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A narrative review of intermittent fasting with exercise

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RESEARCH SNAPSHOT

Research question: How does the combination of exercise and intermittent fasting affect body weight, body composition, cardiometabolic risk factors, and physical fitness?

Key Findings: When combined with different modalities of exercise, intermittent fasting can reduce body weight and fat mass while eliciting training adaptations. Evidence is equivocal regarding the impact on lean mass and cardiometabolic markers, and there is a need for longer and better-powered interventions in this area. Combining intermittent fasting with exercise may provide an accessible, low burden alternative to traditional caloric restriction. Future trials should prioritize recruitment of well-powered samples comprising both males and females, a broad range of ages, and those at risk for cardiometabolic disease.

ABSTRACT

Intermittent fasting is a dietary pattern that encompasses the 5:2 diet, alternate day fasting (ADF), and time restricted eating (TRE). All three involve alternating periods of fasting and ad libitum eating. Like other dietary strategies, intermittent fasting typically induces loss of both fat mass and lean mass. Exercise may thus be a useful adjuvant to promote lean mass retention while adding cardiometabolic, cognitive, mental, and emotional health improvements. In this narrative review, we summarize current evidence regarding the combination of intermittent fasting and exercise and its impacts on body weight, body composition, cardiometabolic risk, and muscular and cardiorespiratory fitness. A PubMed search was conducted to identify all trials lasting >4 weeks that combined 5:2, ADF, or TRE with any modality exercise and had body weight as an endpoint. A total of 23 trials (26 publications) were identified. Evidence suggests that combining intermittent fasting with exercise leads to decreased fat mass regardless of weight

status. However, evidence is equivocal for the impact on other aspects of weight loss and body composition, fat free mass and cardiometabolic risk factors and may be dependent on weight status or exercise dosages (i.e., frequency, intensity, duration, and modality). Higher-powered trials are needed to determine the efficacy of combining exercise and intermittent fasting for benefits on bodyweight and cardiometabolic risk. Current evidence suggests that intermittent fasting does not impair adaptation to exercise training, and may improve explosive strength, endurance, and cardiopulmonary measures such as maximal oxygen consumption. Additionally, we discuss limitations in the current evidence base, and opportunities for continued investigation. Future trials in this area should consider interventions that have 1) increase sample size, 2) longer intervention duration, 3) broadened inclusion criteria, 4) objective measures of diet and exercise adherence, and 5) diversity of sample population.

INTRODUCTION

Obesity and overweight continues to be a significant issue in the United States (U.S.) with 30% of Americans having overweight, 40% having obesity, and almost 10% having severe obesity.[1] While the use of anti-obesity drugs has increased, dietary behavioral interventions remain necessary for overall health, increased efficacy of pharmacological treatment, and weight loss maintenance. Intermittent fasting, a dietary behavioral intervention for weight management, has increased in popularity in the last two decades due to the ease of implementation and less stringent food restriction requirements than traditional caloric restriction (CR). Three main forms of intermittent fasting have emerged, namely, the 5:2 diet, alternate day fasting (ADF), and time-restricted eating (TRE). Each form alternates "feast" periods (ad libitum intake) with "fast" periods (calorie abstention), yet in different ways. The 5:2 diet consists of 2 consecutive or non-consecutive "fast days" of 0-500kcal (or up to 25% of energy needs) each week with the remaining five days as "feast days". Similarly, ADF consists of eating 0-500kcal (or up to 25% of energy needs) on the "fast day" but this is alternated every other day throughout the week with ad libitum eating on the "feast day". TRE consists of ad libitum eating during a 6- to 10-hour daily window, while fasting the remaining 14-18 hours. Prior research suggests that the 5:2 diet and ADF may be as efficacious as traditional CR for weight loss,[2,3] with 6-12 weeks of either approach resulting in weight loss of 3-8% and decreases in blood pressure, insulin resistance, and other cardiometabolic markers.[4] Evidence is less conclusive for TRE, but 8-12 weeks appears to result in a calorie deficit of 20-40% and weight loss of 2-4% with uncertain effects on cardiometabolic outcomes.[5]

Recently, interest has grown in the combined effects of intermittent fasting and exercise. Exercise, planned physical activity, is a key determinant of energy balance and may therefore result in an augmented effect on body weight while also contributing to improvements in serum lipids, blood pressure, fasting glucose. The current Physical Activity Guidelines for Americans call for 150-300 minutes of moderate-intensity aerobic activity per week and two days of muscle strengthening activities weekly for disease prevention, health promotion, and weight loss. However, 55% of Americans don't meet these recommendations,[6,7] which compounds the cardiovascular and cardiometabolic impact of overweight and obesity. Furthermore, as exercise is a key regulator of lean mass, the addition of exercise to a dietary regimens such as intermittent fasting may help to mitigate lean mass loss typically experienced when undertaking energy restricted diets.[8,9] This is critical to pursue because lean mass (especially skeletal muscle) plays a central role in regulating basal metabolism and peripheral glucose uptake.[6,10,11] These benefits underscore the potential benefits of combining exercise with intermittent fasting, but to date there has been limited synthesis of evidence from studies examining the joint effects of intermittent fasting and exercise on weight loss and related health markers.

