

Although the present data strongly supports the potential of IF to improve cardiovascular health markers, it is vital to recognise that more study is needed to define the appropriate fasting protocols, duration of intervention, and long-term sustainability for various groups. It is getting more and more evident as the scientific community investigates the mechanics and uses of IF that this dietary approach has great potential as a strong tool for enhancing cardiovascular health and lowering the risk of chronic diseases.

Potential Risks and Side Effects of IF

While intermittent fasting has garnered significant interest for its potential health advantages, it is important to acknowledge that this dietary approach may not be appropriate for everyone and can result in various adverse effects. Individuals who adhere to intermittent fasting (IF) may have a variety of unfavourable symptoms, such as weakness, heightened appetite, dehydration, frequent headaches, diminished focus, hypotension, or syncope (15). The detrimental consequences that occur during fasting periods are often ascribed to the metabolic modifications and calorie restriction that the body undergoes as it adjusts to the changes in eating patterns and energy intake.

Prior to commencing an intermittent fasting (IF) regimen, individuals should seek guidance from a trained nutritionist to minimise the potential for adverse reactions and guarantee sufficient nutrient consumption. It is particularly crucial for some groups, such as pregnant or nursing women, frail elderly adults, those with weakened immune systems, and those with a past of eating problems, to be cautious about intermittent fasting (IF) as it may not be suitable or safe for them (16). Frail elderly individuals and those with weakened immune systems may be more susceptible to the potential negative consequences of calorie restriction and changes in eating habits. However, pregnant and nursing women require greater nutritional intake to support the growth of the foetus and the production of milk.

Furthermore, people with diabetes should exercise great caution when thinking about IF since the nutritional approach may cause hypoglycemia, or low blood sugar (17). The changed meal schedule and longer fasting times linked with IF can upset the delicate equilibrium between medicine, insulin, and glucose levels, therefore greatly raising the risk of hypoglycemic episodes. For those with diabetes, hypoglycemia can be very harmful as untreated it can cause confusion, dizziness, seizures, and even unconsciousness. Therefore, before trying IF to completely understand the possible benefits and risks in the context of their specific health status and to create a customised plan that guarantees their safety and well-being, people with diabetes or other chronic health conditions must see their healthcare provider.



Significance

The great promise of intermittent fasting as an effective tool for weight control, general health enhancement, and the avoidance of chronic diseases explains the growing curiosity in this practice. IF has become a more flexible and sustainable way to reach and keep a healthy weight as obesity rates are rising at an alarming speed worldwide and alternative to conventional calorie restriction diets (18). For many people trying to change their body composition and metabolic health, IF is a more flexible and practical choice because of its emphasis on the timing of food intake rather than the rigorous restriction of particular foods or total calorie intake.

Apart from its well-documented impact on weight control, IF has been repeatedly linked to a broad spectrum of health advantages going much beyond simple changes in body composition. Many research have shown how well IF might raise insulin sensitivity, lower systemic inflammation, boost brain performance, and possibly extend lifespan (19). The complicated metabolic and physiological changes that arise during fasting periods—such as enhanced glucose control, more fat oxidation, and the activation of cellular repair mechanisms—are believed to be mediators of these advantages.

Given the worldwide burden of several chronic diseases is rising at an unheard-of pace, the potential of IF to prevent and control several diseases has also attracted major attention recently. Based on accumulating data, IF might be protective against various major chronic diseases including cardiovascular disease, type 2 diabetes, neurodegenerative diseases, and potentially some forms of cancer (20). The development of cellular stress resistance, the encouragement of autophagy (a cellular self-cleaning process), and the modification of important metabolic pathways engaged in the pathogenesis of these diseases define the several processes behind these protective effects (21).

The interest among healthcare professionals, academics, and the general public in this exciting dietary strategy rises along with the volume of data confirming the health advantages of IF. IF's growing popularity has also spurred a more general conversation on the need of meal timing and the possible benefits of matching eating patterns with the body's inherent circadian rhythms (22). Growing understanding of the chronobiological aspects of nutrition has led to a paradigm change in our comprehension of the complex relationship of food intake, metabolic state, and overall well-being.

As more research serve to understand the basic mechanisms and long-term effects of IF, thus optimising health, preventing chronic diseases, and promoting lifespan in the current period. This dietary strategy is likely to keep increasing popular. Under the leadership of qualified healthcare professionals, it is thus essential to approach IF carefully considering individual health status, dietary demands, and lifestyle concerns to ensure its safe and effective implementation.

Physiological and Metabolic Effects

IF is one increasingly popular technique for improving body composition and regulating body weight. With an eye towards its effects on body weight, fat loss, and muscle mass, an increasing body of research has looked at the metabolic and physiological effects of IF. After a thorough review and meta-analysis comparing IF with continuous calorie restriction, Cho et al. (2019) found that both approaches were comparable successful in lowering body weight; IF showed a little edge in fat mass reduction. Higher norepinephrine levels and enhanced insulin sensitivity, which promote lipolysis and fat oxidation, are thought to be hormonal and metabolic ones among the basic mechanisms (24).

