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Intermittent Fasting: Weighing the Benefits and Drawbacks for Health and Longevity – A Comprehensive Literature Review

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ABSTRACT

Introduction:

Obesity rates have risen sharply in recent decades, with one in eight people worldwide living with obesity in 2022. This has driven interest in the search for effective and sustainable dietary strategies. Intermittent fasting (IF), which alternates periods of eating and fasting, has gained considerable attention as a tool for weight management and overall health improvement. Unlike traditional calorie-restricted diets, IF's simplicity and flexibility make it more accessible, potentially increasing adherence and long-term sustainability.

Purpose:

This study reviews current knowledge on IF, evaluating its physiological mechanisms, health benefits, risks, and long-term implications. It focuses on weight management, glucose metabolism, cardiovascular health, cognitive function, circadian rhythm, and sports performance, while addressing challenges related to safety and sustainability.

Materials and Methods:
This study reviews existing literature, including clinical trials, meta-analyses, and observational studies. It compares IF protocols such as alternate-day fasting (ADF), the 5:2 diet, and time-restricted eating (TRE), emphasizing physiological effects and practical implications.
Conclusion:
Intermittent fasting represents a promising dietary intervention with wide-ranging health benefits, from weight management to improved metabolic and cognitive health. However, challenges such as nutritional deficiencies, risks of hypoglycemia, and limited long-term data highlight the need for personalized approaches and further investigation. Future research should prioritize large-scale, long-term studies to refine fasting protocols and ensure safety and effectiveness across diverse populations. By addressing these gaps, IF could evolve into a sustainable, evidence-based strategy for improving global health outcomes.

Keywords: intermittent fasting, metabolic health, weight management

INTRODUCTION

We live in an era where all knowledge, discovery and information known to humans is just a few taps away. In medicine one can consider this the greatest revolution since the discovery of antibiotics. With that in mind, the authors of this study wanted to review the current state of knowledge regarding Intermittent Fasting (IF).

Latest research shows that in 2022 1 in 8 people in the world were living with obesity and since 1990 adult obesity more than doubled, while adolescent obesity has quadrupled [1]. Alongside this trend the search for the perfect diet intensified. In recent years IF gained public attention as a tool for weight loss [2]. IF is a diet involving alternating periods of eating and not eating. Its simplicity might be one of the reasons for the sudden rise in popularity. Unlike many other diets IF does not require individuals to drastically change their eating patterns, avoid certain food groups, meticulously count ingested calories and macronutrients. Such features make the diet more accessible which might be the reason why IF became so widely adopted [3]. Studies suggest that the IF diet may increase adherence and long-term sustainability to the diet [4].

PURPOSE OF THE STUDY

The purpose of this study was to consolidate and critically evaluate the current body of knowledge regarding IF, focusing on its physiological mechanisms, health benefits, challenges, and potential risks. By exploring its impact on weight management, metabolic health, glucose metabolism, and cardiovascular function, the study aimed to assess the efficacy of IF as a tool for addressing obesity and related health concerns.

Additionally, this study sought to examine the role of IF in cognitive function, sports performance, and circadian rhythm regulation, highlighting both the potential advantages and the limitations associated with its practice. By addressing gaps in long-term safety, sustainability, and adherence, the research aimed to provide a comprehensive understanding of IF while identifying areas that require further investigation to refine fasting protocols and support diverse populations effectively.

METHODS OF INTERMITTENT FASTING

Methods of IF are usually categorized into one of three types: alternate-day fasting (ADF), the 5:2 diet and time-restricted eating (TRE) [4]. Using ADF method individuals alternate between day of no food intake and a day of unrestricted eating. The 5:2 diet is characterized by limiting energy intake for two non-consecutive days per week (500 calories/day for women and 600/day calories for men) and allowing unrestricted eating for the rest of the week. TRE differs from the former approaches. It involves following a consistent routine where you eat within a designated time frame each day and fast during the remaining hours. For example, the 16:8 method restricts eating to an 8-hour window (known as Eating Window), with fasting occurring for the remaining 16 hours [5]. In this approach, meals are typically consumed within a set period, such as between 12 p.m. and 8 p.m., while the rest of the time is spent fasting. This is the most popular method of IF, however, one can adjust the hours to individual preferences. Comparison of those 3 methods are shown in Table 1 [4, 5].

