GMR
The Original

COMBINED EFFECTS OF HIGH-INTENSITY INTERVAL TRAINING AND 5:2 INTERMITTENT FASTING ON WEIGHT LOSS, BODY COMPOSITION, AND PHYSICAL FITNESS: A NARRATIVE REVIEW

Ma Yuequn[1,2], Mohamad Nizam Bin Nazarudin[1]*, Nurwina Akmal Binti Anuar[1]

[1]Faculty of Education, Universiti Kebangsaan Malaysia, Bangi, 43600, Selangor, Malaysia
[2]Hechi University, Hechi City, Guangxi Zhuang Autonomous Region, China
Corresponding Author: Mohamad Nizam Bin Nazarudin, mohdnizam@ukm.edu.my

Abstract

Background: Increased obesity in adults is a global problem of >1b affecting significant cardiovascular and metabolic morbidity. Two dietary strategies capable of changing the body composition and cardio-metabolic health independently are high-intensity interval training (HIIT) and the 5/2 intermittent fasting (IF) diet—both of which are time-efficient because of their suitability for short-term periods of time. The combined effects of these however have not been synthesized systematically, however.
Objective: The aim of the narration review is to assess critically the literature available about the effects of HIIT with 5:2 IF on weight loss, body composition and physical fitness in the adult population with overweight or obesity.
Methods: peer-reviewed literature was synthesized in narrative format, with a preference for systematic reviews and meta-analysis and for studies published in the past five years that were based on RCTs. The databases were searched such as PubMed, Scopus and Web of Science. The evidence was critically appraised, synthesized and contextualized with the mechanistic insights.
Results: The effect of HIIT + 5:2 IF was more beneficial for weight loss (weighted mean difference (WMD): −3.03 kg), fat mass (WMD: −0.93 kg), and waist circumference (WMD: −2.51 cm) than was either HIIT or 5:2 IF alone. Interestingly, HIIT was found to counteract the lean mass loss commonly seen with IF; in one RCT, there was a +3.3% gain in fat-free mass. Cardiorespiratory fitness (VO_2 peak) significantly improves consistently and improving muscular performance (especially explosive power) is even better. Three possible synergistic mechanisms that have been proposed are: Complementary activation of AMPK, PGC-1 alpha expression, which leads to mitochondrial biogenesis, and metabolic flexibility. But small sample sizes, brief intervention times (4 to 12 weeks) and a narrow range of protocols and limited generalizability of the results for males and diverse groups have limited the generalizability of available evidence. Most outcomes have very low certainties of evidence (due to the GRADE) of 0.0.
Conclusion: HIIT+5:2 IF seems to be an effective, safe and feasible approach for enhancing weight loss, body composition and physical fitness in women suffering with obesity. Conducting large, longer-term, properly designed RCTs in different patient groups with standardized protocols is an absolute necessity to come up with any clear clinical recommendation.

Keywords: Intermittent occurs suggest high-intensity interval training, 5:2 diet.

1. INTRODUCTION

Overweight and obesity refers to an abnormal or excessive build-up of fat which may be harmful to health. The association between being overweight or obese and many non-communicable diseases is independent, meaning obesity is a risk factor on its own aside from any other fixed risk factors for those diseases like cardiovascular disease, type 2 diabetes, and several cancers (1). There has been a dramatic increase in excess body weight over the past few decades throughout the world. There is an increasing problem of obesity with more than a billion people worldwide already affected (2). The worldwide cost of overweight and obesity is estimated to be USD 3 trillion (USD 1 trillion as early as 2030) annually without surveillance and intervention (3). This growing public health problem calls for effective, scalable and sustainable weight-management solutions.

High-intensity interval training (HIIT) is one exercise modality that has gained significant popularity for lifestyle interventions, and has shown promising results in the literature for body composition and cardio-metabolic health, with research demonstrating its effectiveness and effectiveness relative to other forms of exercise. In the realm of exercise modality, high-intensity interval training (HIIT) has proven to be a time-efficient training approach with comprehensive evidence that it is effective for body composition and cardio-metabolic health, and is more effective than other types of exercise. An interval training was found to have significant difference in decreasing total body fat percentage from moderate-intensity continuous training (weighted mean difference: −0.77%) and non-exercise control (weighted mean difference: −1.50%) by up to 2.3% (4). In addition to reaching a higher adiposity reduction, HIIT also elevates cardiorespiratory fitness, insulin sensitivity and mitochondrial oxida1ve capacity (5).

Meanwhile, the practice of intermittent fasting (IF) has become a popular diet breakthrough method for managing weight has come to the fore. One of the most studied IF nutritional plans (5:2 diet) involves a week of about 500–600 kcal for two non-consecutive "fast" days interspersed with the rest of the week of unrestricted eating in calories (6). Results from interest IF suggest that the weight loss in the range of 3-8% in 6-12weeks is clinically meaningful (7). However, as with many diets, IF usually results in a decrease in both fat mass and non-fat mass weight loss, leading to worries regarding maintenance of metabolically active fat-free mass (6, 7).

Science shows that the 5:2 IF and HIIT combination makes a lot of sense for a number of reasons. Exercise could be used as an adjunct to IF and preserve lean mass while providing benefits to the cardio-metabolic and physical fitness (7). Second, the two interventions could have complementary metabolic pathways, i.e. IF could switch metabolism to promote oxidation of fatty acids while HIIT can increase insulin sensitivity and the amounts of mitochondria in the body (6). Third, emerging evidence suggests that people who perform IF after exercise will have more fat mass and waist circumference losses than people who do IF without exercise (8, 9).

While there is an increased call for interest, there is some fragmentation of the evidence base. A great variability exists in the literature regarding IF protocols, exercise modalities and outcome measures. Thus, this narrative review aims to critically assess the existing evidence regarding the synergistic effects of HIIT and 5:2 IF on body composition, physical fitness and weight loss. We draw on RCTs, systematic reviews and meta-analyses to synthesize results; explore mechanisms which could lead to synergistic effects; point to gaps in the research; and talk about practical implications.