Many studies have particularly focused on the relationship between IF and body weight and fat loss. Varady et al. (2011) for example found that alternate-day fasting produced appreciable declines in body weight and body fat percentage in overweight adults without compromising lean body mass (25). Increased growth hormone release during fasting periods is probably the reason muscular mass is maintained during IF (26).

The literature also covers questions of probable muscle loss under IF. When Tinsley et al. (2016) applied the 16/8 IF method—16 hours fasted, 8 hours eating window—on those engaged in resistance exercise, they found no noticeable difference in muscle building when compared to a normal diet group (27). This suggests that IF has no deleterious effect on muscle protein synthesis under suitable protein intake during meals.

Apart from affecting body composition, IF has been proven to produce many metabolic reactions. Examining how IF might support metabolic health, Mattson et al. (2017) found that it can help reset metabolic pathways, hence enhancing glucose management and more efficient fat metabolism. Further supporting these metabolic changes are studies demonstrating IF's positive effects on insulin sensitivity, inflammatory markers, and lipid profiles (29,30).



The physiological changes induced by IF are defined by improved cellular stress tolerance and increased mitochondrial efficiency. Anton et al. (2018) noted that the metabolic alterations associated with IF, particularly the change from glucose to ketone-based energy consumption, can aid to improve weight loss results and maybe contribute to extended lifespan and neuroprotection. The present analyses the many metabolic and physiological effects of intermittent fasting on body weight, fat loss, and muscle mass. Though IF seems to be a viable approach to maximise body composition and general health, further research is needed to understand its long-term repercussions and appropriate application strategies for different groups.

Impact on Body Weight and Fat Loss

Reducing body weight and encouraging fat reduction have repeatedly been demonstrated by intermittent fasting as a successful approach. Strong evidence confirming the effectiveness of IF in lowering body weight and body fat (23) was supplied by the methodical review and meta-analysis by Cho et al. (2019). Several processes are believed to be mediators of this effect, including enhanced lipolysis and fat oxidation during fasting periods, which are enabled by hormonal and metabolic alterations including higher norepinephrine levels and better insulin sensitivity (24,32).

Individual studies have strengthened these conclusions even more. Varady et al. (2011) for example showed that among overweight adults, alternate-day fasting resulted in notable decreases in body weight and body fat percentage without sacrificing lean body mass (25). One clear benefit of maintaining muscle mass during IF is that it implies that fat loss rather than muscle catabolism is mostly responsible for the weight loss generated by IF.

Muscle Mass Preservation

Potential loss of muscle mass is one of the main worries about weight loss programs. Still, the research indicates that intermittent fasting might be especially helpful for maintaining muscle mass—especially in relation to resistance training. After a normal diet, Tinsley et al. (2016) examined the effects of the 16/8 IF approach on those undergoing resistance training and observed no appreciable change in muscle development relative to a control group. This result suggests that, given enough protein intake during the feeding times, IF does not adversely affect muscle protein synthesis.

There are probably multiple reasons why muscle mass preserves during IF. First of all, it has been demonstrated that preserving muscle mass depends critically on the higher production of growth hormone during fasting times (26). Furthermore, by encouraging the use of fat for fuel, the metabolic changes linked with IF—especially the change to ketone-based energy consumption—may aid to spare muscle protein(33).

Metabolic Enhancements

Numerous metabolic changes induced by intermittent fasting have been demonstrated to help to improve health outcomes by themselves. After a thorough investigation of the effects of IF on metabolic health, Mattson et al. (2017) found that it can assist reset metabolic processes, hence improving glucose control and more effective fat metabolism (28). Rising insulin sensitivity, lower inflammation, and favourable changes in lipid profiles are among the several processes suggested to explain these improvements (29,30).

Research studies repeatedly show how well IF increases insulin sensitivity. For overweight women, for instance, Harvie et al. (2011) observed that intermittent calorie restriction enhanced insulin sensitivity and lowered insulin resistance. Likewise, early time-restricted eating enhanced insulin sensitivity, blood pressure, and oxidative stress in males with prediabetes—even in the absence of weight loss—Sutton et al. (2018) reported. These results imply that the metabolic advantages of IF go beyond what weight loss by itself produces.

Physiological Adaptations

A range of physiological changes brought about by intermittent fasting adds to its general health advantages. Enhanced cellular stress resistance is one of the main adaptations; it is hypothesised that the metabolic changes brought about during fasting periods influence this resistance. Stress-resistant proteins, including brain-derived neurotrophic factor (BDNF) and sirtuins, which are absolutely vital for cellular repair and lifespan, have been demonstrated to be expressed in response to the change from glucose to ketone-based energy use (34).



Increased mitochondrial efficiency is another significant physiological adaptation brought on by IF. According to Anton et al. (2018), the metabolic changes linked to IF—especially the greater reliance on fat for fuel—may improve mitochondrial function and biogenesis (31). Along with the possible neuroprotective and anti-aging effects (35), this improved mitochondrial efficiency may help explain the weight loss and metabolic health advantages shown with IF.

