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Clinical Trials on Intermittent Fasting Effects on Health and Diseases published from January 2022 to January 2024: A literature review

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Abstract

Background and Objective: Intermittent fasting (IF) encompasses dietary approaches such as the 16/8 and 5:2 diets, alternate-day fasting (ADF), and other regimens involving alternating periods of fasting and eating. Recently, IF has gained significant attention for its potential health benefits and has been extensively studied in clinical settings. This review critically examines clinical trials published from January 2022 to January 2024, focusing on the efficacy, safety, and mechanisms of IF as a dietary intervention to promote health and address diseases in adults.

Materials and Methods: A systematic analysis of recent clinical trials was conducted using PubMed and Google Scholar as the primary databases. Studies involving religious fasting, animal models, or participants under 18 years old were excluded from this review. A total of 23 articles meeting the inclusion criteria were analyzed.

Results: The findings indicate that IF is effective in promoting weight loss, managing diabetes, regulating blood pressure, and reducing risks associated with cardiovascular and liver diseases. Furthermore, evidence suggests that IF may enhance immune function and provide positive effects in cancer management, offering a promising avenue for improving health outcomes across multiple domains.

Conclusion: This review highlights the emerging evidence supporting IF as a safe and effective dietary intervention for weight management, metabolic health, and disease prevention. However, further research is required to refine IF protocols, assess long-term safety, and explore its mechanisms across diverse populations to establish it as a reliable strategy for promoting health and combating chronic diseases.

Keywords: Intermittent Fasting, Health, Diseases.

INTRODUCTION

Intermittent fasting (IF) refers to a dietary pattern that alternates between periods of fasting and non-fasting, with intervals ranging from a few hours to 24 hours or more [(1)]. IF encompasses at least two primary variants: time-restricted feeding (TRF) and intermittent energy restriction. TRF involves limiting food consumption to a shorter timeframe than usual, whereas intermittent energy restriction entails regular periods of restricted energy intake followed by periods of unrestricted intake [(1)]. Common fasting patterns include alternate-day fasting (ADF), two-day-a-week fasting (5:2), and prolonged fasting lasting from 5 to 40 days [(1)].

In recent years, IF has gained significant attention as a dietary strategy with potential benefits for health and disease management [(2)]. Research has shown that IF may promote weight loss, with studies highlighting the efficacy of ADF, the 5:2 diet, and TRF as weight-loss interventions [(2)]. Additionally, IF has demonstrated improvements in metabolic health, including reduced insulin resistance and favorable changes in leptin and adiponectin levels [(3)]. Evidence also suggests that intermittent energy restriction may help prevent and manage pre-diabetes and diabetes mellitus (DM), with notable improvements in metabolic and cardiovascular biomarkers [(4)]. Moreover, IF has been linked to benefits for hypertension, cardiovascular risk factors, and potential longevity [(3)].

However, contrasting perspectives caution against the potential risks of IF, such as nutrient deficiencies, hormonal imbalances, and adverse mental health effects. Fasting may pose dangers for certain populations, including individuals with hormonal disorders, pregnant and breastfeeding women, children, older adults, and immunocompromised individuals [(3)].

This research aims to review clinical trials on intermittent fasting published between January 2022 and January 2024, critically evaluating its potential benefits and risks to provide a comprehensive understanding of its impact on health and disease.

METHODOLOGY

A systematic electronic search was conducted to identify clinical trials examining the effects of intermittent fasting (IF) on health and disease. PubMed and Google Scholar served as the primary databases for this search. The following keywords were used: "Intermittent Fasting," "Autoimmune Diseases," "Blood Pressure," "Cancer," "Cardiovascular," "Diabetes Mellitus," "Liver Diseases," "Metabolic Health," "NAFLD," "Obesity," "Sleep," and "Time-Restricted Eating."

Studies were included based on the following criteria: (1) clinical trials conducted on human participants, (2) adult population aged ≥ 18 years, (3) publication dates between January 2022 and January 2024, and (4) availability of free full texts.

The exclusion criteria were: (1) studies focusing on religious fasting, (2) trials conducted on pediatric populations, (3) trial durations of less than four weeks, (4) studies limited to a specific country, and (5) clinical trials conducted on animals.

Articles meeting the inclusion criteria underwent a detailed review to determine their relevance to the study objectives. After careful evaluation, 23 articles were selected for inclusion in this literature review. These articles form the foundation of the analysis and are listed in the reference section.

THE EFFECT OF INTERMITTENT FASTING ON HEALTH AND DISEASES

3.1: Intermittent Fasting and Cardiovascular Health

Cardiovascular diseases (CVDs) are the leading cause of death globally, accounting for an estimated 17.9 million deaths annually[5].Behavioral risk factors, including unhealthy diets, physical inactivity, tobacco use, and harmful alcohol consumption, are major contributors to heart disease and stroke[5]. These risk factors manifest as raised blood pressure, glucose, lipids, and overweight or obesity [5]. Assessing cardiovascular risk typically involves parameters such as blood pressure measurements, lipid profiles, fasting blood glucose levels, body mass index (BMI), waist circumference, and lifestyle factors, including smoking status and physical activity[6].

The direct impact of intermittent fasting (IF) on cardiovascular health remains a subject of debate. Some studies indicate potential cardiovascular benefits of IF, such as improved lipid profiles [7, 8], blood pressure [8], and glucose metabolism markers [8]. However, other research has reported inconclusive or conflicting results, with one study finding no effects of IF on cardiovascular risk parameters other than fat mass reduction [9].