The purpose of this narrative review is to summarize the current literature examining the effects of intermittent fasting (5:2, ADF, and TRE) combined with various modalities of exercise on body weight and body composition, cardiometabolic risk, glucoregulatory factors, and muscular and cardiorespiratory fitness.

METHODS

This is a narrative review and as such was not registered. A PubMed search was conducted using the following key words or MeSH terms: "humans", "fasting", “time restricted eating”, “alternate day fasting”, “alternate day modified fasting”, "intermittent fasting", "fasting", "intermittent energy restriction", “exercise”, “exercise therapy”, "resistance training", "resistance exercise", "strength training", “aerobic exercise”, “exercise”, “aerobic training”, “physical activity”, “endurance exercise”, “weightlifting”, “walking”. The inclusion criteria for research articles were as follows: (1) randomized controlled trials and nonrandomized trials; (2) adult male and female participants (>18 years); (3) endpoints that included changes in body weight; and (4) only studies that included intermittent fasting and exercise combined. The following exclusion criteria were applied: (1) cohort, cross sectional, and observational studies; (2) fasting performed as a religious practice (e.g., Ramadan or Seventh Day Adventist); and (3) trial durations <4 weeks.

RESULTS

It is important to consider the effects of intermittent fasting on body weight and composition since weight loss of $\geq$5% can reduce cardiometabolic risk in individuals with overweight and obesity.[12] Even in individuals without overweight or obesity a caloric deficit combined with exercise can improve longevity, cognition, and physical functioning with age.[13,14] Accordingly, several trials have examined the effects of combining intermittent fasting and various forms of exercise on body weight and composition in individuals with and without obesity. Our search retrieved 7 trials (8 publications)[15-22] on 5:2 combined with exercise, 3 trials (4 publications)[23-26] on ADF combined with exercise, and 13 trials (14 publications) on TRE combined with exercise.[27-39] **Table 1** describes the trial design and intervention characteristics. **Table 2** describes the findings on body weight, body composition cardiometabolic factors, and muscular and cardiorespiratory fitness. **Table 3** describes the heterogeneity between trial participants and adherence monitoring.

5:2

Seven trials (8 publications) have examined the effect of the 5:2 diet combined with exercise.[15-22] One was a randomized control trial,[18] 5 trials (6 publications) were randomized trials without a control,[15-17,19,21,22] and 1 trial was not randomized.[20] One trial included participants with normal weight, overweight, or obesity,[15,22] five trials included participants with overweight or obesity,[17-21] and one trial included participants with obesity only.[16] Exercise interventions included aerobic activity, steps/day, resistance training, high intensity interval training or a combination of modalities.

Batitucci et al.[16] conducted a parallel arm trial examining the 5:2 diet (600kcal fast days), high intensity interval training (HIIT) three days a week, or the 5:2 diet and HIIT combined. Only the combination group decreased body weight significantly (-2%) after the 8-week intervention. Fat mass and waist circumference decreased, and fat free mass increased in both the combination and HIIT groups but remained unchanged in the 5:2 alone group. A group difference was reported between the two exercise groups compared to diet alone at week 8, however, no time by diet effect was reported. Kang et al.[17] compared 5:2 (30% of maintenance calories on fast days), CR alone (30% calorie deficit) and CR plus protein meal replacement (30% calorie deficit) in a parallel arm randomized trial. All participants were instructed to increase their physical activity to 150-300 minutes weekly. The 5:2 diet and the meal replacement groups lost 9% of body weight after 12 weeks, which was significantly more weight loss over time compared to the CR group (-5%, time by diet interaction). Importantly, significantly more participants lost clinically significant (5% and 10%) body weight from baseline in the 5:2 and meal replacement groups than the CR group. Fat mass decreased and fat free mass increased in all three groups with no difference between groups. Hottenrott et al.[18] compared the 5:2 diet to an unrestricted diet group combined with 30–60 min of running and 20 min of resistance training 3-4 days a week throughout the 12-week intervention in healthy individuals with obesity. Additionally, both groups were divided and randomized to ingest an alkaline supplement or placebo. The 5:2 groups lost significantly more body weight and fat mass than the ad libitum groups with or without the alkaline supplement over time (time by diet interaction). Additionally, the 5:2 group combined with the alkaline supplement lost significantly more body weight, fat mass, and visceral fat mass than the 5:2 diet group alone. Keenan et al.[15] compared 5:2 (30% of maintenance calories on fast days) or CR (20% calorie deficit) combined with 2 supervised resistance training sessions and 1 unsupervised aerobic or resistance training session in individuals with normal weight, overweight, or obesity. Body weight (5:2: -5% males, -3% females; CR -7% males, -3% females), and fat mass decreased significantly, and fat free mass significantly increased in both IF and CR groups after 12 weeks. No time by diet interaction was reported for body weight or composition; however, time by sex interactions were reported with males losing more weight than females and females gaining more lean mass than males. The increase in lean mass in the females may account for the difference in weight loss between the sexes. Additionally, the CR group increased muscle surface area significantly more than the 5:2 group over time (time by diet interaction). Cooke et al.[21] examined 5:2, sprint interval training sessions 3 times a week, or a combination of 5:2 and sprint interval training for 16 weeks in individuals with overweight or obesity. Body weight and fat mass decreased significantly more over time in the 5:2 alone or combination group (data not provided) than sprint training alone (time by diet interaction). At 8 weeks both 5:2 groups lost lean body mass compared to the sprint group alone, however this was not significant at week 16. Waist circumference decreased in all three groups after 16 weeks. Headland et al.[19] compared the 5:2 diet (500kcal for females and 600kcal for males on fast days) to a week-on week-off diet (1000kcal/d for females and 1200kcal/d for males) or CR (30% calorie deficit) in individuals with overweight and obesity. Participants were advised to increase their steps to 10,000 per day. After 52 weeks, all groups decreased lean mass and fat mass from baseline, resulting in 6-7% mean body weight reduction in each group with no time by diet interaction. Jospe et al.[20] compared the 5:2 diet, a Mediterranean diet (mostly plant based foods with mono and polyunsaturated fats), and paleolithic diet (restriction of grains, legumes, and dairy) in individuals with overweight or obesity in a non-randomized parallel-arm trial. Participants were able to choose their diet arm and one of two exercise interventions, 1) 150-300 minutes of aerobic activity plus two days of resistance training (58% of participants) or 2) at home-based HIIT program (42% of participants). All three diet groups reported significant weight loss after 24 weeks. However, only the 5:2 diet and Mediterranean diet groups significantly decreased body weight, fat mass, and visceral fat mass after 52 weeks of the intervention. Lean mass was not reported in this trial, but when considering changes in body fat percentage and mean changes in weight, it appears that both the Mediterranean diet and paleolithic diet retained or gained lean mass compared to a loss in lean mass in the 5:2 group (non-significant). However, these results may be skewed as the 5:2 diet group had more than double the participants of the Mediterranean diet and paleolithic diet groups.