Metabolic Changes

Significant metabolic alterations induced by intermittent fasting have been demonstrated and have broad consequences for the prevention of diseases and general state of health. The increase in glucose homeostasis and insulin sensitivity among other things is really remarkable (36). Reduced insulin release during fasting causes the organism to become more sensitive in target tissues like the liver, skeletal muscle, and adipose tissue (37). Those with type 2 diabetes or those who run the danger of acquiring the disorder especially benefit from this increase in insulin sensitivity. Additionally demonstrated to be beneficial for lipid metabolism is IF. While raising levels of high-density lipoprotein (HDL) cholesterol, studies have shown that IF can cause declines in total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides (38). Reduced lipogenesis during fasting periods and higher fat oxidation are supposed to be mediators of these alterations in lipid profiles (39).

Moreover, IF has been linked to lower inflammation and oxidative stress, main causes of several chronic illnesses (40). Particularly the higher synthesis of ketones, the metabolic changes generated by IF have been demonstrated to reduce inflammation and enhance the expression of antioxidant enzymes like catalase (41). In general, IF has complex and broad physiological and metabolic impacts. IF has become a promising approach for maximising health and avoiding chronic diseases by encouraging fat loss while keeping muscle mass, improving metabolic health, producing positive physiological responses, and pushing favourable alterations in glucose and lipid metabolism. More study is required, nevertheless, to completely clarify the processes behind these effects and identify the best IF strategies for various groups.

Intermittent Fasting (IF) and Health Outcomes

Extensive studies examining the impact of IF on a broad spectrum of health outcomes—including cardiovascular health, diabetes management, cancer prevention, cognitive performance, psychological well-being, and longevity—have been conducted. The findings draw attention to the possibilities as well as the constraints of IF as a health intervention.

Cardiometabolic health

Studies on how intermittent fasting affects cardiovascular health point to its major influence on risk factors for heart disease. Research on important cardiovascular risk factors including blood pressure, resting heart rates, LDL cholesterol, and triglycerides (42) has revealed improvements in each. Moreover, intermittent fasting could enhance cardiac structure and function, especially in respect to the efficiency of heart muscle performance(43). Nevertheless, the degree of these advantages may differ greatly depending on the kind of fasting program and the personal traits of the subjects (44).

Probably the most successful non-pharmacological technique to increase healthspan is a calorie restriction (CR), a steady decrease in caloric intake while preserving ideal nutrition. Long-term adherence to continuous daily CR is poor, nevertheless, because of biological, behavioural, psychological, environmental, and environmental factors(45). Promising alternative intermittent fasting (IF) involves alternating periods of fasting and unrestricted eating, therefore helping adherence (46). It encompasses multiple strategies: religious fasting, alternate-day fasting (ADF), alternate-day modified fasting (ADMF), the 5:2 diet, fasting-mimicking diet, and time-restricted eating (TRE)(47). Every technique differs in length and intensity of fasting intervals. Most research find that it effectively lowers calorie intake, weight loss results; current studies also show that IF can enhance cardiometabolic health even without lowering energy intake (48).

Common during human development, prolonged episodes of food shortage resulted in adaptations allowing survival in a fasting state. Among these adaptations is a coordinated metabolic reaction to a brief fast lasting 0–72 hours (49). Blood glucose levels rise following a meal, which causes insulin to be released, therefore preventing the release of glycerol and free fatty acids (FFA) from adipose tissue and so limits ketone generation(50). Blood glucose and insulin levels drop when fasting passes beyond 12 hours; catabolic hormones, FFA, glycerol, and ketones rise (51). Within 24 hours, the glycogen level of the liver runs low;



gluconeogenesis then takes front stage as the main source of glucose (52). Key drivers of IF's health effects include this metabolic change from glycogenolysis to gluconeogenesis, fat oxidation, and ketogenesis (53).

If regimens lower ectopic fat, improve body composition, and raise cardiometabolic risk factors relative to unrestricted eating (54), IF can significantly lower body weight, fat mass, and cardiometabolic indicators including triglycerides, cholesterol, and blood pressure according meta-analyses (55). But IF does not seem to offer any more advantages than daily CR, implying that the net energy deficit is the primary driver of these health advantages (56). New technologies like continuous glucose, FFA, and ketone monitoring should be used in next studies to better grasp the function of the metabolic switch in IF's health advantages (57).

To appreciate IF's cardiometabolic effects, one must first grasp how it affects energy metabolism. More research is needed to ascertain whether IF regimens increase fat oxidation and improve metabolic flexibility, which is fundamental in preventing ectopic fat accumulation and insulin resistance even if studies have shown that IF regimens can improve postprandial metabolism and substrate oxidation (58). Combining IF with exercise—especially endurance and resistance training—may maximise the health advantages by promoting the metabolic transition and maintaining fat-free mass (59). Future research should investigate, in the framework of IF (60), the most practical and efficient workout timing.