Method	Eating Day - kcal intake	Fasting Day - kcal intake	Fast days during the week	Feeding Window
ADF	unrestricted	0	3-4	unrestricted
5:2	unrestricted	limited: - 500 kcal/day for women - 600 kcal/day for men	2	unrestricted
TRF	unrestricted	unrestricted	7	restricted to a set time frame each day f.e. 8 hours

Table. 1 Comparison of ADF, 5:2 and TRF methods [4, 5]

BENEFITS

Studies suggest that IF has a wide range of health benefits. Those include increased health and life span, decreased cardiovascular risk and improved cognition [6]. Furthermore IF restores healthier circadian clock and improves gut microbiota [7], protects against hepatosteatosis and improves gut function [8]. Those findings are supported by additional research which emphasizes the physiological responses of major organs triggered by the metabolic switch during fasting [9].

DOWNSIDES

Many studies on IF highlight several potential drawbacks, including hunger, irritability, fatigue, reduced cognitive function, negative impacts on both physical and mental well-being, and the risk of hypoglycemia. Despite these challenges, IF has shown promise for weight loss and improvements in cardiovascular and metabolic health [10]. However, IF as a dietary pattern is a complex topic, with both benefits and potential risks. To fully assess its effectiveness, it's crucial to weigh these factors carefully, considering existing research and insights from diverse perspectives. The lack of well - designed clinical trials makes it difficult to draw firm conclusions about its long-term effects [11].

PHYSIOLOGY OF INTERMITTENT FASTING

The prime source of energy during fasting are ketones. Metabolic transition occurs when the body shifts from using glucose to ketones, which are derived from fatty acids. That, in consequence, moves the metabolism from synthesizing lipids, cholesterol and storing fat, to activating fat breakdown through fatty acid oxidation. Glucose levels typically begin to drop about six hours after a meal, continuing to decrease and remain low until the following day [12]. However, the metabolic switch to ketone production doesn't occur solely due to falling glucose levels. It typically happens after 10 to 14 hours of fasting, once liver glycogen stores are depleted - though some research suggests this may take up to 36 hours - it depends on factors like food intake, liver glycogen levels, and physical activity during fasting. Once glycogen reserves are exhausted, fats stored in adipocytes are broken down into free fatty acids (FFAs) through lipolysis, which are then released into the bloodstream. These FFAs are transported to the liver, where they are converted into ketones, such as acetone.

SIRT1 - a gene that plays a key role - is activated during the transition from glycogen breakdown (glycogenolysis) to ketone production. Its role involves reduction of glucose production, prevention of fat accumulation in the liver, and regulation of energy expenditure [9]. As a result, ketones serve as an energy source and promote the growth of new mitochondria, boost synaptic flexibility, and improve cellular resilience to stress by increasing the production of BDNF (brain-derived neurotrophic factor). Additionally, the metabolic shift encourages the release of GLP-1 (glucagon-like peptide 1) into the bloodstream. GLP-1 is a hormone that takes part in glucose clearance and enhances insulin sensitivity in cells [13].

Additionally ketones are metabolized into adenosine triphosphate (ATP), which fuels cells with high metabolism, such as muscle and neurons. This mechanism enables continuous and unobstructed muscle and brain function during fasting and extended physical activity. Evidence suggests that certain organs respond to IF in a similar way as to aerobic exercise, exhibiting effects like the inhibition of mTOR, activation of autophagy, and promotion of mitochondrial biogenesis [9]. Research has also highlighted the role of autophagy in cancer, with growing interest in its potential as a therapeutic target [14].

IMPACT ON WEIGHT MANAGEMENT

IF has emerged as a potential strategy for weight loss, fat reduction, and improving blood lipid levels, positioning it as a useful tool in addressing obesity and related health issues [15]. Studies have shown that IF is effective in decreasing body weight and visceral fat among adults that are overweight or obese [16, 17].

Moreover, following IF diet lowers cardiovascular risk by targeting abdominal fat and also promotes favorable changes in body composition - reduction of fat mass while preserving muscle mass. These results highlight IF as a promising method for managing body weight, particularly in individuals who are overweight or obese [18]. However, further investigation is needed to understand the long-term implications and challenges associated with sustaining weight loss over extended periods.