A secondary data analysis comparing IF with continuous energy restriction combined with exercise highlighted the impact of these dietary interventions on blood lipid profiles [7]. Both approaches improved lipid profiles, but the IF group exhibited a greater reduction, suggesting that IF may be a promising dietary strategy for enhancing lipid profiles and reducing cardiovascular risk [7].

A cross-sectional study investigating meal timing and cardiometabolic health in young men revealed intriguing findings. Participants with a longer daily eating window and those consuming their first meal earlier in the 24-hour cycle demonstrated better cardiometabolic outcomes, including improved blood pressure, lipid profiles, glucose metabolism markers, and body composition[8]. These findings emphasize the potential importance of meal timing in promoting cardiovascular health and suggest that optimizing food intake timing may improve cardiometabolic outcomes.

An experimental study on 24-hour shift workers examined time-restricted eating (TRE) and its effects on CVD risk [10]. While no significant changes were observed in LDL levels, blood pressure, or other parameters among healthy participants, those with elevated cardiometabolic risk factors showed significant reductions in blood pressure and HbA1c levels following TRE. This suggests that TRE may be particularly beneficial for individuals with heightened cardiometabolic risk factors.

Additionally, research on long-distance runners has provided insights into the effects of dietary interventions like TRE. One study found no adverse changes in cardiometabolic risk factors among runners following TRE [9]. However, athletes aiming to reduce fat mass before events may benefit from TRE, as it supports fat-free mass maintenance and resting energy expenditure compared to a caloric deficit diet.

The evidence presented underscores the potential of intermittent fasting and time-restricted eating as strategies for improving cardiovascular health, particularly among individuals with existing cardiometabolic risk factors. However, conflicting findings highlight the need for further research to determine optimal fasting protocols and identify populations most likely to benefit from such interventions. The author believes that while IF shows promise, tailoring fasting strategies to individual health profiles and lifestyle needs will be crucial for maximizing its benefits.

Intermittent fasting and Cardiovascular Health[table 3.1.1]

Author (Year)	IF Regimen	Duration	Sample Size (N)	Description of Participants	Changes	Additional Considerations
Dote-Montero (2023)	Meal timing (three non-consecutive 24-h dietary recalls)	3 months	N = 118	Young adults (82 women; 22 ± 2 years old; BMI: 25.1 ± 4.6 kg/m²)	Longer daily eating window and a shorter time from midsleep point to first food intake associated with a healthier cardiometabolic profile (lower HOMA-IR and cardiometabolic risk score)	Meal timing is not related to anthropometry or body composition
Richardson, C (2023)	Time-restricted eating (TRE) pattern (16 h fast; 8 h eating) or the reverse	4 weeks	N = 15	Long-distance male runners	No significant differences were observed in resting energy expenditure, markers of insulin resistance, serum lipids, or blood pressure. Body composition did change significantly in TRE group	
Manoogian, E. (2022)	10-h time-restricted eating (TRE)	12 weeks	N = 137	Firefighters working 24-h shifts (23-59 years old, 9% female)	In participants with elevated cardiometabolic risks at baseline, significant reductions in glycated hemoglobin A1C and diastolic blood pressure were observed compared to SOC	
Keenan, S (2022)	Twice-weekly fast (5:2 IF; IFT group) and CER (CERT group) when combined with resistance exercise	12 weeks	N = 34	Healthy participants (17 males and 17 females, mean BMI: 27.0 kg/m², mean age: 23.9 years)	Combined with resistance training, both dietary patterns (CER, IF) improved blood lipids, with greater reductions observed in the IFT group	

3.2: Intermittent fasting and NAFLD – Non-alcoholic Fatty Liver Disease

Non-alcoholic fatty liver disease (NAFLD) is characterized by the accumulation of fat in the liver, independent of excessive alcohol consumption (11). Approximately 65% of adults with obesity are affected by NAFLD, which is closely linked to the development of insulin resistance and type 2 diabetes. While some pharmacological agents, such as thiazolidinediones, have shown effectiveness in reducing hepatic steatosis, concerns remain regarding their safety and potential weight-gaining effects (11). NAFLD includes two forms: non-alcoholic fatty liver (NAFL) and non-alcoholic steatohepatitis (NASH). Individuals typically develop one form, but some may progress from one type to the other (12). Given these concerns, recent research has focused on non-pharmacological interventions, particularly intermittent fasting (IF), to address hepatic steatosis.

One study evaluated the combination of alternate-day fasting (ADF) and aerobic exercise for reducing intrahepatic triglyceride (IHTG) content in patients with obesity and NAFLD. The results showed that the combination of ADF and exercise was more effective than exercise alone or no intervention, demonstrating significant reductions in body weight, fat mass, waist circumference, alanine aminotransferase (ALT) levels, fasting insulin, and insulin resistance, while enhancing insulin sensitivity. Despite these positive outcomes, the study acknowledged limitations, including the short duration of the intervention, the need for long-term studies, and the potential impact of the COVID-19 pandemic on participant activity levels (11).

Another study compared Time-Restricted Feeding (TRF) with standard care (SC) and found that TRF significantly improved various parameters in patients with NAFLD, including steatosis, weight, BMI, waist circumference, blood pressure, visceral fat, and total body fat. The study highlighted TRF's practical application and ease of adherence, as it focuses on limiting eating windows rather than restricting specific foods. However, limitations such as small sample size and self-reported dietary data were noted, and further research comparing TRF to other dietary approaches, such as the Mediterranean diet, was suggested (13).