Particularly in lowering body weight and decreasing cardiometabolic risk factors, IF regimens seem to give health advantages comparable to continuous daily CR. More long-term, well-powered research is required, nevertheless, to validate these conclusions and grasp the fundamental processes (61). Further research on the possibility of IF to improve cardiometabolic health without weight reduction is justified as is the effect of IF on ectopic fat deposition and postprandial metabolism (62). Combining wearable technologies with tailored techniques might offer more thorough understanding of how IF affects human health (63).

Diabetes and Metabolic Syndrome

Among obese people, IF has become well-known as a weight-loss tactic. Still lacking, though, is studies on its impact in those with type 2 diabetes (T2D), prediabetes, and metabolic syndrome. This review intends to clarify the biochemical and physiological processes behind the favourable effects of IF, especially the "metabolic switch," and assess the effectiveness and safety of IF regimens in these groups (64).

Four studies on those with metabolic syndrome, one on those with prediabetes, and eight studies on those with T2D were found using a MEDLINE PubMed search. Although hampered by small sample sizes and short trial lengths, the existing data points to IF regimens as equally effective as calorie-restriction diets for weight reduction and glycaemic variable improvement (65). Most IF programs are safe and successful generally. Long-term adherence to these regimens is unclear, though, and T2D patients treated with insulin or sulphonylureas run more danger of hypoglycaemia (66).

Particularly in those with metabolic syndrome and prediabetes, large controlled randomised studies are required to assess the efficacy of IF regimens (67). Should IF prove sustainable and effective over extended periods of time, it presents a viable method for enhancing population-wide health, hence generating major public health gains (68).

Regarding the therapy and prevention of diabetes as well as its common comorbidity, metabolic syndrome, IF has showed potential. Important in control of type 2 diabetes, fasting schedules can improve insulin sensitivity and assist in lowering blood glucose levels (69). Moreover, the weight loss usually connected with IF can also help to lower other metabolic syndrome elements including hypertension and abdominal obesity (70). Still, the frequency and length of fasting periods affect the efficacy of IF; so, more study is required to maximise fasting guidelines for diabetic patients (71).

Cancer

Numerous research have investigated the possible preventive properties of IF against different malignancies; results imply that IF could lower cancer risk by numerous different ways. These include lower insulin resistance, which is usually linked with cancer progression, reduction of inflammation, and improvement of cellular repair mechanisms (72). Nonetheless, compared to animal research, human studies are somewhat few; hence, more strong clinical trials are required to validate these results in human populations (73). IF has attracted attention because its possible advantages in treatment and prevention of cancer. Though in animal models calorie restriction (CR) has showed promise in lowering cancer risk, it is difficult to maintain. If marked by intervals of fasting and unrestricted eating, could present a more practical substitute (74).



In animal models, IF has produced conflicting findings about cancer development and prevention. According to some studies, IF can stop tumour development, slow down tumour progression, and lower metastases (75). For example, intermittent fasting slowed tumour growth in a mouse model of colon cancer (76) and delayed tumour initiation in p53-deficient animals. Other investigations, especially in some rat models, however, revealed no appreciable effect on tumour growth or even detrimental effects (77). Variations in fasting times, cancer kinds, and particular animal models employed could explain differences in outcomes (78). Though few, human studies on IF and cancer are expanding. Several short-term trials show that IF can lower insulin and leptin levels and raise adiponectin, hence improving metabolic indicators linked with cancer risk (79). Long-term studies have not, however, consistently shown appreciable increases in insulin sensitivity or cancer-related outcomes (80).

Early research on cancer patients indicates that fasting both before and during chemotherapy may lower treatment-related toxicity and improve treatment efficacy (81). For patients undergoing chemotherapy for breast cancer, for instance, short-term fasting revealed lower DNA damage and better blood counts(82). Likewise, fasting lessened chemotherapy-induced damage in patients with different malignancies, albeit following fasting guidelines differed (83).

Many clinical studies are under way to investigate how IF affects survival and cancer recurrence (84). These studies seek to ascertain if, either alone or in conjunction with conventional treatments, IF can enhance results for cancer patients. Trials evaluating the viability and effects of IF in several cancers—including breast, prostate, colon, and gliomas—are under way (85).

Reduced insulin-like growth factor 1 (IGF-1), improved autophagy (86), and metabolic shift from glucose to ketone use are the possible ways IF can influence cancer. These medicines might theoretically slow down the spread of cancer cells and enhance the body's reaction to cancer treatments (87).

More study is required to validate the advantages of IF in cancer prevention and therapy even if first findings show great promise. Long-term, well-controlled research is required to ascertain IF(88) durability and effectiveness. Moreover, knowledge of the fundamental processes will help to comprehend how IF affects cancer results (89).

IF should not be advised as a normal procedure for cancer patients not involved in research trials right now (90). IF could be a choice for overweight and obese people looking for weight loss to lower cancer risk, particularly when coupled with a good diet and exercise(91). Given the paucity of clear data and particular patient demands, clinicians should talk with patients about the possible risks and rewards (92).

