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Intermittent Fasting for Weight Management and Metabolic Health: An Overview

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ABSTRACT

Obesity and overweight contribute significantly to cardiometabolic disorders worldwide. Traditional caloric restriction often faces challenges like poor adherence and rebound weight gain. Intermittent fasting (IF) offers an alternative approach that focuses on meal timing rather than quantity, including methods such as alternate-day fasting, the 5:2 diet, and time-restricted feeding. IF reduces energy intake and activates metabolic pathways that promote lipid oxidation, ketone production, and hormonal regulation for energy balance. It also influences AMPK and mTOR pathways, enhances autophagy, and aligns with circadian rhythms to improve glucose and lipid metabolism. Furthermore, IF positively modulates gut microbiota, enhancing insulin sensitivity and energy homeostasis. Clinical studies indicate that IF effectively reduces body weight and fat mass while preserving lean muscle. It also improves insulin sensitivity, lipid profiles, blood pressure, and inflammation. However, variations in fasting protocols and limited long-term studies necessitate further research to assess its long-term safety and efficacy.

Keywords: Intermittent fasting, weigh, Time-restricted feeding, body composition

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Introduction

The problems of obesity and overweight are the primary global health concerns and a significant part of the modern cardiometabolic disease burden [1]. The rate of overweight and obese has also been rising sharply in the last three decades globally and this poses a huge challenge to the general population, in terms of health. The most recent statistics show that in both high-income and middle-income nations, a significant part of the adult population is now in the ranges of overweight or obese, which increases their susceptibility to a variety of chronic illnesses [2]. Conventional weight loss dietary interventions have mainly been based on sustained energy or caloric restriction whereby the individual consumes less calories than expended, over a long period of time. Although caloric restriction has been demonstrated to cause significant weight loss and metabolic profile changes in the short term, its long-term efficacy is often limited by a low adherence rate, countermeasures by the body (including low basal metabolic rate and increased appetite) and recovery of weight gains after the active dieting period ends [3].Some believe that it is not an easy task to continue with the daily caloric cutting due to behavioural, social or psychological restraints; and many of the studies indicate that even though the weight is brought off initially, most of the participants gain back part of the weight, one to two years into it.

The concept of intermittent fasting has become a different model of dieting; instead of counting calories per day, it is emphasized when to eat. Intermittent fasting is a continuum of eating behaviours that alternate fasting and normal or regular consumption. Such patterns may be alternate-day fasting, the 5:2 technique and time-restricted feeding [4]. IF focuses on the timing of food intake, but not the food content intake, and has received plenty of research attention due to the potential to reduce total energy intake but activate fasting-associated metabolic processes that may affect adiposity and cardiometabolic risk [5].Moreover, time-restricted eating or alternate-day fasting as an IF regimen, is becoming a growing topic of investigation not only as to its impact on adiposity and the metabolism but also in terms of its effects on skeletal muscle integrity and functioning [6].IF has received great interest as a cardiometabolic risk factor modifying metabolic intervention that can potentially be beneficial in body composition, insulin sensitivity, and other metabolic factors by changing substrate use (e.g., by increasing fat oxidation), changing circadian metabolic rhythms, and lowering overall energy expenditure [7].

Types of Intermittent Fasting

Alternate-Day Fasting (ADF)

Alternate-day fasting is a common type of fasting, where fatigue consumption is substantially reduced usually about 25% of normal on a day when energy consumption is restricted, and this pattern is balanced with an eating day that permits an ad libitum or normal consumption .Syntheses of meta-analyses and randomized controlled trials suggest that Alternate Day Fasting is one of the most consistent intermittent fasting regimens in terms of short-term decreased body weight over many other IF regimens, but heterogeneity between studies is high [8].Alternate-Day Fasting has a greater commitment and a longer-term data-void relative to simpler protocols, including the 5:2 or time-restricted feeding, and some studies report greater early weight loss but have difficulty maintaining the pattern over a good many-month period [8,9]

Time-Restricted Feeding (TRF)

Time-restricted feeding limits the daily energy intake to a stable daily duration usually 610 hours, hence creating a daily fasting duration usually 1418 hours [10].Randomized studies of TRE have shown inconsistent effects; some RCTs have found some small incremental weight loss or metabolic effect (especially with an earlier eating window), whereas larger pragmatic studies that compared TRE with calorie targets showed no effect compared to calorie restriction alone [10,3]. TRE can lead to weight loss in part since it leads to ending up with an overall energy intake reduction, and timing (early versus late window) and coexisting calorie objectives alter the results [11,10].