In a post-hoc analysis of a randomized clinical trial, the effects of a Low Carbohydrate High Fat (LCHF) diet, the 5:2 diet, and standard care (SOC) were compared. Both the LCHF and 5:2 diets resulted in greater weight reduction than SOC over a 12-week period. The study reported favorable changes in visceral adipose tissue (VAT) volume compared to subcutaneous adipose tissue (SAT), improved waist circumference, and enhanced insulin sensitivity, particularly in the 5:2 and LCHF groups. The study recognized the short duration (12 weeks) and insufficient statistical power to detect body composition changes as limitations, suggesting the need for larger studies to evaluate long-term outcomes (14).

The studies reviewed offer promising evidence for the role of intermittent fasting and diet modifications in the management of NAFLD. The combination of ADF and exercise appears to be a particularly effective strategy for reducing hepatic steatosis. The research on TRF also presents a compelling case for its potential benefits, particularly for patients with NAFLD, as it is a simple and adaptable approach to dietary modification. However, the limitations noted across the studies—such as small sample sizes, short intervention periods, and reliance on self-reported data—underscore the need for more robust, long-term clinical trials. Additionally, the comparative effectiveness of TRF and other dietary interventions, like the Mediterranean diet or LCHF, warrants further exploration. This will help clarify the optimal approach to managing NAFLD and inform future treatment guidelines.

Intermittent fasting and NAFLD[table 3.2.1]

Author (Year)	Sample Size (N)	Type of Participants	Intervention Duration & Type of Fasting	Comparison Group or Condition	Weight Change	Changes
Time-Restricted Eating						
Jack Feehan (2023)	28	Adults with an ultrasound diagnosis of fatty liver	12 weeks, Time-Restricted Eating (TRE) for 16 hours (from 8 pm to 12 noon the following day).	Standard care	↓	HDL ↓, ALT ↓, Total body fat ↓, Triglycerides ↓, Adiponectin (ns), Leptin ↓
Alternate-Day Fasting						
Mark Ezpeleta (2023)	80	Adults with obesity and NAFLD	3 months, 2 groups: 1 combination group and ADF group were instructed to consume 600 kcal for dinner (between 5:00 pm and 8:00 pm) on fasting days and eat food freely on feast days. Exercise: moderate-intensity aerobic exercise 5x/week.	Control (no change in eating/physical activity)	↓	IHTG (ns), ALT ↓, AST ↓, Fasting insulin ↓, LDL ↓, HDL ↓
Calorie-restricted Intermittent Fasting						
Catarina Lindqvist (2023)	64	Adults with NAFLD	12 weeks, Calorie-restricted intermittent fasting (5:2), calorie-restricted low-carbohydrate high-fat (LCHF)	12 weeks of healthy lifestyle advice (standard-of-care) diet	↓	Total serum cholesterol ↓, LDL ↓

3.3: Intermittent fasting and sleep disorders

Getting adequate sleep is essential for both physical and mental well-being. Sleep plays a crucial role in repairing, relaxing, and rejuvenating the body, helping to reverse the effects of stress (15). Several factors influence sleep, including stress, daily habits, physical activity, mental health conditions, sleep environment, dietary intake, and obesity, particularly in individuals with obstructive sleep apnea (15). Although time-restricted feeding (TRF) and intermittent fasting (IF) have demonstrated positive effects on body weight and metabolic health, only a limited number of studies have explored the effects of TRF on sleep.

The first study presents a randomized controlled trial comparing early time-restricted eating (eTRE) with a control group that ate over a ≥12-hour period (16). Participants in the eTRE group who adhered to the protocol at least five days per week showed greater improvements in overall mood. However, those in the eTRE group took slightly longer to fall asleep (a few minutes more) and reported sleeping half an hour less compared to the control group. Despite the reduced sleep duration, eTRE participants reported less fatigue and similar sleep quality to those in the control group. A post hoc analysis revealed no significant correlations between sleep duration, sleep latency, and hunger levels either during fasting or mean hunger. The study acknowledged limitations such as the reliance on self-reported data, a moderate sample size, and potential bias from the per-protocol analysis.

The second study investigated the effects of Alternate-Day Fasting (ADF) combined with exercise in adults with obesity and non-alcoholic fatty liver disease (NAFLD) (17). Despite showing positive effects on weight and intrahepatic triglyceride content, the combination of ADF and exercise did not result in any improvements in sleep parameters. Specifically, no changes were observed in sleep quality, duration, insomnia severity, or the risk of obstructive sleep apnea in individuals with NAFLD. The study acknowledged several limitations, including a small sample size, reliance on self-reported sleep measures, and potential confounding factors such as the impact of the COVID-19 pandemic on participants' sleep patterns.

The third study examined the effects of 4-hour versus 6-hour time-restricted feeding (TRF) on sleep in adults with obesity (18). Contrary to the hypothesis, the study found that the mild weight loss induced by both 4-hour and 6-hour TRF did not lead to improvements in sleep quality, duration, insomnia severity, or the risk of obstructive sleep apnea. The discussion suggests that a weight loss of at least 5% may be necessary to observe significant changes in sleep quality. As with the other studies, limitations included a small sample size, reliance on self-reported sleep measures, and potential confounding factors, such as caffeine consumption during fasting periods. The findings indicate that the modest weight loss achieved through 4- and 6-hour TRF may be insufficient to induce meaningful improvements in sleep quality or duration.