CONCLUSION

In conclusion, while intermittent fasting (IF) presents a promising dietary strategy with multiple health benefits, careful consideration of individual circumstances and comprehensive research are essential to fully understand its efficacy and safety. Intermittent fasting has garnered growing interest as a method for weight management, health improvement, and disease prevention. Studies suggest that IF can contribute to significant weight loss, improved metabolic health, and reduced risk factors for various chronic diseases, such as diabetes and cardiovascular conditions. These benefits have driven the popularity of IF among diverse populations seeking effective and sustainable dietary interventions.

However, despite the potential advantages, it is crucial to address the existing gaps in the literature to clarify the role of intermittent fasting in health promotion and disease management. Research should focus on understanding the long-term effects of IF, identifying the most effective fasting protocols, and determining the populations that can benefit the most from this dietary approach. Moreover, potential risks and side effects associated with IF, such as nutrient deficiencies, psychological impacts, and adverse effects on certain medical conditions, must be thoroughly investigated to ensure safe and effective implementation.

By addressing these research gaps, we can develop a clearer understanding of intermittent fasting's potential and limitations, ultimately guiding individuals and healthcare providers in making informed decisions about its use for health improvement and disease prevention.

REFERENCES

1. Mattson MP, Longo VD, Harvie M. Impact of intermittent fasting on health and disease processes. *Ageing Res Rev.* 2017;39:46-58.
2. Ganesan K, Habboush Y, Sultan S. Intermittent Fasting: The Choice for a Healthier Lifestyle. *Cureus.* 2018;10(7):e2947.



3. Harvie M, Howell A. Potential Benefits and Harms of Intermittent Energy Restriction and Intermittent Fasting Amongst Obese, Overweight and Normal Weight Subjects-A Narrative Review of Human and Animal Evidence. *Behav Sci (Basel)*. 2017;7(1):4.
4. Hoddy KK, Kroeger CM, Trepanowski JF, Barnosky AR, Bhutani S, Varady KA. Safety of alternate day fasting and effect on disordered eating behaviors. *Nutr J*. 2015;14:44.
5. de Cabo R, Mattson MP. Effects of Intermittent Fasting on Health, Aging, and Disease. *N Engl J Med*. 2019;381(26):2541-2551.
6. Stockman MC, Thomas D, Burke J, Apovian CM. Intermittent Fasting: Is the Wait Worth the Weight? *Curr Obes Rep*. 2018;7(2):172-185.
7. Malinowski B, Zalewska K, Węsierska A, Sokołowska MM, Socha M, Liczner G, et al. Intermittent Fasting in Cardiovascular Disorders-An Overview. *Nutrients*. 2019;11(3):673.
8. Moro T, Tinsley G, Bianco A, Marcolin G, Pacelli QF, Battaglia G, et al. Effects of eight weeks of time-restricted feeding (16/8) on basal metabolism, maximal strength, body composition, inflammation, and cardiovascular risk factors in resistance-trained males. *J Transl Med*. 2016;14(1):290.
9. Stockman MC, Thomas D, Burke J, Apovian CM. Intermittent Fasting: Is the Wait Worth the Weight? *Curr Obes Rep*. 2018;7(2):172-185.
10. 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):1645.
11. 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;27(6):1212-1221.e3.
12. Santos HO, Macedo RCO. Impact of intermittent fasting on the lipid profile: Assessment associated with diet and weight loss. *Clin Nutr ESPEN*. 2018;24:14-21.
13. Anton SD, Moehl K, Donahoo WT, Marosi K, Lee SA, Mainous AG 3rd, et al. Flipping the Metabolic Switch: Understanding and Applying the Health Benefits of Fasting. *Obesity (Silver Spring)*. 2018;26(2):254-268.
14. Headland ML, Clifton PM, Keogh JB. Effect of Intermittent Compared to Continuous Energy Restriction on Weight Loss and Weight Maintenance after 12 Months in Healthy Overweight or Obese Adults. *Int J Obes (Lond)*. 2019;43(10):2028-2036.
15. Stockman MC, Thomas D, Burke J, Apovian CM. Intermittent Fasting: Is the Wait Worth the Weight? *Curr Obes Rep*. 2018;7(2):172-185.
16. Hoddy KK, Marlatt KL, Çetinkaya H, Ravussin E. Intermittent Fasting and Metabolic Health: From Religious Fast to Time-Restricted Feeding. *Obesity (Silver Spring)*. 2020;28 Suppl 1(Suppl 1):S29-S37.
17. 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):588-594.
18. Rynders CA, Thomas EA, Zaman A, Pan Z, Catenacci VA, Melanson EL. Effectiveness of Intermittent Fasting and Time-Restricted Feeding Compared to Continuous Energy Restriction for Weight Loss. *Nutrients*. 2019;11(10):2442.
19. de Cabo R, Mattson MP. Effects of Intermittent Fasting on Health, Aging, and Disease. *N Engl J Med*. 2019;381(26):2541-2551.
20. Mattson MP, Longo VD, Harvie M. Impact of intermittent fasting on health and disease processes. *Ageing Res Rev*. 2017;39:46-58.
21. Bagherniya M, Butler AE, Barreto GE, Sahebkar A. The effect of fasting or calorie restriction on autophagy induction: A review of the literature. *Ageing Res Rev*. 2018;47:183-197.
22. Manoogian ENC, Panda S. Circadian rhythms, time-restricted feeding, and healthy aging. *Ageing Res Rev*. 2017;39:59-67.
23. 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):1645.