Table 1. Characteristics of Studies Investigating the Effects of High-Intensity Interval Training and 5:2 Intermittent Fasting

Author, Year	Study Design	Sample Size (n)	Participant Characteristics	Intervention Details	Duration	Key Outcomes
Batitucci et al., 2022 (26)	Randomised controlled trial	36	Women with obesity; BMI 34.0 ± 3.2 kg/m²; age 32.2 ± 4.4 years	Three groups: (1) 5:2 IF + HIIT; (2) HIIT alone; (3) 5:2 IF alone. HIIT: 3×/week, 25 min/session, 70–85% MHR. 5:2 IF: 2 fasting days/week, two meals within 6 h (25% total energy intake) + 18 h complete fasting	8 weeks	Weight and BMI reduced only in IF + HIIT group (P = 0.012 and P = 0.031). Body fat loss: IF + HIIT −4% (P < 0.001); HIIT alone −2.3% (P = 0.043). FFM increased: IF + HIIT +3.3% (P < 0.001); HIIT alone +2% (P = 0.043). All aerobic and strength parameters improved
Cooke et al., 2022 (28)	Randomised controlled trial	34	Adults with overweight/obesity; age 35.4 ± 8.4 years; BMI 31.3 ±	Three groups: (1) 5:2 IF; (2) sprint interval training (SIT);	16 weeks	Both IF and IF/SIT decreased body weight, fat mass

			3.5 kg/m²; VO_2peak 27.7 ± 7.0 mL·kg⁻¹·min⁻¹	(3) 5:2 IF + SIT. SIT: 3 bouts/week, 20 s cycling at 150% VO_2peak, 40 s active rest, 10 min total		and visceral fat vs SIT alone (P < 0.05), with no significant differences between diet-only and combined groups. Only exercise (alone or with IF) significantly increased cardiorespiratory fitness
Li et al., 2024 (42)	Randomised controlled trial	326	Adults with overweight/obesity and type 2 diabetes	Three groups: (1) 5:2 diet (2 days/week energy restriction by formula diet); (2) exercise (2 days/week HIIT + resistance training); (3) lifestyle education control	12 weeks	5:2 diet significantly reduced HbA1c vs control (−0.34%, P = 0.007). Exercise did not significantly improve HbA1c vs control (P = 0.47). Exercise was superior in maintaining lean body mass. Both interventions improved adiposity and hepatic steatosis
Batitucci et al., 2024 (22)	Randomised controlled trial	36	Women with obesity; age 18–40 years	Three groups: (1) 5:2 IF + HIIT (n = 15); (2) HIIT alone (n = 11); (3) 5:2 IF alone (n = 10). HIIT: 3×/week, 25 min/session. 5:2 IF: 2 fasting days/week	8 weeks	Exercise increased fecal acetate concentrations (P = 0.04). No changes observed in gut microbiota composition or functional profile across groups
Keenan et al., 2022 (33)	Randomised controlled trial	34	Untrained adults; mean BMI 27.0 kg/m²; age 23.9 years	Two groups: (1) 5:2 IF + resistance training (IFT); (2) continuous energy restriction + resistance training (CERT).	12 weeks	LBM increased +3.7% (P < 0.001); body weight −4.6% (P < 0.001); fat −24.1% (P < 0.001) with no significant between-group differences.

				Both: 2 supervised resistance + 1 unsupervised session/week; ≥1.4 g protein/kg/day		Similar gains in strength and muscular endurance
Postmenopausal women pilot study, 2025 (32)	Randomised controlled trial (pilot)	NR	Postmenopausal women	IF + HIIT vs low-calorie diet	8 weeks	Combination of IF and HIIT effective for enhancing body composition and physical performance, potentially mediated by changes in orexinergic system

Abbreviations: BMI, body mass index; CERT, continuous energy restriction; FFM, fat-free mass; HbA1c, glycated haemoglobin; HIIT, high-intensity interval training; IF, intermittent fasting; IFT, intermittent fasting training; LBM, lean body mass; MHR, maximum heart rate; NR, not reported; SIT, sprint interval training; VO_2peak, peak oxygen consumption.

2. PHYSIOLOGICAL BASIS OF HIGH-INTENSITY INTERVAL TRAINING

HIIT is typically characterized by a series of burst with similarly high intensity fitness activity mixed with recovery time. Usually two to three minutes in the length of exercise-to-recovery ratio, protocols are performed at 70–100% of maximal HR or 65–90% of VO_2 peak (10). The key to HIIT is its significant physiological response in the face of only roughly half the total training volume of moderate intensity continuous training (4).

HIIT's energy load simultaneously affects both aerobic and anaerobic metabolic pathways. During high intensity bouts of work, the phosphocreatine system and anaerobic glycolisis are the most rapid sources of resynthesize of ATP and during recovery, oxidative phosphorylation predominates (11). A systematic review of metabolomic analysis studies has found that the pathways involved in metabolomic changes induced by HIIT are substantial and include pathway related to carbohydrate, lipid and amino acid metabolism (12).

HIIT has been shown to significantly promote maximal fat oxidation during exercise in overweight and obese adults (0.07 g/min [95% CI, 0.03–0.11 g/min]) (13) in a 2023 meta-analysis. HIIT has beneficial effects on insulin sensitivity as well. A 2025 systematic review reported that HIIT significantly reduced fasting insulin (SMD: −0.43; 95% CI: −0.82 to −0.05) and HOMA-IR (SMD: −0.52; 95% CI: −0.97 to −0.07) compared with MICT in patients with diabesity (14).