IMPACT ON GLUCOSE METABOLISM AND INSULIN SENSITIVITY

The modern trend of excessive calorie consumption, which is largely driven by the widespread availability of processed foods that are high in sugar and fat, has contributed to increasing rates of obesity and associated health conditions [19]. This overconsumption can result in glucotoxicity, where prolonged exposure to high glucose levels causes damage to pancreatic beta-cells, impairing insulin secretion and glucose regulation [20]. IF has demonstrated potential benefits in regulating blood sugar levels, particularly for individuals with metabolic syndrome, by significantly improving insulin sensitivity. It has shown to be helpful in managing abnormal glucose levels, thereby reducing the risks and progression of chronic illnesses such as cardiovascular disease, atherosclerosis, insulin resistance, diabetes, and associated complications like strokes and neurological issues [21].

Research indicates that IF lowers insulin levels and enhances insulin sensitivity [22 - 24], often outperforming unstructured eating habits in addressing insulin resistance conditions [25]. Some studies even suggest that IF may be more effective at reducing insulin levels compared to calorie-restricted diets [26, 27]. However, findings also reveal variability: for instance, no significant improvement in insulin sensitivity was observed between individuals practicing long-term ADF and a control group of non-obese participants [28]. These differences suggest that the impact of IF on insulin sensitivity may depend on the individual's level of insulin resistance.

IMPACT ON CELLULAR REPAIR PROCESSES AND LONGEVITY

IF has been shown in numerous studies to provide neuroprotective benefits, including reducing brain damage and neurological deficits following ischemic stroke. It also inhibits inflammatory pathways and inflammasome activation, both of which can worsen stroke outcomes [29 - 31]. Research further suggests that IF can shift metabolism, decrease inflammation and oxidative stress, and promote neural plasticity and regeneration [29]. However, individual responses to IF may vary, particularly for individuals with conditions such as diabetes or hypertension. While most studies report no adverse effects of IF on cardiovascular disease incidence or cardiac-related hospitalizations, exceptions exist, and additional research is necessary to understand its specific impact on ischemic stroke in individuals with diabetes [32].

IMPACT ON LIPID PROFILES AND CARDIOVASCULAR HEALTH

Elevated triglycerides (TG) and decreased high-density lipoprotein (HDL) levels in the bloodstream are two of the five markers used to identify metabolic syndrome, a condition closely tied to lipid profile imbalances [33].

Metabolic syndrome is a significant risk factor for the development of type 2 diabetes, cardiovascular diseases, strokes, and other health complications.

Sedentary lifestyles and diets high in calories but low in fiber are primary contributors to these health issues [34]. Adjusting dietary habits can help mitigate the risks of developing diabetes and heart-related diseases, often leading to improvements in lipid profiles and reductions in body weight [35 - 37].

Studies indicate that individuals practicing IF or energy-restricted diets (ERD) experience notable enhancements in their lipid profiles compared to those who follow no structured diet [38]. However, evidence comparing IF and ERD remains inconclusive, as both approaches show similar effectiveness in improving body composition, physical metrics, and lipid profiles among overweight or obese individuals [26, 39]. Research highlights reductions in total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and TG with these dietary interventions. While changes in HDL-C levels are inconsistent - some studies report no significant differences [38, 40], while others indicate improvements [41 - 43]. IF has been found to lower the risk of cardiovascular disease in obese and in metabolically healthy, non-obese individuals. Substantial improvements in blood lipid levels have been observed in cases where ADF was maintained for over six months [28].

IMPACT ON COGNITIVE FUNCTION

IF appears to offer various benefits for brain health and cognitive performance. When combined with regular physical activity and exercise, IF has been associated with improved physical and mental performance, particularly in athletes [44]. Potential advantages have been identified for brain-related conditions, including epilepsy, Alzheimer's disease, and multiple sclerosis. Animal studies further suggest that IF may benefit neurological disorders such as Parkinson's disease, autism spectrum disorder, and mood and anxiety disorders. However, more research is necessary to understand the effects of IF on neurological diseases in human populations thoroughly [45].

Despite these potential benefits, critics have raised concerns about the negative psychosocial effects of IF. Issues related to social relationships and mental well-being should be carefully considered. Daylight fasting, in particular, may lead to adverse physical and mental health effects. Reported drawbacks include hunger, irritability, and reduced cognitive function [10]. During fasting periods, individuals often experience increased eating-related thoughts, heightened hunger, and fears about losing control over their eating habits, which are more pronounced compared to non-fasting days [46]. However, these symptoms may subside within about a month of initiating the fasting regimen [10].