24. Heilbronn LK, Smith SR, Martin CK, Anton SD, Ravussin E. Alternate-day fasting in nonobese subjects: effects on body weight, body composition, and energy metabolism. *Am J Clin Nutr.* 2005;81(1):69-73.
25. Varady KA, Bhutani S, Church EC, Klempel MC. Short-term modified alternate-day fasting: a novel dietary strategy for weight loss and cardioprotection in obese adults. *Am J Clin Nutr.* 2009;90(5):1138-43.
26. Hartman ML, Veldhuis JD, Johnson ML, Lee MM, Alberti KG, Samojlik E, et al. Augmented growth hormone (GH) secretory burst frequency and amplitude mediate enhanced GH secretion during a two-day fast in normal men. *J Clin Endocrinol Metab.* 1992;74(4):757-65.
27. Tinsley GM, Forsse JS, Butler NK, Paoli A, Bane AA, La Bounty PM, et al. Time-restricted feeding in young men performing resistance training: A randomized controlled trial. *Eur J Sport Sci.* 2017;17(2):200-207.
28. Mattson MP, Longo VD, Harvie M. Impact of intermittent fasting on health and disease processes. *Ageing Res Rev.* 2017;39:46-58.
29. Harvie MN, Pegington M, Mattson MP, Frystyk J, Dillon B, Evans G, et al. 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 (Lond).* 2011;35(5):714-27.
30. 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;27(6):1212-1221.e3.
31. Anton SD, Moehl K, Donahoo WT, Marosi K, Lee SA, Mainous AG 3rd, et al. Flipping the Metabolic Switch: Understanding and Applying the Health Benefits of Fasting. *Obesity (Silver Spring).* 2018;26(2):254-268.
32. Zauner C, Schneeweiss B, Kranz A, Madl C, Ratheiser K, Kramer L, et al. Resting energy expenditure in short-term starvation is increased as a result of an increase in serum norepinephrine. *Am J Clin Nutr.* 2000;71(6):1511-5.
33. Koutnik AP, Poff AM, Ward NP, DeBlasi JM, Soliven MA, Romero MA, et al. Ketone Bodies Attenuate Wasting in Models of Atrophy. *J Cachexia Sarcopenia Muscle.* 2020;11(4):973-996.
34. Mattson MP, Moehl K, Ghena N, Schmaedick M, Cheng A. Intermittent metabolic switching, neuroplasticity and brain health. *Nat Rev Neurosci.* 2018;19(2):63-80.
35. Rubinsztein DC, Mariño G, Kroemer G. Autophagy and aging. *Cell.* 2011;146(5):682-95. 3
36. Barnosky AR, Hoddy KK, Unterman TG, Varady KA. Intermittent fasting vs daily calorie restriction for type 2 diabetes prevention: a review of human findings. *Transl Res.* 2014;164(4):302-11.
37. Heilbronn LK, Civitarese AE, Bogacka I, Smith SR, Hulver M, Ravussin E. Glucose tolerance and skeletal muscle gene expression in response to alternate day fasting. *Obes Res.* 2005;13(3):574-81.
38. Santos HO, Macedo RCO. Impact of intermittent fasting on the lipid profile: Assessment associated with diet and weight loss. *Clin Nutr ESPEN.* 2018;24:14-21.
39. Anton SD, Moehl K, Donahoo WT, Marosi K, Lee SA, Mainous AG 3rd, et al. Flipping the Metabolic Switch: Understanding and Applying the Health Benefits of Fasting. *Obesity (Silver Spring).* 2018;26(2):254-268.
40. Faris MA, Kacimi S, Al-Kurd RA, Fararjeh MA, Bustanji YK, Mohammad MK, et al. Intermittent fasting during Ramadan attenuates proinflammatory cytokines and immune cells in healthy subjects. *Nutr Res.* 2012;32(12):947-55.
41. Wegman MP, Guo MH, Bennion DM, Shankar MN, Chrzanowski SM, Goldberg LA, et al. Practicality of intermittent fasting in humans and its effect on oxidative stress and genes related to aging and metabolism. *Rejuvenation Res.* 2015;18(2):162-72.
42. Malinowski B, Zalewska K, Węsierska A, Sokołowska MM, Socha M, Liczner G, et al. Intermittent Fasting in Cardiovascular Disorders-An Overview. *Nutrients.* 2019;11(3):673.
43. Godar RJ, Ma X, Liu H, Murphy JT, Weinheimer CJ, Kovacs A, et al. Repetitive stimulation of autophagy-lysosome machinery by intermittent fasting preconditions the myocardium to ischemia-reperfusion injury. *Autophagy.* 2015;11(9):1537-60.
44. Stockman MC, Thomas D, Burke J, Apovian CM. Intermittent Fasting: Is the Wait Worth the Weight? *Curr Obes Rep.* 2018;7(2):172-185.