Regarding cardiovascular disease risk, four trials have examined the effect of the 5:2 diet with exercise on fasting lipids, glucose, insulin, and measures of insulin sensitivity or resistance. [15,19-21] Two of the trials also examined the effect on blood pressure.[20,21] Keenan et al.[15] reported a significant decrease in LDL cholesterol and HDL cholesterol from baseline in both the 5:2 and CR groups when combined with resistance training. The 5:2 group decreased LDL cholesterol significantly more than the CR group over time (time by diet interaction). Additionally, females decreased HDL significantly more over time than males (time x sex interaction). No changes were reported for triglycerides, fasting glucose, fasting insulin or insulin resistance via homeostatic model assessment – insulin resistance (HOMA-IR=(fasting plasma insulin/fasting plasma glucose/22.5).[40] Cooke et al.[21] reported a significant decrease in LDL cholesterol over time when combining the 5:2 diet with sprint interval training, whereas no changes were observed in the 5:2 diet alone and sprint interval training alone. HDL cholesterol, triglycerides, blood pressure, fasting insulin, fasting glucose, and HOMA-IR also remained unchanged in all three groups. Headland et al.[19] reported a significant increase in HDL cholesterol and a significant decrease in triglycerides after 52 weeks of 5:2, week on week off, and CR combined with 10,000 steps/day, with no between group differences reported. Fasting glucose remained unchanged. Jospe et al.[20] reported a significant decrease in LDL cholesterol in the

Mediterranean and paleolithic diets combined with exercise, and an increase in HDL cholesterol with 5:2 combined with exercise. Triglycerides remained unchanged in all groups. Systolic and diastolic blood pressure decreased significantly in the Mediterranean and 5:2 diet, whereas only diastolic blood pressure decreased in the Paleolithic diet group after 52 weeks. The Mediterranean diet group significantly lowered their HbA1c over time and this changed resulted in a time by diet interaction.

In regards to muscular strength or cardiorespiratory performance, four studies have examined the effects of 5:2 combined with exercise.[16,18,21,22] Batitucci et al.[16] reported that HIIT alone and 5:2 combined with HIIT improved shuttle walking test, strength (abdominal test, push up test, squat test, 1 repetition maximum leg 45° test, 1 repetition maximum bench press test, dorsal dynamometer, handgrip), observed maximal heart rate, and VO_{2max} after 8 weeks. Keenan et al.[22] reported increased upper and lower body strength (3-repetition maximum and volume test of bench press and leg press) from baseline when combining resistance training with 5:2 or CR. The CR group increased muscle surface area significantly more than the 5:2 group over time (time by diet interaction). Hottenrott et al.[18] reported an increase in maximum running velocity from baseline in the 5:2 group combined with exercise and an alkaline supplement compared to 5:2 combined with exercise and a placebo. No changes were reported in 5:2 alone or the ad libitum groups independent of the alkaline supplement. Lastly, Cooke et al.[21] reported a significant increase in VO_{2peak} with sprint interval training alone and in the combination group compared with 5:2 alone. The combination group increased VO_{2peak} significantly more over time than sprint interval training alone (time by diet interaction).