The studies reviewed suggest that any improvements in sleep quality or duration are either minimal or nonexistent, with some participants even experiencing reduced sleep duration. This lack of correlation between intermittent fasting and sleep may be attributed to the limited weight loss achieved through these interventions, which might be insufficient to elicit significant changes in sleep parameters. Further research with larger sample sizes, longer durations, and more objective sleep measurements is needed to better understand the relationship between intermittent fasting and sleep.

Intermittent fasting and sleep disorders table[3.3.1]

Author (Year)	Sample Size (N)	Type of Participants	Intervention Duration & Type of Fasting	Comparison Group or Condition	Weight Change	Changes
Time-Restricted Eating						
Felicia L. Steger (2022)	90	Adults with obesity	14 weeks eTRE; 8-hour eating window from 07:00–15:00	14 weeks control schedule (≥12-hour window)	↓	- Fasting glucose ↓ - Insulin resistance ↓ - Total cholesterol ns - Triglycerides ns - LDL ns - HDL ns There were no differences in sleep onset, sleep offset, chronotype, or sleep quality
Sofia Cienfuegos (2022)	49	Adults with obesity	8 weeks- 2 groups: 4-h TRF (eating only between 3 and 7 p.m.), 6-h TRF (eating only between 1 and 7 p.m.)	For 8 weeks control group (no meal timing restrictions)	↓	- 4- and 6-h TRF have no effect on sleep quality, duration, insomnia severity, or the risk of obstructive sleep apnea
Alternate-Day Fasting						
Mark Ezpeleta (2023)	80	Adults with obesity and NAFLD	3 months ADF (600 kcal "fast day," alternated with an adlibitum intake "feast day") and moderate-intensity aerobic exercise (5/WEEK; 60 min/session); ADF alone; exercise alone	No-intervention control group	↓	- Triglyceride ↓ Sleep quality (PSQI) score did not change Insomnia severity did not change Risk of obstructive sleep apnea did not change

3.4: intermittent fasting and type 2 diabetes

Diabetes mellitus (DM) encompasses autoimmune, genetic, and metabolic chronic disorders characterized by elevated blood glucose levels, or hyperglycemia [19]. While preventable, DM is influenced by various risk factors such as increased BMI, low physical activity, diets high in processed foods and sugar, and pregnancy [20]. These factors contribute to insulin resistance, the primary mechanism underlying type 2 diabetes. The global prevalence of diabetes rose from 200 million in 1990 to 830 million in 2022, with a faster increase in low- and middle-income countries compared to high-income nations due to limited access to preventive care and lifestyle changes [21]. As a systemic disease, DM leads to complications including heart disease, kidney damage, nerve damage, and vision impairment. It is a leading cause of blindness, kidney failure, heart attacks, strokes, and lower-limb amputations. In 2021, diabetes was the direct cause of 1.6 million deaths and 47% of all deaths due to diabetes occurred before the age of 70 years. Another 530 000 kidney disease deaths were caused by diabetes, and high blood glucose causes around 11% of cardiovascular deaths [21]. However, effective interventions, including dietary modifications, physical activity, medications, and regular screenings, can prevent or delay these complications.

Intermittent fasting (IF) has gained attention for its potential benefits in managing DM, particularly in improving glycemic control. Studies suggest that IF reduces calorie intake during fasting periods, leading to decreased insulin demand and enhanced insulin sensitivity [22]. For instance, a systematic review conducted in 2023 examined the metabolic impact of intermittent energy restriction and periodic fasting in patients with type 2 diabetes. The study, reported according to PRISMA guidelines, demonstrated that IF could improve glucose regulation in the short term and facilitate dosage reductions of glucose-lowering medications. These results highlight the role of fasting-induced metabolic shifts, such as increased reliance on fat oxidation and reduced hepatic glucose production, in improving glycemic control [23].

A 2022 study systematically explored the effects of various IF regimens compared to non-intervention diets and continuous calorie restriction (CR). It found that participants following IF exhibited improved insulin resistance and lipid profiles. However, while IF supports weight management and metabolic health by promoting caloric deficits and reducing insulin variability, it was less effective than CR for sustained glycemic control. This difference likely arises from CR's consistent energy restriction, which provides a more stable reduction in glucose levels over time [24].

Despite promising findings, evidence remains mixed, with some studies indicating no significant impact of IF on glycemic control in diabetes. Such discrepancies may result from variations in study designs, fasting regimens, and participant adherence. Overall, while IF shows potential as a complementary strategy for diabetes management, its effectiveness relative to other interventions warrants further investigation.

Intermittent fasting and T2DM[table 3.4.1]

Author (Year)	Type of Fasting	Duration	Sample Size	Description of Participants	Changes	Additional Consideration
Elske L. van den Burg (2023)	IER/PF	4 weeks-16 weeks	817 patients	Adult patients with T2DM, mean age 55.6 years, mean HbA1c from 7.2% to 8.5%	IER and PF can increase glucose regulation at least in the short term.	The review was very broad, studying IER and PF on T2DM, but short-term studies were included.
Lihu Gu (2022)	ADF/IER/TRF/RF	1-3 months	2483 participants	1277 in the interventional group, 1206 in the control group	IF led to more reduction in insulin concentration than non-interventional diet (SMD = -0.21, p = 0.03).	There was also reduction in BMI, WC, FM, and insulin resistance more effectively compared to non-interventional diet.