The 5:2 Diet (Intermittent Energy Restriction)

The 5:2 diet recommends two non-consecutive fast days per week (usually around 500 kcal in women and 600kcal in men) and normal eating on the other five days [9].Pragmatic interventions of the 5:2 diet document a minor weight decrease that is equivalent to traditional brief weight-loss suggestions in 12 months, and group support has the capability to enhance transient adherence and initial weight loss, although effects subside with time [9].Recent randomised controlled trials involving a 5:2 design and meal replacements or targeted clinical care demonstrate promising short-term glycaemic and weight improvements in individuals with type 2 diabetes, but 3-year follow-up is not yet done [12].

Religious Fasting (e.g., Ramadan)

Religious fasting including Ramadan is daytime fasting between sunrise and sunset for 29-30 days and is typified by unique patterns of eating schedules, sleep, and action, unlike most of the controlled IF routines [13]. Systematic evidence suggests that Ramadan fasting tends to induce minor changes in body weight and fat mass in healthy adults, though the effect relies on cultural changes in diet, physical activity, and whether participants are voluntarily limiting their energy consumption outside of fasting [13].

Mechanisms Behind Weight Reduction

Hepatic glycogen is depleted and the substrate-utilization profile changes from dominant glucose oxidation to enhanced adipose lipolysis and hepatic β-oxidation of free fatty acids when the body enters a condition of prolonged fasting or restricted eating window [14]. The "metabolic transition" from carbohydrate to fat utilization is marked by an increase in circulating free fatty acids, which causes ketone bodies like β-hydroxybutyrate to rise and act as alternate fuels for the brain and muscle [15].The increased metabolic health seen in intermittent-fasting programs is a result of the ketones produced during this transition acting as both fuels and signalling molecules that alter mitochondrial biogenesis, redox status, and epigenetic regulators [14].

Long-term fasting causes glucagon levels to rise and insulin levels to fall, reducing the insulin: glucagon ratio and encouraging lipolysis, gluconeogenesis, and ketogenesis instead of fat storage [16]. While increased glucagon promotes hepatic fatty acid oxidation and ketone generation, decreased insulin transmission inhibits lipogenesis [17]. While ghrelin increases, triggering hypothalamic NPY/AgRP neurons and regulating appetite and energy intake variability, circulating leptin decreases, showing decreased fat storage signalling [15]. During fasting or restricted feeding, these hormonal changes regulate hunger, mobilize substrates, and maintain energy balance.

Fasting raises the AMP:ATP ratio and activates AMPK, which suppresses anabolic pathways and encourages autophagy, mitochondrial biogenesis, and fatty acid oxidation [18]. By inhibiting mTORC1, food and insulin deprivation promotes catabolic adaptation and decreases protein/lipid synthesis [19]. To preserve energy and metabolic equilibrium, autophagy is induced by AMPK activation and mTOR inhibition working together. When energy is limited, these mechanisms allow cells to switch from growth to repair [20].