Summary of findings: Altogether, the results of the above studies suggest that the 5:2 diet combined with exercise appears to produce weight loss of 2-9% and significant decreases in fat mass after 8-52 weeks of the diet these reductions. Additionally, 5:2 appears to produce similar weight and fat mass loss to traditional CR or the Mediterranean diet. It is unclear if the 5:2 diet ameliorates lean mass loss, which may be dependent on the magnitude of caloric deficit and or modality of exercise. However, it does appear that 5:2 combined with exercise improves lipid profile, blood pressure, and insulin sensitivity, although the data are not entirely conclusive. According to the data presented here, diets that affect diet quality, such as the Mediterranean diet, may be more beneficial for glucose regulation and insulin sensitivity. These data suggest that training adaptations are not impaired by the caloric restriction of 5:2 and may improve both strength, running velocity and $V0_{2peak}$.

ADF

Three trials (4 publications) have examined the effect of ADF combined with exercise on body weight and body composition.[23-25] All three trials utilized a randomized controlled factorial design.[23-25] One trial included participants with overweight and obesity,[25,26] whereas the others included only participants with obesity.[23,24] One trial examined resistance and aerobic training[25,26] and the other two examined aerobic activity only.[23,24] Cho et al.[25,26] compared ADF, exercise (resistance and aerobic exercise 3 times a week), and ADF combined with exercise to a control group. However, this search revealed two manuscripts for NCT03652532, with varying results.[25,26] The manuscript from Cho et al[25], analyzed 31 completers. The ADF, exercise, and combination groups all reduced body weight, body fat percentage, and fat mass significantly after 8 weeks of the intervention. A significant time by diet interaction was reported for both ADF and combination groups compared to controls for body weight change and fat mass loss.

Skeletal muscle decreased in the combination group from baseline. Under the same clinicaltrials.gov registration, Oh et al.[26] analyzed 35 completers. Body weight decreased in the ADF and combination groups. Fat mass and fat free mass decreased in the combination group only. Waist circumference decreased significantly from baseline in ADF, combination, and exercise groups. Body fat percentage decreased over time in the ADF group and combination group, with a significant time by diet interaction between the combination and control groups. Bhutani et al.[23] compared ADF, aerobic exercise 3 days a week, and ADF and exercise combined compared to a no intervention control group in individuals with obesity. All three intervention groups lost a significant amount of body weight from baseline (ADF + exercise: -7%, ADF: -3%, Exercise: -1%) and decreased waist circumference after 12 weeks. Participants in the combination group lost significantly more body weight and decreased waist circumference significantly more than the other groups over time (time by diet interaction). Fat mass decreased in the ADF and combination group whereas fat-free mass decreased in the ADF group only. Ezpeleta et al.[24] performed a similar factorial trial to Bhutani et al.,[23] however the exercise dose was higher (aerobic exercise 5 days/week). Participants had obesity and non-alcoholic fatty liver disease. After 12 weeks, body weight decreased significantly by -5% in both the ADF and combination groups, and -2% for exercise alone. Body weight, fat mass, fat free mass, and visceral fat decreased significantly more in the combination group over time (time by diet interaction) compared to exercise alone and the controls. However, no differences were reported between ADF alone or ADF combined with exercise for body weight, fat mass, lean mass, or visceral fat mass.

Regarding cardiometabolic risk, three trials have examined the effect of ADF combined with exercise on fasting lipids and glucoregulatory factors,[23-25] two of which also examined effects on blood pressure.[23,24] Cho et al.[25] reported no changes in LDL cholesterol or HDL cholesterol after 8 weeks of ADF or exercise alone or combined. However, the combination group significantly decreased triglycerides from baseline whereas the control group increased triglycerides significantly more over time when compared with the ADF and combination groups (time by diet interaction). No changes were reported in fasting glucose, fasting insulin, or insulin resistance. Bhutani et al.[23] reported a significant decrease in LDL cholesterol and an increase in HDL cholesterol (time by diet interaction compared to controls) in the ADF combined with exercise groups; ADF and exercise alone remained unchanged. Triglycerides remained unchanged in all groups. Only the ADF group reported a significant decrease in both systolic and diastolic blood pressure from baseline however, the ADF group had significantly higher blood pressure at baseline. Fasting glucose decreased significantly from baseline in all treatment groups and remained unchanged in the control group. Fasting insulin decreased from baseline in the ADF group only, while insulin resistance remained unchanged in all groups. Lastly, Ezpeleta et al.[24] reported no changes in LDL and HDL cholesterol in ADF, exercise alone, or the combination groups. ADF alone reduced triglycerides significantly from baseline. Diastolic blood pressure decreased from baseline in the combination group only. Fasting insulin significantly decreased and insulin sensitivity via the quantitative insulin sensitivity check index (QUICKI= 1 / [log [insulin (mlU/ml)] + log [glucose (mg/dl)])[41] statistically increased in the ADF, aerobic exercise, and combination groups, but not the control group. The combination group also decreased fasting insulin and increased insulin sensitivity significantly more over time compared to the exercise and control groups (time by diet interaction). No difference was reported between the ADF and combination groups, and HbA1c remained unchanged in all groups.