3.5: Intermittent fasting and blood pressure

Hypertension, defined as a consistent blood pressure reading of ≥130/80 mm Hg, often presents without symptoms, making regular monitoring essential. Alarmingly, an estimated 46% of adults with hypertension are unaware of their condition, highlighting the silent nature of the disease and the need for increased awareness and screening efforts [25, 26]. Modifiable risk factors include unhealthy diets—such as excessive salt intake and high consumption of saturated and trans fats—low fruit and vegetable consumption, physical inactivity, tobacco and alcohol use, and obesity. Non-modifiable risk factors include family history, age over 65, and comorbid conditions like diabetes or kidney disease [26]. Prevention strategies emphasize lifestyle modifications such as reducing dietary salt, avoiding excessive alcohol, quitting smoking, maintaining a balanced diet, engaging in regular exercise, and achieving weight loss [27].

Emerging evidence suggests that intermittent fasting (IF) could serve as a complementary approach to hypertension management. A 2023 study demonstrated that IF significantly reduced patients' blood pressure levels when compared to pre-IF measures. The study attributed this improvement to mechanisms such as enhanced heart rate variability (HRV), reduced angiotensin-converting enzyme

(ACE) activity, and lowered angiotensin II levels post-IF. These findings underscore the physiological benefits of fasting-induced hormonal shifts, which may contribute to improved cardiovascular health [28].

In a separate study conducted with adults aged 25 to 75 years, early time-restricted eating (eTRE)—a form of intermittent fasting involving eating within a shorter daily window—was found to be more effective for weight loss and diastolic blood pressure improvement over 14 weeks than a typical eating schedule of 12 hours or longer. The authors highlighted that the observed benefits of eTRE could stem from aligning food intake with circadian rhythms, which optimizes metabolic processes and reduces late-day calorie consumption. Furthermore, the study reported enhanced mood among participants practicing eTRE, potentially linked to stabilized glucose levels and improved dietary patterns [29].

These findings collectively suggest that IF, particularly in the form of eTRE, offers promise as a non-pharmacological intervention for hypertension. However, it is crucial to note that these outcomes need confirmation through further research, particularly focusing on the long-term effects and the most effective fasting protocols suited to individual patient needs. This area warrants further exploration to refine the approach to managing hypertension through dietary interventions.

Intermittent fasting and blood pressure[table 3.5.1]

Author (Year)	Type of Fasting	Duration	Sample Size	Description of Participants	Changes	Additional Consideration
Erkan Demirci, Bekir Calapkourur, Ziya Simsek (2023)	IF	30 days	58 patients	Age 40-60; exclusion criteria: smoking, BMI > 30 kg/m², hyperlipidemia, diabetes, GFR < 50	A significant decrease in mean systolic and diastolic blood pressures measured.	No statistically significant changes in fasting blood glucose, HbA1c, creatinine, GFR, BUN, total cholesterol, LDL, HDL, or TG levels. Significant decrease in CRP levels after IF.
Humaira Jamshed, Felicia L. Steger, David R. Bryan, MA1 (2022)	TRE	14 weeks	90 participants	Adults aged 25 to 75 years with obesity	The eTRE + ER intervention improved diastolic blood pressure (−4 mm Hg; 95% CI, −8 to 0 mm Hg; P = .04)	No statistically significant differences in systolic blood pressure, heart rate, glucose levels, insulin levels.

3.6: Intermittent fasting and obesity

Obesity results from a complex interplay of genetic, socioeconomic, cultural, and lifestyle influences, including dietary habits and urban development [30]. According to the World Health Organization (WHO), key drivers of obesity are maladaptive dietary patterns, insufficient physical activity, and underlying genetic predispositions [31]. The condition exacerbates physiological and metabolic dysregulation, heightening the risk of cardiovascular diseases such as strokes, insulin resistance, type 2 diabetes, and respiratory conditions like sleep apnea. It also negatively impacts musculoskeletal health, leading to joint pain and decreased mobility. Furthermore, obesity is associated with psychological consequences, including compromised self-esteem, social isolation, mood disturbances, and body image issues, as outlined by the NIH [32].

In recent years, intermittent fasting (IF) has emerged as a promising strategy for obesity management. Reducing calorie intake and adopting healthier eating habits are central to combating obesity [33]. Numerous studies conducted from 2022 to 2024 have explored the relationship between intermittent fasting and weight loss in overweight and obese individuals, examining various IF regimens with diverse parameters such as meal timing, combination with exercise, and energy intake restriction. Kleinman et al. stated that, given its promising outcomes in animal studies, additional research into intermittent fasting is needed, but it is crucial that clinical conclusions and recommendations are based on the limited clinical evidence currently available[34].

One study demonstrated significant reductions in body weight and fat mass among participants following both 1-day and 2-day fasting regimens, with the latter showing greater effects. This suggests that the intensity and frequency of fasting play a crucial role in its outcomes [35]. Another study confirmed similar weight and fat loss results in fasting groups, with the added focus on the effect of IF on sleep patterns. Interestingly, while weight and fat mass decreased, visceral fat remained unaffected, indicating that the impact of IF on fat distribution may vary [18].

A different study investigated the combination of IF with exercise, revealing that participants in the combination group and the IF-only group both experienced significant reductions in body weight, fat mass, and waist circumference. These findings suggest that IF, even without exercise, has substantial health benefits, though combining the two may optimize outcomes [11]. Similarly, another study found comparable weight and fat mass reductions between participants following IF and those engaging in Sprint Interval Training (SIT), suggesting that IF can achieve results similar to intensive exercise programs [36].