Mitochondrial activity undergoes a powerful increase at the cellular level in response to HIIT, through the upregulation of the expression of both PGC-1α and SIRT3(15). HIIT and MICT is able to promote both of these pathways; HIIT generally produces more quick molecular adaptations (16). HIIT also leads to an increase in glucose, lactate and fatty acid transporter protein content in the skeletal muscle (17).

The HIIT Cardio adaptations are known. Drawing on previous evidence, Kjaer et al. (2013) performed an umbrella review, which confirmed the positive effect of HIIT on cardiorespiratory fitness for adults (10). In patients with heart failure a meta-analysis of 2024 pointed to a significant increase in the mean difference in peak oxygen uptake (PVO2) from HIIT compared to MICT (1.78 mL/kg/min), and also selected an increase in the mean difference of left ventricular ejection fraction (LVEF) with HIIT compared to MICT (18). An increase in VO_2 max was also reported by a 2024 systematic review for both men (g = 0.57) and women (g = 0.57) after HIIT (19).

In summary, physiologic mechanisms of the benefits of HIIT involve whole system adaptations (metabolic, mitochondrial & cardiovascular systems). All these adaptations help to establish HIIT as a powerful exercise approach in the field of obesity management and enhancement of metabolic health.

3. PHYSIOLOGICAL BASIS OF 5:2 INTERMITTENT FASTING

The 5:2 IF approach involves eating as much as you want on 5 days a week and on 2 days, not every two days, a week you will consume about 500-600 Kcal to complete the fast (6). In this way, intermittent and not prolonged energy deficit is achieved, thus resulting in calories deficit over the week (20).
The induction of a metabolic switch, changing from glucose oxidation to ketone oxidation is a process that is a key physiological change present in the central manner (21). On a fasting day, glycogen levels in the liver decrease allowing for more fatty acid oxidation or ketone body production in the liver (22). Measurable ketosis can occur with short-term IF and generally, reduced carbohydrate consumption increases ketosis levels during brief periods (6). Many of the purported benefits of IF have been proposed to stem from this metabolic switch, such as improved metabolic flexibility (21).
Another critical hormonal axis is also involved: hormonal adaptations. By comparison, fasting leads to a fall in the level of plasma insulin and an increase in the glucagon: insulin ratio which promotes lipolysis in white adipose tissue (22). Secretion of growth hormone is significantly stimulated (up to fivefold) which can help in fat oxidation and seems to be beneficial for preserving muscle (22). Additionally, when it comes to hunger regulation, some hormones are under the command of IF such as leptin and adiponectin (21).
Human studies have also more recently helped to clarify the physiology. The 5:2 diet has been found to have a beneficial impact on levels of LDL cholesterol, and a recent review (2025) offered high-quality evidence for this (23). An RCT in the year 2025 showed that the glycemic control and anthropometric indices were improved in pre-diabetic patients (24). In the study published in 2024, weight loss, fat mass loss, 90% reduction in hepatic steatosis and diminished inflammatory biomarkers were associated with metabolic-associated fatty liver disease (MAFLD) (25). Another narrative review suggests that IF can be used safely and effectively for weight loss and that the advantages, although similar, are just as effective as a continuous calorie restriction (7).
Overall, the 5:2 IF method works by triggering metabolic switching, inducing hormonal changes that make fat burning more efficient, and via thermogenic effects. The amount of evidence has increased, but exactly how each of these mechanisms contributes to the effects of IF—and if there are any effects beyond the caloric deficit—are still being investigated.

4. COMBINED EFFECTS ON WEIGHT LOSS

Based on the available evidence presented in the RCTs, systematic reviews and meta-analyses, there is some beneficial evidence regarding the use of HIIT combined with 5:2 IF, but not all of the studies could be regarded as conclusive.
The most relevant evidence was provided by the 8-week RCT by Batitucci et al. (2022) with 36 women suffering from obesity who were randomized to either 5:2 IF + HIIT or HIIT alone or 5:2 IF alone (26). HIIT consisted of three sessions weekly for 25 min/session with exercises performed at 70–85% of the individual's maximal heart rate. Only IF+ HIIT showed significant results with regards to body weight ($P = 0.012$) and BMI ($P = 0.031$) when compared with other groups, while there was no significant difference between the HIIT alone and IF alone groups (26). This indicates that treatment could be required for 8 weeks to show clinically significant weight loss, and may need to be used together.
Guo et al. carried out a systematic review and meta-analysis in 2022 of nine RCTs included in which body mass and waist circumference were assessed in 230 participants using HIIT intervention plus fasting applied with and without other combinations of fasting and exercise, yielding better results with HIIT plus fasting when compared to control conditions (9). The level of certainty that these conclusions can be drawn from the evidence, however (GRADE certainty of evidence), was very low (9). A meta-analysis by Khalafi et al. that was conducted in 2025 showed that there was a weighted mean difference (WMD) of −3.03 kg (95% CI: −3.44 to −2.61) in favour of exercise plus IF for body weight reduction and a similar WMD of −2.63 cm (95% CI: −4.16 to −1.11) for waist circumference compared with exercise alone (8). Likewise, a review published in 2025 showed that when exercise was added to IF, it led to greater fat mass amount (−0.93 kg) and waist circumference (−2.51 cm) reduction than IF alone (27).
Yet some studies don't reaffirm that the combined interventions are better. A 2022 analysis, which utilized IF along with sprint interval training (SIT), revealed that IF and IF/SIT both very effectively reduced body weight, body fat, and abdominal fat levels—versus SIT alone—and had no noticeable distinction between groups (28). The authors found that "energy restriction is the prime factor to enhancing body composition" (28). The differing results are possible because of differences in volume of HIITs/SITs interventions, length of the interventions and fasting protocols.
On the whole, the evidence collected right now suggests that pairing HIIT and 5:2 IF may help you lose extra weight more efficiently than one or the other intervention alone, but the potential benefit may not be that significant.