Regarding muscular strength or cardiorespiratory performance only one study has examined the effect of ADF with exercise on muscular strength or cardiorespiratory performance. Cho et al.[25] reported a significant increase VO_{2max} from baseline in the ADF combined with exercise group. Muscle strength (chest press and pulldown) was significantly increased in the exercise and combination group from baseline. Chest press significantly decreased in the ADF alone group while no changes were reported in the controls.

Summary of findings: These data suggest that ADF combined with aerobic training may improve body weight by 4-7% in 8-12 weeks as well as significant decreases in fat mass, and waist circumference. When considering lean mass, the results are incongruent. Cho et al.[25,26] and Ezpeleta et al.[24] did not report lean mass change with the addition of exercise, however, Bhutani et al.[23] only reported lean mass loss in the diet alone group indicating that exercise mitigated this loss. Due to the paucity of data and inconsistency of results, the effect of ADF combined with exercise is unclear for triglycerides and blood pressure. Regarding glucose regulation, data from Ezpeleta et al.[24] appears promising, yet it is also uncertain if combining ADF and exercise results in favorable impact on glucoregulatory factors. Lastly, only one trial examined muscular strength or cardiorespiratory in ADF combined with exercise. More studies will need to examine if these data can be replicated.

TRE

Thirteen studies (14 publications) have examined the effect of TRE combined with different modalities of exercise on body weight and body composition.[27-39] Nine[27,29,31,33-37,42] were randomized control trials wherein controls were prescribed a 12-h eating window or instructed to maintain current eating patterns, one[38] was a randomized trial with no controls, two were randomized crossover design[28,39] and one (two publications) was a single arm design.[30,43] Three trials included participants with overweight or obesity[33,37,38] with the remaining ten trials including participants with normal weight only.[27-32,34-36,39] Exercise interventions included aerobic and endurance activity, resistance training, high intensity interval training or a combination of modalities. Haganes et al.[33] examined TRE, HIIT (3 days per week), or TRE combined with HIIT compared to controls in individuals with overweight or obesity. Compared to the control group, the TRE, HIIT, and combination groups significantly reduced their body weight (TRE: -2%, HIIT: -2%, combination -4%), fat mass, and visceral fat mass from baseline (time by diet interaction). Fat free mass decreased significantly in the TRE group over time compared to the control group (time by diet interaction). Isenmann et al.[38] examined 8-h ad libitum TRE with macronutrient recommendations (45-65% carbohydrate, 20-35% fat, 20-35% protein) compared to a Macronutrient based diet which consisted of 80% unprocessed foods, in participants with overweight or obesity for 14 weeks (8 week intervention period and 6 week independent period). A 500kcal deficit was included during the independent period of the macronutrient diet. Both groups were asked to follow their diet and attend two training sessions a week. After 14 weeks, both groups significantly decreased body weight (-5%), fat mass, and waist circumference from baseline with no differences between groups. No changes were reported in fat free mass. Kotarsky et al.[37] examined 8-h TRE or a “normal” eating window combined with 300 minutes of moderate or 150 minutes of vigorous aerobic activity and resistance training on three non-consecutive days per week in individuals with overweight or obesity. After 8 weeks, the TRE group lost significantly more body weight (-4%) and fat mass over time compared to the normal eating group (time by diet interaction). Both the TRE and normal eating group increased fat free mass and decreased waist circumference from baseline with no differences between groups. Morro et al.[27] compared 8-h TRE compared to a control (12-h) diet in young healthy male elite cyclists for four weeks. Both groups combined their dietary intervention with cycling (500km/week in six training sessions/week) and were given a weight maintenance calorie goal to control for energy intake. The TRE group significantly reduced body weight (-2%). Fat mass was significantly lower in the TRE group than the controls at week 4 (group difference), however this change was not significant over time or time by diet. No changes were reported in fat free mass. Richardson et al.[28] also compared isocaloric 8-h TRE to a 12-hour control diet group in healthy male endurance trained runners. Participants were asked to maintain their current training regimen for both arms of the study. No changes were reported in body weight or fat free mass after 4 weeks, but fat mass decreased significantly during the TRE intervention over time. Correia et al.[29] randomized healthy trained young males to TRE or normal diet (12-h), both of which were combined with 3 resistance training sessions per week. After 4 weeks, no changes in body weight, fat free mass, or skeletal muscle were reported in either group. Fat mass decreased in both groups from baseline, with no differences between groups. Waldman et al.[30,43] examined 8-h TRE in middle-aged competitive male cyclists for 8 weeks. Participants self-selected their eating window to fit their family's eating schedule. All cyclists reported exercise over 150 min/week and were asked to continue their current habitual exercise during the dietary intervention. Participants significantly reduced body weight (-3%)