45. Mattson MP, Longo VD, Harvie M. Impact of intermittent fasting on health and disease processes. *Ageing Res Rev.* 2017;39:46-58.
46. Heilbronn LK, Ravussin E. Calorie restriction and aging: review of the literature and implications for studies in humans. *Am J Clin Nutr.* 2003;78(3):361-9.
47. Anton SD, Moehl K, Donahoo WT, Marosi K, Lee SA, Mainous AG 3rd, et al. Flipping the Metabolic Switch: Understanding and Applying the Health Benefits of Fasting. *Obesity (Silver Spring).* 2018;26(2):254-268.
48. 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;27(6):1212-1221.e3.
49. de Cabo R, Mattson MP. Effects of Intermittent Fasting on Health, Aging, and Disease. *N Engl J Med.* 2019;381(26):2541-2551.
50. Rizza W, Veronese N, Fontana L. What are the roles of calorie restriction and diet quality in promoting healthy longevity? *Ageing Res Rev.* 2014;13:38-45.
51. Longo VD, Mattson MP. Fasting: molecular mechanisms and clinical applications. *Cell Metab.* 2014;19(2):181-92.
52. Cahill GF Jr. Fuel metabolism in starvation. *Annu Rev Nutr.* 2006;26:1-22.
53. Mattson MP, Longo VD, Harvie M. Impact of intermittent fasting on health and disease processes. *Ageing Res Rev.* 2017;39:46-58.
54. Varady KA, Bhutani S, Klempel MC, Kroeger CM, Trepanowski JF, Haus JM, et al. Alternate day fasting for weight loss in normal weight and overweight subjects: a randomized controlled trial. *Nutr J.* 2013;12(1):146.
55. Barnosky AR, Hoddy KK, Unterman TG, Varady KA. Intermittent fasting vs daily calorie restriction for type 2 diabetes prevention: a review of human findings. *Transl Res.* 2014;164(4):302-11.
56. Trepanowski JF, Kroeger CM, Barnosky A, Klempel M, Bhutani S, Hoddy KK, et al. Effects of alternate-day fasting or daily calorie restriction on body composition, fat distribution, and circulating adipokines: Secondary analysis of a randomized controlled trial. *Clin Nutr.* 2018;37(6 Pt A):1871-1878.
57. 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. *Trials.* 2018;19(1):86.
58. 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):507-516.
59. Tinsley GM, La Bounty PM. Effects of intermittent fasting on body composition and clinical health markers in humans. *Nutr Rev.* 2015;73(10):661-74.
60. Moro T, Tinsley G, Bianco A, Marcolin G, Pacelli QF, Battaglia G, et al. Effects of eight weeks of time-restricted feeding (16/8) on basal metabolism, maximal strength, body composition, inflammation, and cardiovascular risk factors in resistance-trained males. *J Transl Med.* 2016;14(1):290.
61. Harris L, Hamilton S, Azevedo LB, Olajide J, De Brún C, Waller G, et al. Intermittent fasting interventions for treatment of overweight and obesity in adults: a systematic review and meta-analysis. *JBI Database System Rev Implement Rep.* 2018;16(2):507-547.
62. Welton S, Minty R, O'Driscoll T, Willms H, Poirier D, Madden S, et al. Intermittent fasting and weight loss: Systematic review. *Can Fam Physician.* 2020;66(2):117-125.
63. Cioffi I, Evangelista A, Ponzio V, Ciccone G, Soldati L, Santarpia L, et al. Intermittent versus continuous energy restriction on weight loss and cardiometabolic outcomes: a systematic review and meta-analysis of randomized controlled trials. *J Transl Med.* 2018;16(1):371.
64. 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):3.
65. 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):1645.