5. EFFECTS ON BODY COMPOSITION

Measures of body composition such as fat mass (FM), visceral adipose tissue (VAT) and fat-free mass (FFM) are more clinically proposed than body weight.

FAT MASS AND VISCERAL ADIPOSITY

A meta-analysis of Guo and others (2022) found significant decreases in FM from HIIT + fasting as compared to control (9)]. A larger multilevel meta-analysis by Jiao et al. (2026) included 65 RCTs with 3293 participants and showed similar findings, which is that body fat percent, FM, WC and visceral fat decreased significantly with a combination of exercise and IF (29). Of particular interest, there was no significant difference in EX + IF on FFM or lean body mass, which has significant implication for preserving muscle (29).

The effects on the visceral adiposity are of special interest. In 2022, a RCT study compared IF and IF/SIT with SIT, and showed that both IF and IF/SIT groups had a reduction of vs.fat, which has been seen to be more than just in SIT group (28). This indicates that not only is IF a powerful tool for visceral adiposity reduction, but that there is a small, additional, and synergistic advantage to be obtained from combining exercise to IF.

LEAN BODY MASS AND SKELETAL MUSCLE PRESERVATION

There is conflicting evidence for the use of FFM. A +3.3% increase in FFM with the IF + HIIT group, versus a +2% increase in FFM with the HIIT alone group ($p < 0.001$), was reported in the Batitucci et al. (2022) RCT, whereas the IF alone group was not significant (26). This refutes the notion that energy restriction necessarily results in reductions of lean mass. However, no significant difference in FFM was found with the HIIT + fasting versus control groups based on the meta-analysis of Guo et al., 2022 [9]. Likewise, Jiao et al. (2026) conducted a meta-analysis on this and did not observe significant changes in FFM (29). The null responses may be due to variation in the HIIT protocols; HIITs with higher volume may be required to induce accretion of FFM.

SEX-SPECIFIC FINDINGS

There is increasing evidence that there is a sex dimorphism in response. Results from a systematic review published in 2023 revealed that BMI, body weight and body fat was more reduced in males than females after IF (30). Sex specific analyses however, are limited with regards to IF combined with HIIT and most studies are not sufficiently powered to reveal sex differences (27).

Overall, a combination of HIIT and 5:2 IF is consistently effective for the reduction of FM and VAT, IF seemingly being the greater contributor of fat loss. It is not clear what impact it will have on FFM, probably due to heterogeneity in HIIT protocols used.

6. EFFECTS ON PHYSICAL FITNESS

Based on the results of the Guo et al 2022 meta-analysis [9], HIIT during fasting showed a significant effect on VO_2 peak, when compared with the control conditions. The improvement seems to be mostly due to the exercise aspect—fasting without exercise doesn't really significantly improve aerobic capacity. Batitucci et al. (2022) conducted an RCT and found that all parameters of aerobic capacity and strength were enhanced in the IF + HIIT group (26). A narrative review found no detrimental effect of IF on adaptation to exercise training and it might be beneficial for cardiopulmonary measures (7).

MUSCULAR STRENGTH, ENDURANCE, AND FUNCTIONAL PERFORMANCE

The Batitucci et al. 2022 study found that IF and HIIT was successful in enhancing physical fitness and strength (26). In 2021 a crossover trial was conducted with active females to investigate the effects of HIIT with and without IF. This fat loss combined with an increase in counter-movement jump height by 6.2 cm ($p < 0.001$, $d = 1.8$) (31) was also observed in the HIIT + IF group. The difference in the change of CMJ height between HIIT + IF and HIIT alone was larger (5.2 cm) (31). In a pilot study, there was observed an increase in body composition and physical performance in postmenopausal women as a result of IF combined with HIIT (32).

EXERCISE ADHERENCE

The extent of adherence is an important influence on the effectiveness in the real world. Studies indicate that intermittent fasting diets have a high level of compliance in the short- to medium-term (33)]. Adherence is not completely consistent though; one study in MS found that adherence to calorie reduction regimens was in general suboptimal (34).

Overall, HIIT plus 5:2 IF drastically enhances CRF and certain aspects of MP, without compromising exercise training adaptation.

Table 2. Summary of Effects of High-Intensity Interval Training and 5:2 Intermittent Fasting on Weight Loss, Body Composition, and Physical Fitness

Outcome	HIIT Effect	5:2 IF Effect	Combined Effect	Overall Evidence Strength
Body weight	Modest reduction; may not achieve statistical significance in isolation	Reduction; typically 3–8% weight loss over 6–12 weeks	Superior to either alone (WMD: −3.03 kg vs. exercise alone). Statistically significant reductions observed only in combined group in some RCTs (8,26)	Low to moderate
BMI	Modest reduction	Reduction	Significant reduction only in combined group in some RCTs (P = 0.031) (26)	Low
Fat mass	Reduction (−2.3%, P = 0.043 (26)	Reduction	Greater reduction than IF alone (−0.93 kg; 95% CI: −1.69 to −0.18) (27). IF+EX: −4% (P < 0.001); HIIT alone: −2.3% (P = 0.043) (26)	Low to moderate
Visceral adiposity	Reduction when combined with IF	Reduction; primary driver of visceral fat loss	Significant reduction; IF appears to be main driver, with exercise providing modest additive benefit (28)	Low
Lean body mass	Increase (+2%, P = 0.043) (26)	No significant change	Increase (+3.3%, P < 0.001) in some studies (26); no significant difference in meta-analyses (9,29)	Low
VO_2max / Cardiorespiratory fitness	Significant improvement	No significant improvement	Significant improvement vs. control (9). Additional improvement vs. IF alone: +1.92 ml/kg/min (8)	Low to moderate
Insulin sensitivity	Improvement; reduces fasting insulin and HOMA-IR (14)	Improvement; primary driver of glycaemic control (24)	Greater improvement vs. IF alone (8)	Low to moderate
Cardiovascular fitness	Significant improvement	No significant improvement	Significant improvement; driven primarily by HIIT component (9)	Low to moderate
Exercise adherence	Generally acceptable in short-term studies (33)	High compliance reported in short-to-medium term (33)	Feasible in motivated populations; long-term adherence data lacking (34)	Low

7. POTENTIAL MECHANISMS UNDERLYING SYNERGISTIC EFFECTS

HIIT and the 5:2 IF could have synergistic effects via several overlapping, molecular pathways (Figure 1). While the precise mechanisms remain incompletely elucidated, emerging evidence points to coordinated regulation of energy sensing, mitochondrial biogenesis, substrate metabolism, and inflammatory signalling.