and fat mass after 8 weeks. Fat free mass and abdominal skin fold remained unchanged. Morro et al.[31] compared a modified form of TRE (4-h window on 4 days per week) against a normal diet (12-h) control in lean healthy young males. Participants were instructed to eat calories for weight maintenance and perform resistance training on 3 non-consecutive days/week. No changes were reported in body weight or fat free mass after 8 weeks, but fat mass decreased significantly more over time in the TRE compared to the normal diet group (time by diet interaction). Moro et al. then performed a follow-up at one year from baseline (10 months after the completion of the previous trial). The TRE group significantly decreased their body weight (-3%) and fat mass, while the normal diet group significantly increased their body weight and fat mass. These changes were significant over time and reporting a significant time by diet interaction. No changes were reported in visceral fat mass at follow-up.[42] However, at 12 months, TRE observed a significant decrease in arm and thigh circumference (cross-sectional area) from baseline compared to the normal diet group (time by diet interaction). Tinsley et al.[34] recruited healthy trained males and compared an isocaloric 7-h TRE diet to a normal diet (12-h) control for 8 weeks. Both groups performed resistance training on three non-consecutive days each week throughout the trial. Body weight, fat mass, fat free mass, and visceral fat mass remained unchanged in both groups. Brady et al.[36] examined 8-h TRE versus a control group in 17 male middle- and long-distance runners who were asked to maintain their habitual exercise. The TRE group lost significantly more body weight (-3%) than the control at 8 weeks (time by diet interaction). No changes were reported in fat mass or fat free mass. Tinsley et al.[35] also examined 8-h TRE or normal (12-h) control diet combined with resistance training (three non-consecutive days per week) in 40 resistance trained females for 8 weeks. Both diet groups were tested with and without Hydroxymethylbuterate (HMB) supplementation, which may promote muscle growth. All groups increased body weight (1-2%) and fat free mass significantly. Fat mass was reduced in the TRE groups independent of HMB supplementation. No differences in body weight, fat mass or fat free mass were reported between groups in the intention to treat analysis. However, the per protocol analysis (n=24) reported a significant time by diet interaction with larger reductions in fat mass and body fat percentage in the TRE plus HMB group and significant increases in fat free mass in all groups. Martinez-Rodriguez et al.[39] examined HIIT (3 times per week) alone compared to HIIT combined with every other day TRE (<14-h eating window with first meal close to waking) using a randomized crossover design in 14 active, normal weight females. HIIT alone had no effect on body weight and body fat, but HIIT combined with TRE produced a significant reduction (time by diet interaction) in fat mass. Fat free mass remained unchanged.

In regards to cardiovascular risk, eight studies have examined the effect of TRE combined with exercise on fasting lipids,[28,30,31,33,35,37,42] four on blood pressure,[28,33,35,37] and ten on glucoregulatory factors.[27,28,30,31,33-37,42] Richardson et al.[28] reported no changes in LDL cholesterol, HDL cholesterol, triglycerides or blood pressure after 4 weeks of TRE or a normal diet in male elite endurance runners. Fasting glucose, fasting insulin, insulin resistance (HOMA-IR), and insulin sensitivity (QUICKI) also remained unchanged. Tinsley et al.[35] reported no changes in LDL cholesterol, HDL cholesterol, triglycerides, fasting insulin, or fasting glucose after 8 weeks of TRE or a control diet combined with resistance independent of HMB supplementation in trained lean females. Diastolic blood pressure significantly decreased in both the TRE and normal diet groups independent of HMB supplementation. Haganes et al.[33] reported no changes in LDL cholesterol, triglycerides, blood pressure, fasting glucose, fasting insulin, and insulin resistance (HOMA-IR) after 7 weeks of TRE or HIIT alone or combined in individuals with overweight or obesity. The combination group reported a greater reduction in HDL cholesterol over time than the other groups (time by diet interaction). Nocturnal glucose decreased significantly in the TRE and combination groups and HbA1c decreased significantly in the combination group compared to controls (time by diet interaction). Waldman et al.[30] reported no changes in LDL cholesterol or triglycerides, however HDL cholesterol increased after 4 weeks of 8-h TRE in male cyclists. Fasting glucose significantly decreased while fasting insulin and insulin resistance (HOMA-IR) remained unchanged. Kotarsky et al.[37] reported no changes in HDL, blood pressure, fasting insulin or HbA1c after TRE combined with 150-300 minutes of exercise for 8 weeks. Brady et al.[36] also reported no change in triglycerides, fasting glucose, fasting insulin or insulin resistance (HOMA-IR). Moro et al.[42] reported a significant increase in HDL cholesterol and a significant reduction in triglycerides, glucose, insulin, and insulin resistance (HOMA-IR) after 8 weeks of 4h TRE four days per week combined with resistance training in lean trained males. At a year follow-up of the same participants significantly decreased LDL cholesterol and increased HDL. Compared to the controls over time, triglycerides decreased significantly (time by diet interaction). Additionally, fasting glucose, fasting insulin, and insulin resistance decreased significantly more over time compared to the normal diet controls (time by diet interaction). In a different trial, Morro et al.[27] reported no differences in triglycerides, fasting glucose or fasting insulin, insulin resistance (HOMA-IR) or insulin sensitivity (QUICKI) after 4 weeks of isocaloric TRE or normal diet in elite cyclists.