One study highlighted that IF demonstrated superior results in weight loss and fat reduction compared to traditional calorie-restriction diets. This indicates that the timing and structure of eating periods in IF may provide metabolic advantages beyond mere calorie reduction [37]. Another study reported consistent outcomes in terms of body weight and fat mass loss but noted intriguing gender-specific differences. Men experienced reductions in visceral fat and waist circumference, while women showed increases in skeletal muscle mass. The researchers hypothesized that these differences could be attributed to hormonal variations between genders [38].

The evidence from the reviewed studies indicates the promising potential of intermittent fasting (IF) as an intervention for managing obesity. Nevertheless, the variations in outcomes, particularly across genders and among different fasting regimens, suggest that personalized approaches based on individual metabolic and hormonal profiles may enhance the effectiveness of IF. Further research is needed to elucidate the mechanisms underlying these variations and to establish standardized guidelines for implementing intermittent fasting in diverse populations.

Intermittent fasting and obesity[table 3.6.1]

Author (Year)	IF Regimen	Duration	Sample Size (N)	Description of Participants	Changes	Additional Considerations
Paul J Arciero (2022)	IF-P1 (36h) vs. IF-P2 (60h)	4 weeks	N = 20	Overweight/obese men and women, non-smokers, 30–65 years	**IF1-P**: ↓ BW (-5.2%), ↓ WC (-5 cm) **IF2-P**: ↓ BW (-7%), ↓ WC (-7.6 cm)	Reductions in total energy intake (-1000 kcal/day) Unchanged levels of energy expenditure (200–300 kcal/day)
Sofia Cienfuegos (2022)	4h vs. 6h vs. control group	10 weeks	N = 49	Healthy, BMI (30–49.9)	**IF groups**: ↓ BW, ↓ FM, no effect on visceral fat	4h: 4-h TRF (eating only between 3 and 7 p.m.) 6h: 6-h TRF (eating only between 1 and 7 p.m.) Control group: No meal timing restrictions No calorie restriction.
Mark Ezpeleta (2022)	Combination vs. ADF vs. Exercise vs. Control group	12 weeks	N = 80	Overweight/obese men and women, non-smokers, 81% female, 23–65 years	**Combination**: ↓ BW (-4.58%), ↓ FM (-3.24 kg), ↓ WC (-5.02 cm) **ADF**: ↓ BW (-5.06%), ↓ FM (-3.32 kg), ↓ WC (-4.59 cm) **Exercise**: ↓ BW (-2.11%), ↓ FM (-1.34 kg), ↓ WC (-3.24 cm) **Control**: ↓ BW (-0.60%), ↓ FM (-0.62 kg), ↓ WC (-0.52 cm)	ADF and combination groups: 600 kcal (as dinner, 5–8 p.m. on fast days / as desired on alternating feast days) Exercise and control groups: Moderate-intensity aerobic exercise (5 times/week)
Matthew B. Cooke (2022)	5:2 IF vs. SIT vs. Combination	16 weeks	N = 34	BMI (25–35), non-smokers, 18–45 years	↓ BW, ↓ FM	**5:2 IF**: 2 non-consecutive fasting days per week, 5 days on ad libitum eating **SIT**: Supervised SIT (3 bouts/week of 20s cycling at 150% VO2peak followed by 40s active rest, total 10 min duration)
Felicia L. Steger (2023)	16:8 TRE vs. Control Group	14 weeks	N = 90	25–75 years	↓ BW (-3.7 ± 1.2 kg), ↓ FM (-2.8 ± 1.3 kg)	eTRE: 8-hour eating window from 07:00–15:00 Control group: ≥12-hour eating window
Przemysław Domaszewski (2023)	16:8 TRE vs. Control Group	6 weeks	N = 116	BMI (25–29.9), non-smokers, 65–74 years	↓ BW, ↓ FM, ↓ WC & visceral fat in men only, ↑ skeletal mass in women	Energy restriction included Baseline activity

3.7: Intermittent fasting and cancer

Cancer imposes a profound burden not only on affected individuals but also on their families and healthcare systems. It remains a feared global health challenge, significantly reducing the quality of life of its victims. Despite considerable advancements in cancer treatments, awareness and prevention remain crucial strategies for reducing the global burden of this devastating disease [39, 40]. Effective prevention strategies often focus on addressing modifiable risk factors such as obesity and poor dietary habits, both of which are linked to an increased risk of various cancer types [44, 45].

Recent studies have highlighted the potential benefits of intermittent fasting (IF) in cancer prevention and metabolic syndrome management [41, 42, 43]. For instance, a study examined the effects of a four-week intermittent fasting regimen from dawn to sunset on metabolic health and cancer prevention [41]. This research analyzed peripheral blood mononuclear cells (PBMC) proteomics, a highly sensitive tool that provides insights into the body’s response to diseases like cancer [46]. PBMC proteomics revealed that dawn-to-dusk fasting induced anti-atherosclerotic, anti-inflammatory, and anti-tumorigenic effects at the cellular level in individuals with metabolic syndrome. These findings suggest that IF may influence metabolic pathways and protein expression, potentially reducing risk factors associated with tumorigenesis.

However, this study had notable limitations. Being a pilot study with a small sample size, its findings require validation through larger and more diverse clinical trials. Additionally, as the study was limited to individuals with metabolic syndrome, the generalizability of its results to other populations remains uncertain. This highlights the need for further research to explore the broader applicability of IF in cancer prevention.