IMPACT ON SPORTS PERFORMANCE

IF has demonstrated a positive influence on body composition and lean muscle mass without compromising physical performance [47]. Research has also shown promising outcomes in overweight women, where IF improved body composition and muscle oxidative capacity [48]. Among active women, combining high-intensity interval training (HIIT) with IF has been found to reduce fat mass and improve jumping performance [49].

When paired with resistance training, IF has been shown to significantly reduce body mass, fat mass, body mass index (BMI), and body fat percentage, while preserving fat-free mass [50].

Additionally, various IF protocols result in comparable improvements in body composition, muscle quality, and strength [51].

Despite these encouraging findings, further research is needed to fully understand the mechanisms and energy pathways that enable athletes to maintain their performance capacities during IF.

IMPACT ON CIRCADIAN RHYTHM

Circadian rhythm regulates various physiological processes, including sleep, hormone secretion, and metabolism. Disruptions to this system can contribute to metabolic disorders such as obesity. Although this synchronization provides notable advantages, it also poses certain challenges.

By restricting eating times, IF may help to synchronize food intake with the body's circadian clock, a concept known as chrononutrition. Studies support this, showing that time-restricted eating (TRE) improves factors like sleep quality and gene expression related to circadian rhythms [52].

However some studies have reported delays in bedtime and wake time during IF, as well as a reduction in the proportion of rapid eye movement (REM) stage sleep [53]. Nevertheless, IF doesn’t seem to result in a feeling of excessive sleepiness during daytime or any noticeable changes in cognitive functions; it also has no adverse effect on circadian rhythms if the schedules of sleep/wake are properly controlled [54]. However, more research is needed to fully understand the exact impact of TRE on the circadian system in humans. A greater understanding of this connection will allow individuals to implement these protocols better into personalised diets [52].

SUSTAINABILITY AND ADHERENCE

Sustainability and adherence to IF remain key concerns, particularly regarding long-term commitment to the practice. Critics highlight that its effectiveness may be hindered without personalized approaches that account for individual preferences, lifestyles, and cultural factors. Research suggests that while older adults typically adapt well to time-restricted eating, additional guidance and support may be needed for understanding and sticking to the regimen, especially for individuals with conditions like type 2 diabetes and metabolic syndrome. Tailoring IF protocols to individual needs is crucial for improving adherence and ensuring sustainable benefits [55 - 57].

CHALLENGES AND POTENTIAL RISKS

Research highlights several limitations and potential risks associated with IF. Nutritional concerns, such as deficiencies and imbalances, are commonly noted, particularly for individuals who struggle to meet their dietary requirements within the constrained eating windows of IF. Weakness that can occur in some individuals during prolonged fasting is another commonly mentioned concern.

The long-term safety and effectiveness of IF remain uncertain, and it is not advised for certain populations, including pregnant women, nursing mothers, children, the elderly, and those with eating disorders [10].

LIMITATIONS AND FUTURE DIRECTIONS

While some benefits of IF are well-documented, significant gaps remain in our understanding. These include:

1. The long-term safety and sustainability of IF, particularly in vulnerable populations.
2. The impact of IF on hormonal balance, particularly in women.
3. Variability in individual responses based on genetics, age, and lifestyle.

Future research should prioritize large-scale, long-term trials to address these gaps and refine fasting protocols for different populations.

CONCLUSION

IF represents a promising dietary strategy with notable potential benefits for weight management, metabolic health, and longevity. Its simplicity and adaptability have contributed to its widespread popularity, making it accessible for individuals seeking effective alternatives to traditional calorie-restricted diets. Research indicates that IF can improve body composition, insulin sensitivity, lipid profiles, and cognitive function while promoting mechanisms such as autophagy and mitochondrial biogenesis.

However, IF is not without challenges. Nutritional deficiencies, risks of hypoglycemia, and long-term safety concerns require careful consideration. Vulnerable populations, including pregnant women, nursing mothers, children, and individuals with eating disorders, are advised against adopting IF without medical guidance. The variability in individual responses, driven by factors such as genetics, age, and lifestyle, further underscores the need for personalized approaches to fasting protocols.

As the popularity of IF continues to grow, future research must address critical gaps in our understanding of its long-term effects, particularly in diverse populations. Large-scale clinical trials and comprehensive studies will be essential to refine fasting protocols, maximize benefits, and minimize risks. By advancing evidence-based insights, IF can evolve into a sustainable and scientifically grounded strategy for improving global health outcomes.

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