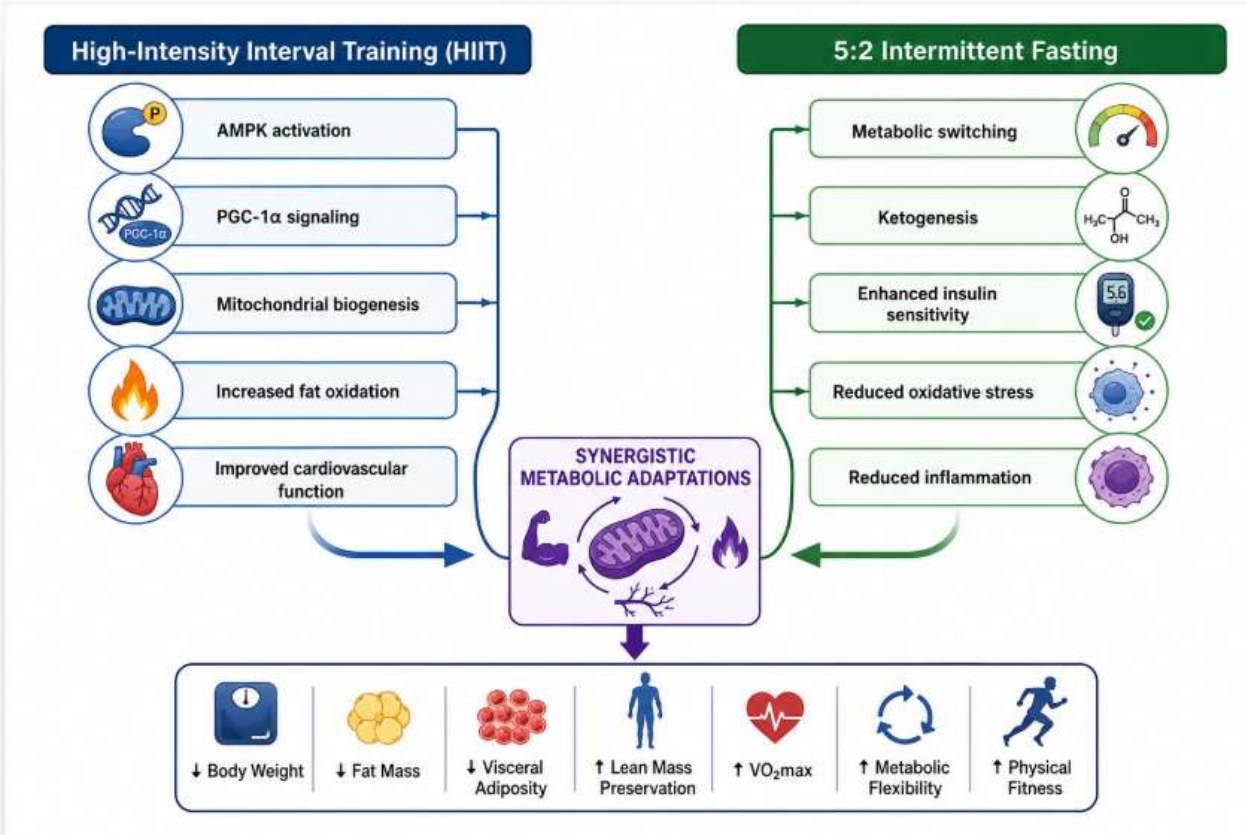

Figure 1: Proposed synergistic mechanisms of high-intensity interval training (HIIT) and 5:2 intermittent fasting (IF).

The graphical abstract illustrates the complementary molecular and physiological mechanisms through which HIIT and 5:2 intermittent fasting may improve metabolic health. HIIT activates AMP-activated protein kinase (AMPK) and peroxisome proliferator-activated receptor gamma coactivator-1 alpha (PGC-1α), promoting mitochondrial biogenesis, enhanced fat oxidation, and improved cardiovascular function. Concurrently, 5:2 intermittent fasting induces metabolic switching and ketogenesis while enhancing insulin sensitivity and reducing oxidative stress and systemic inflammation. The convergence of these adaptive pathways may produce synergistic metabolic adaptations, resulting in reductions in body weight, fat mass, and visceral adiposity, alongside preservation of lean mass, improved maximal oxygen uptake (VO_2max), enhanced metabolic flexibility, and better overall physical fitness.

ABBREVIATIONS: HIIT, High-Intensity Interval Training; IF, Intermittent Fasting; AMPK, AMP-Activated Protein Kinase; PGC-1α, Peroxisome Proliferator-Activated Receptor Gamma Coactivator-1 Alpha; VO_2max, maximal oxygen uptake.

AMPK ACTIVATION

AMPK acts as a sensor of cellular energy, is activated by a rise in the AMP/ATP ratio in energy stress (35) AMPK is activated independently by both IF and HIIT, in different ways but both complement each other. Both prolonged fasting and HIIT can favour the activation of AMPK: Prolonged fasting does it by lowering the energy stores of the cell and HIIT does it with an intense muscular contraction (35). Preclinical studies show that, following caloric restriction, HIIT activates AMPK (36), but after IF + HIIT there is an increase in AMPK gene expression over IF alone (37).