Cancer prevention can be achieved by minimizing exposure to modifiable risk factors such as poor diet, sedentary lifestyles, and obesity [47]. To further investigate this, a 12-month randomized controlled trial was conducted to compare three intervention groups: 8-hour time-restricted eating (TRE), daily calorie restriction (Cal-R), and a control group. The trial aimed to assess the impact of these interventions on weight loss, metabolic biomarkers, inflammation, oxidative stress, gene expression profiles in colonic mucosa, and colorectal cancer risk markers[48].

The study revealed that TRE resulted in 3% to 5% weight loss, reduced insulin resistance, and most notably, a decrease in oxidative stress. These outcomes underscore the potential of TRE in mitigating cancer-related metabolic risks. However, the study also faced challenges, including participant adherence to long-term dietary regimens. Issues with compliance and dropout rates may have influenced the reliability and validity of the findings.

These studies collectively indicate the promising role of intermittent fasting in cancer prevention, particularly through its effects on metabolic health and inflammation. However, the current body of evidence underscores the need for larger, more inclusive trials to validate these findings. Further research is essential to address the limitations of existing studies and to determine the long-term benefits of IF in cancer prevention.

Intermittent fasting and cancer[table 3.7.1]

Author (Year)	IF Regimen	Duration	Sample Size (N)	Description of Participants	Changes	Additional Consideration
Mindikoglu et al. (2022)	4-week dawn-to-dusk dry fasting (not related to any religion)	4 weeks	N = 14	Subjects with Metabolic Syndrome, mean age of 59, fasting from dawn to dusk for more than 14 hours daily for 29 days	Down-regulation of apolipoprotein B (APOB) gene protein products (GP), alteration in lipid and atherosclerosis pathways, up-regulation of tumor-suppressor effect genes	Prospective clinical trial study design. The assessment was performed before, at the end, and one week post-fasting.
Kelsey Gabel (2022)	8-hour TRE	12 months	N = 255	Adults with obesity, elevated CRC risk, and prediabetes, age: 45-65 years, BMI: 30-49.99	TRE causes weight loss and reductions in oxidative stress and insulin resistance.	This is a new clinical trial that did not confirm its hypothetical results yet. The TRE-CRC trial will serve as the first study to assess the efficacy on weight loss and CRC risk reduction in adults with obesity, and it will serve as the largest study in humans to assess the systemic and colon tissue molecular mechanisms that mediate the anticancer effects of both TRE and CR.

3.8: Intermittent fasting and immune system

Intermittent fasting (IF) has emerged as a promising approach to enhancing immunity, offering benefits that range from cellular repair and inflammation reduction to stem cell regeneration and modulation of gut microbiota (43). Although research in this area is still evolving, existing evidence suggests that intermittent fasting can strengthen immune function, contributing to overall health and well-being (49).

One notable randomized controlled feeding study investigated the effects of calorie restriction on 36 patients diagnosed with Multiple Sclerosis (MS), an autoimmune condition. Participants were divided into groups subjected to three distinct dietary approaches, including intermittent fasting (50). The study revealed significant immune-modulating effects among the intermittent fasting group. Specifically, IF resulted in a reduction in memory T cell subsets, which are associated with immune overactivation, as well as specific lipid markers in MS patients. Concurrently, a proportional increase in naive T cells, which play a critical role in maintaining immune balance and responding to new antigens, was observed.

These immune-related changes were not present in patients who followed either a control diet or a daily calorie restriction regimen, underscoring the unique potential of intermittent fasting. The study's authors proposed that IF possesses anti-inflammatory properties and neuroprotective benefits in MS patients. These findings suggest broader implications, indicating that intermittent fasting may have similar immune-enhancing effects in healthy individuals or those with other autoimmune conditions [50].

This research highlights the potential of intermittent fasting (IF) as a strategy for modulating immune function. Although further studies are necessary to confirm its efficacy across diverse populations, the existing evidence suggests that IF could play a valuable role in enhancing immune health and addressing autoimmune diseases. These findings point to the need for continued exploration into dietary interventions like IF for supporting immune function and managing autoimmune conditions.

Intermittent fasting and immune system[table 3.8.1]

Author (Year)	**IF Regimen**	**Duration**	**Sample Size (N)**	**Description of Participants**	**Changes**	**Additional Considerations**
Kathryn C Fitzgerald (2022)	Intermittent Calorie Restriction	8 weeks	N = 36	People with Multiple Sclerosis (MS)	Reductions in effector memory and TH1 subsets and proportional increases in naïve subsets; larger changes in lipid markers are associated with larger T cell subset changes	Daily CR and weight-stable diets showed no significant changes; metabolic and flow cytometry used for assessment.

SUMMARY

The rising prevalence of chronic diseases affecting the heart, endocrine system, and other bodily systems, coupled with the growing reliance on medications, has prompted researchers to explore non-pharmacological treatments. Intermittent fasting (IF) has gained attention as a potential strategy to improve health and manage diseases. This study reviews clinical trials to assess the effects of IF on various chronic conditions, highlighting both its benefits and limitations.

A total of 23 articles were reviewed, including 4 that examined the impact of IF on cardiovascular health. Three studies concluded that IF positively influences cardiovascular health and lipid profiles, while one reported no significant changes or adverse effects on cardiometabolic risk factors.

Three studies focused on non-alcoholic fatty liver disease (NAFLD), reporting significant improvements in ALT, LDH, fat mass, insulin resistance, steatosis, and adipose tissue distribution. However, these findings were limited by short study durations (12 weeks) and small sample sizes.