In regards to muscular strength and cardio respiratory fitness, seven studies have examined the effect of time restricted eating combined with exercise.[29,31,34-36] Correia et al.[29]

reported an increase in explosive upper body strength from baseline in TRE and normal diet groups. A significant time by diet interaction for peak force and peak dynamic bench press throw favoring the TRE group. The normal diet group also increased their explosive upper body strength over time, produced greater improvements over time compared to TRE (time by diet interaction) for squat jump peak force, countermovement jump peak force, countermovement jump height and isometric bench press. Moro et al.[31] reported significant increases in leg press and hip sled in both the TRE combined with resistance training and the normal diet combined with resistance training groups. Bench press and leg press increased over time in both the TRE and normal diet groups with no difference between groups.[42] Tinsley et al.[34] also reported an increase in hip sled, hip sled endurance and bench press when combining resistance training with both TRE and normal diet after 8 weeks in trained healthy males. Brady et al.[36] reported no significant changes in fixed blood lactate concentration, heart rate at fixed blood lactate concentration, and %HR max or VO_{2max} in either group after 8 weeks. Tinsley et al.[35] reported an increase in maximum strength and muscular performance (countermovement vertical jump, mechanized squat, and 1 repetition max and repetitions to failure of bench press and hip sled) when combining resistance training with TRE or normal 12-h diet, independent of HMB supplementation in resistance trained females. Martinez-Rodriguez et al.[39] reported an increase from baseline countermovement vertical jump height in the TRE combined with HIIT group. Additionally, there was a group interaction at week 16 between the combination group and HIIT alone group.

Summary of findings: In individuals with overweight or obesity TRE combined with exercise produced significant decreases in body weight of 2-4% after 7-16 weeks. Body fat mass and waist circumference also seem to decrease significantly. Changes in fat free mass changes were inconsistent and may depend on intensity or volume of aerobic or resistance training. In normal weight, trained individuals body weight appears unchanged in trials prescribed a calorie goal for weight maintenance and decreases in trials with an ad libitum eating window. However, fat mass does appear to decrease significantly when combining TRE and exercise in lean individuals. LDL cholesterol and blood pressure remained largely unchanged, however TRE combined with exercise may increase HDL cholesterol and decrease triglycerides in normal weight individuals. Glucoregulatory factors also appear to be unaffected by TRE and exercise independent of BMI category. However, one long term follow-up did report significantly improved glucose, insulin, and insulin resistance in lean trained males,[42] indicating these changes may improve over longer time periods. It appears that if caloric intake is adequate, improvements in explosive strength, muscular endurance, $V0_{2peak}$ can still be achieved with TRE. It is unclear how TRE may influence adaptations to aerobic or strength training in untrained individuals or those with overweight or obesity.

DISCUSSION

Over 75% of Americans have either overweight or obesity.[1] This is startling as obesity is associated co-morbidities such as heart disease, cancer, stroke, and diabetes.[1] One in five adults in the United States is inactive, which paired with rates of obesity, greatly increase risk of lower quality of life, mental health issues, comorbidities and mortality.[6] While combining different forms of intermittent fasting with exercise has shown favorable effects on body weight and body fat, improvements in cardiovascular and metabolic risk were not consistent. The results are limited by 1) sample size, 2) intervention length, 3) inclusion criteria, 4) objective measures of diet and exercise adherence, and 5) diversity of sample population.