PGC-1A SIGNALLING AND MITOCHONDRIAL BIOGENESIS

PGC-1α is known as a master regulator of mitochondrial biogenesis (38). Only a few minutes of HIIT are enough to induce powerful activation of PGC-1α in human skeletal muscle (38). But, it has been found that IF alone can decrease

the expression of the gene, PGC-1α (39). The leaves of IF and HIIT combined could thus be counterbalanced by the PGC-1α upregulation, as a consequence of the HIIT.

METABOLIC FLEXIBILITY AND SUBSTRATE OXIDATION

Both IF and HIIT improve metabolic flexibility—when a body can easily shift back and forth between using carbohydrates and fat to fuel exercise [21]. Preclinical studies indicate that there is a synergistic effect of combining IF and HIET, with fat levels being prevented from accumulation and better physical performance (40). The mixing resulted in not only a rise in glucose uptake, but also a decrease in the levels of serum insulin and activation of enzymes in the mitochondria (40).

INSULIN SENSITIVITY AND INFLAMMATION

So, both types of fitness training, IF and HIIT, have similarly beneficial effects on insulin sensitivity. Thus, IF reduces insulin action, lowers risk of glucose production and HIIT increases GLUT4 expression and insulin action in skeletal muscle (35). Insulin sensitivity in peripheral tissues is achieved with caloric restriction and HIIT (36).The fasting cells get into autophagy and lower inflammation markers on the cellular level (41).
Overall, the potential for synergy seems to be achieved by promoting coordinated activation of AMPK, complementary regulation of PGC-1α-mediated mitochondrial biogenesis, optimization of metabolic flexibility and improvement of insulin sensitivity. But, mechanistic studies of man are done to a limited extent.

8. CURRENT EVIDENCE, LIMITATIONS, AND FUTURE DIRECTIONS

The evidence base has grown and there are a number of methodological restrictions that limit the extent to which evidence can be interpreted.

SAMPLE SIZE AND STATISTICAL POWER

An endemic constraint is using small sample sizes. The Batitucci et al. 2022 RCT was extremely small – it involved only 36 participants (26). Kandun, et al. (2022) reviewed and combined the results of nine RCTs across their meta-analysis, involving 230 participants (9). In a 2024 systematic review, most articles that they included were small, with fewer than 50 participants in each group [8]. The smaller the samples, the greater will be the possibility of a Type II error.

SHORT INTERVENTION DURATIONS

The majority of the intervention studies reviewed are brief (ranging from 4- to 12-weeks) (9,26,27) Beyond 12 weeks and especially beyond 6 months, the power of the combined HIIT and 5:2 IF are essentially uncharted (27).

HETEROGENEITY IN PROTOCOLS

There is high heterogeneity when it comes to the different types of fast (5:2 IF, alternate day fasting, time-restricted eating) and exercise (time interval training (TIT), high-intensity interval training (HIIT), varying frequency, intensity, duration) (9,27). This makes it difficult to compare with one another and synthesize with a meta-analysis.

SEX DIFFERENCES AND POPULATION DIVERSITY

There is skewed representation in literature who participated in this activity are mostly females (9,27). In a 2025 systematic review, it was noted that 87.3% of the participants were female (27). The generalizability to men, older people and to those with co-morbidities is still not known (30).

ADHERENCE AND LONG-TERM FEASIBILITY

Accurate adherence is difficult to determine and sometimes self-reported (34). Long-term adherence to the treatment has not been studied (34) and short-term adherence seems reasonable (34).

RECOMMENDATIONS FOR FUTURE RESEARCH

Future studies should include: (1) sufficiently large RCTs; (2) interventions lasting 6-12 months; (3) protocols for both 5:2 IF and HIIT which are standardized; (4) population diversity; (5) objective evaluation of dietary adherence and exercise compliance to both protocols; (6) mechanistic studies; and (7) pragmatic implementation trials. Lacking these gaps will be key to take initial evidence to recommendations on clinical practice.

9. CONCLUSION

This Critical Review on the effects of combined HIIT and 5:2 IF on weight loss, body composition and physical fitness was purposefully written to explore the existing evidence in these areas. We draw a number of important inferences from these.

First, the combination results in larger amounts of weight loss (WMD: −3.03 kg) than either type of intervention alone does (WMD: −2.07 kg and −0.95 kg (8,9,27,33–36)). This improvement, though small, is clinically significant as any additional 3-5% weight loss has a positive impact on the cardio-metabolic risk factors (27).

Secondly, the blend has a positive effect on body composition. The significance of this seems to lie in the fact that, compared with HIIT, IF is apparently more important for fat loss (especially visceral fat) and HIIT can help to reverse lean mass loss common with diets (26,29) A meta-analyses, however, has not always substantiated this FFM effect, probably due to differences in the protocol of the HIIT (9,27).

Thirdly, there is enhanced cardiorespiratory fitness (VO_2 peak) together with this combined HIIT and 5:2 IF has no adverse effects on selected parameters of muscular performance while being compared to the adaptation to conventional exercise training (9,26, 31).

Finally, there may be synergistic effects which involve coordinated activation of AMPK, stimulation of mitochondrial biogenesis via PGC-1α, increased metabolic flexibility, and insulin sensitivity (35,38,40). But only a few studies have so far investigated their mechanism in humans.

Fifth, there is a lack of evidence that is influenced by the low number of participants (n = 1–100, below average) in RCTs, limited intervention duration (ranging from 1–12 weeks), protocol diversity, and a scarcity of men and diverse groups (some underrepresented) in RCTs, as well as by the low GRADE certainty of the evidence (9,26.27).

In conclusion, HIIT alongside 5:2 IF seems to be successful, safe as well as feasible strategy to improve body composition, weight burning and physical fitness in ladies of the weight of obesity. It is however; rapidly needed to be followed with larger and longer term RCTs with standardized protocols and different groups to definitively recommend clinical use.