Regarding sleep apnea, 3 studies found no direct evidence linking IF to improvements in the condition. Conversely, 2 studies on type 2 diabetes mellitus (T2DM) demonstrated that IF can reduce blood sugar levels, improve insulin resistance, and enhance glycemic control, suggesting its potential as an adjunctive treatment for T2DM.

Three articles investigating the effects of IF on hypertension consistently reported reductions in blood pressure, particularly in hypertensive patients. Additionally, 6 studies on obesity highlighted significant weight and fat loss, along with decreased waist circumference. Notably, gender-based differences were observed, potentially attributable to hormonal factors.

Two articles explored IF's role in cancer prevention. One demonstrated that IF induced beneficial changes in PBMC proteome, exhibiting anti-atherosclerotic, anti-inflammatory, and anti-tumorigenic effects in individuals with metabolic syndrome. The second study linked time-restricted eating (TRE) to weight loss, reduced insulin resistance, and diminished oxidative stress, a key factor in cancer development.

Lastly, a study on autoimmune conditions, specifically multiple sclerosis (MS), revealed that IF decreased memory T cells and lipid markers while increasing naive T cells, indicating anti-inflammatory effects. These findings suggest that IF may benefit other autoimmune disorders as well.

Overall, the evidence supports IF as a promising non-pharmacological approach for managing chronic conditions, though further research is required to address limitations such as study duration, sample size, and variability in population responses.

CONCLUSION

This research demonstrates that intermittent fasting (IF) can improve metabolic health, including weight loss, insulin sensitivity, and lipid profiles. However, its effects on sleep quality and other health outcomes remain uncertain and require further investigation. The variability in fasting regimens, participant characteristics, and study designs suggests that IF’s effectiveness may depend on factors such as the type of fasting, duration, and individual health conditions. Future studies should include larger, diverse populations and longer follow-up periods, using standardized methods to better understand IF’s long-term effects on sleep, cardiovascular health, and overall well-being.

LIMITATIONS

Although the present literature review offers significant insight into the impact of intermittent fasting (IF) on health and illnesses, it is important to acknowledge several limitations. First, studies' heterogeneity: the clinical trials that make up this review differ in terms of study design, sample size, length, and the particular IF regimens used. Because of this heterogeneity, it is difficult to draw consistent conclusions and the findings may not be as broadly applicable as possible. Second, studies' short follow-up periods of the reviewed trials had brief follow-up periods, which might not have been sufficient to fully capture the sustainability and long-term effects of intermittent fasting. In addition to the limited period of time chosen to review the clinical trials done in the past two years. By addressing these limitations, future research could obtain a deeper understanding of how illnesses and health are affected by intermittent fasting.

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The authors declare no conflict of interest in this study and all of them contributed equally to the conceptualization, drafting and approving the final manuscript. The corresponding author has also oversaw all the steps of the project.

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التجارب السريرية حول تأثير الصيام المتقطع على الصحة والأمراض ، المنشورة من يناير 2022 إلى يناير 2024: مراجعة أدبية

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الملخص

الخلفية والهدف: يشمل الصيام المتقطع أنظمة غذائية مثل حمية 8/16 وحمية 5:2 و الصيام يوما بعد يوم وغيرها من الأنظمة التي تعتمد على التناوب بين فترات الصيام والأكل. في الآونة الأخيرة، حظي الصيام المتقطع باهتمام كبير لما له من فوائد صحية محتملة، وتمت دراسته بشكل موسع في البيئات السريرية. تستعرض هذه المراجعة بشكل نقدي التجارب السريرية المنشورة من يناير 2022 إلى يناير 2024، مع التركيز على فعالية وسلامة وآليات الصيام المتقطع كوسيلة غذائية لتعزيز الصحة وعلاج الأمراض لدى البالغين.

المواد والطرق: تم إجراء تحليل منهجي للتجارب السريرية الحديثة باستخدام قاعدة بيانات PubMed و Google Scholar كمصادر رئيسية. تم استبعاد الدراسات التي تناولت الصيام الديني أو النماذج الحيوانية أو المشاركين الذين تقل أعمارهم عن 18 عامًا. وتم تحليل ما مجموعه 23 دراسة استوفت معايير الإدراج.

النتائج: تشير النتائج إلى أن الصيام المتقطع فعال في تعزيز فقدان الوزن، وإدارة مرض السكري، وتنظيم ضغط الدم، وتقليل المخاطر المرتبطة بأمراض القلب والكبد. علاوة على ذلك، تشير الأدلة إلى أن الصيام المتقطع قد يعزز من وظائف الجهاز المناعي ويوفر تأثيرات إيجابية في إدارة السرطان، مما يجعله وسيلة واعدة لتحسين النتائج الصحية في عدة مجالات.

الاستنتاج: تسلط هذه المراجعة الضوء على الأدلة المتزايدة التي تدعم الصيام المتقطع كوسيلة غذائية آمنة وفعالة لإدارة الوزن، وتحسين الصحة الأيضية، والوقاية من الأمراض. ومع ذلك، هناك حاجة إلى مزيد من الأبحاث لتطوير بروتوكولات الصيام المتقطع، وتقييم سلامته على المدى الطويل، واستكشاف آلياته عبر مجموعات سكانية متنوعة لتأكيد فعاليته كإستراتيجية موثوقة لتعزيز الصحة ومكافحة الأمراض المزمنة.

الكلمات الدالة: الصيام المتقطع ، الصحة ، الأمراض.