Limiting feeding to the body's endogenous active phase optimizes the temporal partitioning of metabolic pathways and enhances metabolic responses by bringing peripheral tissue clocks, liver, adipose, and muscle in line with the central suprachiasmatic-nucleus clock. Research on time-restricted eating indicates that when meal windows are positioned early in the day as opposed to late in the day, improvements are shown in lipid profiles, blood pressure rhythm, and glucose tolerance [21]. Beyond total calorie intake, the timing of nutrient intake is a critical modulator of metabolic health since it affects hormone secretion rhythms, substrate processing, and the temporal regulation of anabolic vs. catabolic processes. In human trials, restricted-eating protocols like TRE and intermittent fasting cause changes in the composition of the gut microbiota and the production of metabolites (such as bile acids and short-chain fatty acids), and these changes are linked to improved insulin sensitivity, decreased inflammation, and fat loss [22]. Human research, however, reveals heterogeneity: people with established metabolic syndrome characteristics may have reduced responses, while lean and overweight people frequently exhibit microbiota alterations [23]. By altering gut-barrier function, bile-acid microbiome signalling, and SCFA-mediated pathways, these microbiota alterations impact host energy balance, establishing the gut microbiota as a mediator of metabolic adaptations during restricted-eating interventions rather than merely a bystander [23].

Effects on Body Weight and Composition

The use of intermittent fasting is found to be an effective method of reducing body weight and fat mass in human subjects. The clinical trials and meta-analyses show that in comparison to baseline or controls, IF interventions result in significant body weight, body mass index, total cholesterol, low-density lipoprotein, and diastolic blood pressure reductions [16,15]. IF has shown similar effects to that of continuous caloric restriction in reducing body weight and fat mass but perhaps has a better adherence and sustainability, indicated by fewer dropouts of people on IF regimens [17]. Notably, Intermittent fasting shows a selective depletion of adipose tissue without involving lean muscle mass thus justifying its ability to enhance body composition [15]. Meta-analyses prove that IF is as effective as daily caloric restriction to achieve weight loss and metabolic improvements, such as positive body composition and cardiometabolic outcome changes [16].

In addition to weight control, IF enhances glycaemic control and insulin sensitivity, and decreases in fasting glucose and insulin levels can be found in numerous studies [15]. The lipid profiles also get better with the total cholesterol, low-density lipoprotein, and triglycerides decreasing after interventions with IF [16]. Moreover, IF is linked to the decreases in the systolic and diastolic blood pressure, and a reduction in the inflammatory markers, which also indicates its possible benefits to the heart [22]. New evidence has indicated that there are other beneficial impacts on the composition of gut microbiota, mood and cognitive capacity, though further research is needed to fully describe the benefits [21].

Although these are the strengths of IF, it has weaknesses. Most of the studies are not long-term and are conducted over several weeks to a few months, which restricts the insight into the long-term effects [15]. The difference in fasting regimes (duration, frequency, and timing) makes it difficult to compare the study directly [16]. Hunger, fatigue, dizziness, and possible nutrient deficiencies are typical undesirable effects and can impact compliance [22].

It is necessary that future studies are carried out on large-scale clinical trials with a long-term viewpoint to assess the sustainability, safety and effectiveness of IF in different populations. Research needs to be done to find out the gender and age-specific responses, culture, and a combination of IF and exercise with balanced dietary intake to best results. Besides, the investigation of the effects of IF on gut microbiota and long-term metabolism adaptation can be considered as a mechanistic understanding of the health benefits of IF [21,15].

Conclusion

Intermittent fasting offers a promising approach for managing weight and improving metabolic health, serving as a viable option to continuous calorie restriction. Intermittent fasting coupled with normal eating patterns reduces total energy expenditure while improving metabolic functions, including increased fat burning, ketone production, and better insulin sensitivity. Hormonal changes, such as decreased insulin and leptin alongside increased glucagon and ghrelin, regulate appetite, substrate mobilization, and energy balance. Cellular mechanisms, including AMPK activation, mTOR inhibition, and autophagy, support energy balance, cellular upkeep, and robustness. IF protocols like alternate-day fasting, time-restricted feeding, and the 5:2 diet have demonstrated reductions in body weight, fat mass, and cardiometabolic risk while preserving lean mass. IF can also influence the makeup of gut microbiota, which subsequently impacts metabolic changes. Despite these benefits, there are limitations, including protocol variability, short-duration studies, and risks specific to certain populations. Subsequent research should examine prolonged effectiveness, protocol refinement, and associations with lifestyle factors to fully harness the intermittent fasting's therapeutic advantages.

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