REFERENCES

1. Jeemon P, Sivasubramonian S. The silent surge: obesity driving a global cardiovascular crisis. Global Heart. 2025;20(1):77.
2. Liu J, Fang Z, Lu Q, Wang Y, Zhang L. Projecting Global Trends and Inequalities in Adult Overweight and Obesity, 2023–2040: Findings From the NCD-RisC Database. Obesity. 2025;33(10):1955–67.
3. Organization WH. Health at a Glance: Asia/Pacific 2024. Health at a Glance: Asia/Pacific. 2024;2024.
4. Poon ET-C, Li H-Y, Little JP, Wong SH-S, Ho RS-T. Efficacy of interval training in improving body composition and adiposity in apparently healthy adults: an umbrella review with meta-analysis. Sports Medicine. 2024;54(11):2817–40.
5. Feng J, Zhang Q, Chen B, Chen J, Wang W, Hu Y, et al. Effects of high-intensity intermittent exercise on glucose and lipid metabolism in type 2 diabetes patients: a systematic review and meta-analysis. Frontiers in endocrinology. 2024;15:1360998.
6. Abou Chaaya J, El Jalbout JD, Nasrallah MP. Effect of intermittent fasting versus continuous caloric restriction on body weight and metabolic parameters in adults with overweight or obesity: A narrative review. Journal of Diabetes and Endocrine Practice. 2023;6(03):118–25.
7. Gabel K, Hamm A, Czyzewski O, Perez JS, Fought-Boudaia A, Motl RW, et al. A narrative review of intermittent fasting with exercise. Journal of the Academy of Nutrition and Dietetics. 2025;125(2):153–71.
8. Khalafi M, Symonds ME, Maleki AH, Sakhaei MH, Ehsanifar M, Rosenkranz SK. Combined versus independent effects of exercise training and intermittent fasting on body composition and cardiometabolic health in adults: a systematic review and meta-analysis. Nutrition journal. 2024;23(1):7.
9. Guo Z, Cai J, Wu Z, Gong W. Effect of high-intensity interval training combined with fasting in the treatment of overweight and obese adults: A systematic review and meta-analysis. International journal of environmental research and public health. 2022;19(8):4638.
10. Poon ETC, Li HY, Gibala MJ, Wong SHS, Ho RST. High-intensity interval training and cardiorespiratory fitness in adults: An umbrella review of systematic reviews and meta-analyses. Scandinavian Journal of Medicine & Science in Sports. 2024;34(5):e14652.
11. Racinais S, Perrey S. Energy Production Pathways During Exercise. IOC Manual of Sports Cardiology. 2016:21–31.
12. Marques de Sá e Silva D, Avgerinou G, Petridou A, Theodoridis G, Mougios V, Gika H. Metabolomic signatures of high-intensity and sprint interval exercise/training in humans: a systematic review. Metabolomics. 2026;22(2):25.

13. Yin M, Chen Z, Nassis GP, Liu H, Li H, Deng J, et al. Chronic high-intensity interval training and moderate-intensity continuous training are both effective in increasing maximum fat oxidation during exercise in overweight and obese adults: A meta-analysis. Journal of Exercise Science & Fitness. 2023;21(4):354–65.
14. Al-Mhanna SB, Poon ET-C, Franklin BA, Tarnopolsky MA, Hawley JA, Jakicic JM, et al. Comparative effectiveness of high-intensity interval training and moderate-intensity continuous training on cardiometabolic health in patients with diabesity: a systematic review and meta-analysis of randomized controlled trials. Diabetology & Metabolic Syndrome. 2025;17(1):331.
15. Heiat F, Shojaei Fard M. Effects of High-Intensity Interval Training and Moderate-Intensity Continuous Training on PGC-1α, SIRT3, and Non-Alcoholic Fatty Liver Disease: A Narrative Review. Journal of Advanced Biomedical Sciences. 2026;16(1):3–16.
16. Hadjispyrou S, Dinas PC, Delitheos SM, Koumprentziotis I-A, Chryssanthopoulos C, Philippou A. The effect of high-intensity interval training on mitochondrial-associated indices in overweight and obese adults: a systematic review and meta-analysis. Frontiers in Bioscience-Landmark. 2023;28(11):281.
17. Li L, Pa Wamw, Anuar Nab. Skeletal Muscle Transcriptional And Regulatory Signaling Adaptations To High-Intensity Interval Training Versus Moderate-Intensity Continuous Training: A Systematic Review. Genetics And Molecular Research. 2026.
18. Yu H, Zhao X, Wu X, Yang J, Wang J, Hou L. High-Intensity Interval Training Versus Moderate-Intensity continuous training on patient quality of life in cardiovascular disease: A systematic review and meta-analysis. Scientific Reports. 2023;13(1):13915.
19. Lock M, Yousef I, McFadden B, Mansoor H, Townsend N. Cardiorespiratory fitness and performance adaptations to high-intensity interval training: are there differences between men and women? A systematic review with meta-analyses. Sports Medicine. 2024;54(1):127–67.
20. Diaz-Garrido N, Zagmutt S, Regaldiz A, Cisternas P, Bastías-Pérez M. Intermittent Fasting: A Metabolically Focused Therapeutic Strategy for Obesity. Nutrients. 2026;18(3):371.
21. Samkari J. Intermittent fasting: a comprehensive review of cellular mechanisms, metabolic processes, and organ health. Journal of Umm Al-Qura University for Medical Science. 2025;11(1):7.
22. Batitucci G, Almeida OG, De Martinis EC, Solar I, Cintra DE, de Freitas EC. Intermittent fasting and high-intensity interval training do not alter gut microbiota composition in adult women with obesity. American Journal of Physiology-Endocrinology and Metabolism. 2024;327(3):E241–E57.
23. Hua Z, Yang S, Li J, Sun Y, Liao Y, Song S, et al. Intermittent fasting for weight management and metabolic health: an updated comprehensive umbrella review of health outcomes. Diabetes, Obesity and Metabolism. 2025;27(2):920–32.
24. Pasdar Y, Saber A, Rezvani N, Bozorgi S, Moradi S, Cheshmeh S, et al. Effect of intermittent fasting, portfolio-moderate-carbohydrate, and anti-inflammatory diets on cardio-metabolic status in pre-diabetic patients; an open-label randomized clinical trial. Diabetology & Metabolic Syndrome. 2025;17(1):319.
25. Wang Y-y, Tian F, Qian X-l, Ying H-m, Zhou Z-f. Effect of 5: 2 intermittent fasting diet versus daily calorie restriction eating on metabolic-associated fatty liver disease—a randomized controlled trial. Frontiers in nutrition. 2024;11:1439473.
26. Batitucci G, Faria Junior EV, Nogueira JE, Brandão CF, Abud GF, Ortiz GU, et al. Impact of intermittent fasting combined with high-intensity interval training on body composition, metabolic biomarkers, and physical fitness in women with obesity. Frontiers in nutrition. 2022;9:884305.
27. Dai Z-h, Wan K-w, Wong P-s, Huang WY, Yu AP-h, Wong SH-s. Additional effect of exercise to intermittent fasting on body composition and cardiometabolic health in adults with overweight/obesity: a systematic review and Meta-analysis. Current Obesity Reports. 2025;14(1):54.
28. Cooke MB, Deasy W, Ritenis EJ, Wilson RA, Stathis CG. Effects of intermittent energy restriction alone and in combination with sprint interval training on body composition and cardiometabolic biomarkers in individuals with overweight and obesity. International journal of environmental research and public health. 2022;19(13):7969.
29. Jiao M, Yan H, Zhang B, Zhao X, Li J, Harun MT. Optimal dosage of exercise combined with intermittent fasting for body composition and cardiometabolic health in adults: a systematic review and multilevel meta-analysis. Frontiers in Nutrition. 2026;13:1772836.
30. Abdelrahim DN, Roky R, Krami AM, Aadil N, Faris ME. Sex as a biological determinant in anthropometric, biochemical, and dietary changes during Ramadan intermittent fasting in healthy people: A systematic review. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2023;17(5):102762.
31. Martínez-Rodríguez A, Rubio-Arias JA, García-De Frutos JM, Vicente-Martínez M, Gunnarsson TP. Effect of high-intensity interval training and intermittent fasting on body composition and physical performance in active women. International journal of environmental research and public health. 2021;18(12):6431.