66. 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.
67. 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):588-594.
68. Patterson RE, Sears DD. Metabolic Effects of Intermittent Fasting. *Annu Rev Nutr*. 2017;37:371-393.
69. Barnosky AR, Hoddy KK, Unterman TG, Varady KA. Intermittent fasting vs daily calorie restriction for type 2 diabetes prevention: a review of human findings. *Transl Res*. 2014;164(4):302-11.
70. Harvie M, Howell A. Potential Benefits and Harms of Intermittent Energy Restriction and Intermittent Fasting Amongst Obese, Overweight and Normal Weight Subjects-A Narrative Review of Human and Animal Evidence. *Behav Sci (Basel)*. 2017;7(1):4.
71. Ganesan K, Habboush Y, Sultan S. Intermittent Fasting: The Choice for a Healthier Lifestyle. *Cureus*. 2018;10(7):e2947.
72. de Groot S, Pijl H, van der Hoeven JJM, Kroep JR. Effects of short-term fasting on cancer treatment. *J Exp Clin Cancer Res*. 2019;38(1):209.
73. Nencioni A, Caffa I, Cortellino S, Longo VD. Fasting and cancer: molecular mechanisms and clinical application. *Nat Rev Cancer*. 2018;18(11):707-719.
74. Lv M, Zhu X, Wang H, Wang F, Guan W. Roles of caloric restriction, ketogenic diet and intermittent fasting during initiation, progression and metastasis of cancer in animal models: a systematic review and meta-analysis. *PLoS One*. 2014;9(12):e115147.
75. Buono R, Longo VD. Starvation, Stress Resistance, and Cancer. *Trends Endocrinol Metab*. 2018;29(4):271-280.
76. Lee C, Raffaghello L, Brandhorst S, Safdie FM, Bianchi G, Martin-Montalvo A, et al. Fasting cycles retard growth of tumors and sensitize a range of cancer cell types to chemotherapy. *Sci Transl Med*. 2012;4(124):124ra27.
77. Shastri AA, Saleh A, Savage JE, DeAngelis T, Camphausen K, Simone NL. Dietary alterations modulate the microRNA 29/30 and IGF-1/AKT signaling axis in breast cancer liver metastasis. *Nutr Metab (Lond)*. 2020;17:23.
78. Brandhorst S, Longo VD. Fasting and Caloric Restriction in Cancer Prevention and Treatment. *Recent Results Cancer Res*. 2016;207:241-66.
79. Hutchison AT, Regmi P, Manoogian ENC, Fleischer JG, Wittert GA, Panda S, et al. Time-Restricted Feeding Improves Glucose Tolerance in Men at Risk for Type 2 Diabetes: A Randomized Crossover Trial. *Obesity (Silver Spring)*. 2019;27(5):724-732.
80. Marinac CR, Nelson SH, Breen CI, Hartman SJ, Natarajan L, Pierce JP, et al. Prolonged Nightly Fasting and Breast Cancer Prognosis. *JAMA Oncol*. 2016;2(8):1049-55.
81. Safdie FM, Dorff T, Quinn D, Fontana L, Wei M, Lee C, et al. Fasting and cancer treatment in humans: A case series report. *Aging (Albany NY)*. 2009;1(12):988-1007.
82. de Groot S, Vreeswijk MP, Welters MJ, Gravesteijn G, Boei JJ, Jochems A, et al. The effects of short-term fasting on tolerance to (neo) adjuvant chemotherapy in HER2-negative breast cancer patients: a randomized pilot study. *BMC Cancer*. 2015;15:652.
83. Dorff TB, Groshen S, Garcia A, Shah M, Tsao-Wei D, Pham H, et al. Safety and feasibility of fasting in combination with platinum-based chemotherapy. *BMC Cancer*. 2016;16:360.
84. Bauersfeld SP, Kessler CS, Wischnowsky M, Jaensch A, Steckhan N, Stange R, et al. The effects of short-term fasting on quality of life and tolerance to chemotherapy in patients with breast and ovarian cancer: a randomized cross-over pilot study. *BMC Cancer*. 2018;18(1):476.
85. Zorn S, Ehret J, Schäuble S, Rautenberg B, Ihorst G, Bertz H, et al. Impact of modified short-term fasting and its combination with a fasting supportive diet during chemotherapy on the incidence and severity of chemotherapy-induced toxicities in cancer patients - a controlled cross-over pilot study. *BMC Cancer*. 2020;20(1):578.
86. Nencioni A, Caffa I, Cortellino S, Longo VD. Fasting and cancer: molecular mechanisms and clinical application. *Nat Rev Cancer*. 2018;18(11):707-719.
87. Mattson MP, Longo VD, Harvie M. Impact of intermittent fasting on health and disease processes. *Ageing Res Rev*. 2017;39:46-58.



88. Clifton KK, Ma CX, Fontana L, Peterson LL. Intermittent fasting in the prevention and treatment of cancer. *CA Cancer J Clin.* 2021;71(6):527-546.
89. O'Flanagan CH, Smith LA, McDonnell SB, Hursting SD. When less may be more: calorie restriction and response to cancer therapy. *BMC Med.* 2017;15(1):106.
90. Caccialanza R, Aprile G, Cereda E, Pedrazzoli P. Fasting in oncology: a word of caution. *Nat Rev Cancer.* 2019;19(3):177.
91. Harvie M, Howell A. Potential Benefits and Harms of Intermittent Energy Restriction and Intermittent Fasting Amongst Obese, Overweight and Normal Weight Subjects-A Narrative Review of Human and Animal Evidence. *Behav Sci (Basel).* 2017;7(1):4.
92. Anton SD, Moehl K, Donahoo WT, Marosi K, Lee SA, Mainous AG 3rd, et al. Flipping the Metabolic Switch: Understanding and Applying the Health Benefits of Fasting. *Obesity (Silver Spring).* 2018;26(2):254-268.