32. Valenzano AA, Vasco P, D'Orsi G, Marzovillo RR, Torquato M, Messina G, et al. Influence of intermittent fasting on body composition, physical performance, and the orexinergic system in postmenopausal women: a pilot study. Nutrients. 2025;17(7):1121.
33. Keenan S, Cooke MB, Chen WS, Wu S, Belski R. The effects of intermittent fasting and continuous energy restriction with exercise on cardiometabolic biomarkers, dietary compliance, and perceived hunger and mood: secondary outcomes of a randomised, controlled trial. Nutrients. 2022;14(15):3071.
34. Xiang Q, Li W, Li Y, Chai X, Ma Y, Yan Z. Single-arm prospective pilot of a 5: 2 intermittent fasting regimen supported by meal replacement and digital coaching in adults with obesity. Clinical Nutrition ESPEN. 2026:103102.
35. Eid SA, Elzinga SE, Kim B, Rumora AE, Hayes JM, Carter A, et al. High-intensity interval training, caloric restriction, or their combination have beneficial effects on metabolically acquired peripheral neuropathy. Diabetes. 2024;73(11):1895–907.
36. Cooke MB, Wilson R, Hayes A, Stathis CG. Effects Of Intermittent Fasting And High Intensity Training On Regulators Of Muscle Mass And Metabolism: 1213 May 30 10: 10 AM-10: 20 AM. Medicine & Science in Sports & Exercise. 2019;51(6S):319–.
37. Valenzano AA, Vasco P, D'Orsi G, Marzovillo RRR, Torquato M, Messina G, et al. Influence of Intermittent Fasting on Body Composition, Physical Performance, and the Orexinergic System in Postmenopausal Women: A Pilot Study. Nutrients. 2025;17(7):1121.
38. Menezes E, Islam H, Arhen B, Wu Z, Pacitti L, Lyrae Silva N, et al. Regulation of PERM1 and select target genes in human skeletal muscle following fasting and exercise. Appl Physiol Nutr Metab. 2026;51:1–15.
39. Menezes ES, Islam H, Arhen BB, Simpson CA, McGlory C, Gurd BJ. Impact of exercise and fasting on mitochondrial regulators in human muscle. Transl Exerc Biomed. 2024;1(3-4):183–94.
40. Real-Hohn A, Navegantes C, Ramos K, Ramos-Filho D, Cahuê F, Galina A, et al. The synergism of high-intensity intermittent exercise and every-other-day intermittent fasting regimen on energy metabolism adaptations includes hexokinase activity and mitochondrial efficiency. PLoS One. 2018;13(12):e0202784.
41. Conde-Pipó J, Mora-Fernandez A, Martinez-Bebia M, Gimenez-Blasi N, Lopez-Moro A, Latorre JA, et al. Intermittent Fasting: Does It Affect Sports Performance? A Systematic Review. Nutrients. 2024;16(1).
42. Li M, Li J, Xu Y, Gao J, Cao Q, Ding Y, Xin Z, Lu M, Li X, Song H, Shen J. Effect of 5: 2 regimens: energy-restricted diet or low-volume high-intensity interval training combined with resistance exercise on glycemic control and cardiometabolic health in adults with overweight/obesity and type 2 diabetes: a three-arm randomized controlled trial. Diabetes Care. 2024 Jun 1;47(6):1074-83.