First, small sample size is a considerable limitation of many of the studies that were reviewed here. Sixteen of the 23 trials reviewed were pilot studies with less than 50 participants, which were then randomized into 2-4 groups. This indicates that most of the trials presented here may be underpowered to report primary and secondary outcomes. Second, current trials lack long-term testing and follow-up. Of the 23 trials reported in this review, 18 were short term (4-12 weeks), 2 were mid-term (16 weeks), and 3 were long term (52 weeks). Two long-term (52 week) studies combining 5:2 with exercise did report significant improvements in blood pressure, HDL cholesterol, and triglycerides. At a follow-up at one year after an 8-week study of TRE combined with resistance training, Moro et al.[42] reported significant improvements in cardiometabolic markers including a significant time by diet interaction in insulin resistance. This may suggest that prior interventions were not long enough to achieve optimal effects. Third, participants included in the current breadth of work, even those with obesity, were metabolically healthy at baseline (being excluded if they had hypertension, dyslipidemia or pre-diabetes). Thus, while participants may have benefited from decreases in body weight and body fat mass, the potential impact on cardiometabolic risk may have been masked by a floor effect related to the inclusion criteria. Specifically, of the 13 trials combining TRE with exercise, only three[33,37,38] examined individuals with overweight or obesity and two[33,37] included people who were not already physically active. Trained individuals are more likely to be euglycemic to begin with, given the direct influence of exercise on glucoregulation.[44-46] Thus, future studies should focus on recruitment of higher risk groups, such as those with prediabetes and untrained individuals. Fourth, objective data on adherence and compliance to both intermittent fasting and exercise interventions are lacking. Currently, food diaries and other self-report techniques are utilized to monitor adherence and compliance to different forms of intermittent fasting. It is well established that individuals under-report energy intake and selectively report foods that are considered to be "healthy" or socially acceptable.[47] It will be important for future studies to explore more objective measures of adherence to these fasting diets such as continuous glucose monitors. As for the exercise interventions, only eleven[16,20,21,23,24,31,33-35,37,39] of the reviewed trials either supervised all exercise or utilized wearables (Actigraph, Pensacola FL or Garmin, Olathe KS) to monitor adherence and compliance. To determine efficacy of these behavioral interventions, high-quality adherence and compliance data are essential. Lastly, racial, ethnic, sex, and age diversity should be considered in future work to increase the external validity of the outcomes. Current data in 5:2 or ADF combined with exercise do include both males and females as well as those aged 18-65 years or older, however, this is a stark contrast when examining the current data in TRE combined with exercise. Of the 13 trials presented combining TRE with exercise, only five[33,35,37-39,48] included women and two[30,37] included those aged 45 years or older. The remaining trials are focused in lean, young, male athletes which is not representative of the U.S. population. While the trials described here span the globe including the US, Brazil, Australia, New Zealand, China, Korea, Germany, Italy, Portugal, Norway, Ireland and Spain, most of these trials have been in European predominantly White countries. Of the seven[23,24,28,30,34,35,37] trials in the US only two[23,24] reported on race and ethnicity. Due to the impact of social determinants of health, including race and ethnicity, on obesity and cardiometabolic risk it is imperative that research includes those from underrepresented backgrounds.

Due to the above limitations, future randomized controlled trials should deliver longer interventions (≥24 weeks) with larger, diverse sample sizes to assess efficacy of intermittent fasting combined with exercise. Individuals who are young, healthy, active, and lean do not have the same heightened risk and are thus unlikely to improve cardiometabolic health based on floor effects. The benefits of intermittent fasting may be greatest for those with obesity, overweight, and/or cardiometabolic risk, and thus more research is needed in these groups. Future studies should utilize tools to measure adherence and compliance to both the diet and exercise programs and explore ways to obtain objective data. Lastly, it is imperative that researchers include both males and females and persons of diverse racial and ethnic backgrounds and across the lifespan in interventions combining diet and exercise, consistent with recent policy advancements and position statements from the U.S. National Institutes of Health and related organizations.

CONCLUSION

The 5:2 diet, ADF, and TRE offer accessible and sustainable alternatives to traditional CR. When combined with different modalities of exercise, these diets can reduce body weight and fat mass. Although there is uncertain impact on chronic disease risk, there is some evidence to suggest that benefits may emerge in higher-powered and longer interventions. Training adaptations are still possible when combining any form of intermittent fasting with exercise. Ongoing research is needed to test the benefits of combined interventions in diverse populations.

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Table 1. Designs: Design, participant characteristics, and intervention descriptions of human trials of intermittent fasting combined with exercise.

Reference	Sample Size	Participant characteristics	Diet length	Design	Intervention arms	Exercise intervention specifics
5:2 Diet						
Batitucci 2022[16]	n=36	Female Obesity	8 weeks	**RT[a]: Parallel- arm**	1. 5:2: Fast day (600kcal) Feast day (ad libitum) 2. 5:2 + Exercise 3. Exercise	HIIT[b] 3 days/week
Keenan 2021, 2022[15,22]	n=44 n=34 analyzed	Male/Female normal weight, overweight, obese recreationally active	12 weeks	**RT[a]: Parallel- arm**	1. 5:2: Fast day (-30% TEE[c]) + resistance training. Fasting meals provided. 2. CR[D] (-20%+) + resistance training	2 supervised resistance training sessions + 1 unsupervised aerobic/resistance training session
Kang 2022[17]	n= 131	Male/Female Overweight or Obesity	12 weeks	**RT[a]: Parallel- arm**	1. 5:2: Fast day (30% TEE[C]) Feast day (70% TEE[C]) 2. CR[D] (70% TEE[C]) 3. High protein meal replacement (70% TEE[C] provided)	150-300m physical activity
Hottenrott 2020[18]	n=80 n=68 analyzed	Male/Female Overweight "Healthy"	12 weeks	**RCT[e]: Parallel- arm**	1. 5:2: Fast day (F: 400, M:600 kcal) Feast day (ad libitum) Alkaline Supplement 2. 5:2: Fast day (F: 500, M:600 kcal) Feast day (ad libitum) Placebo 3. Ad libitum Alkaline Supplement 4. Ad libitum Placebo	Exercise in all groups: 30-60 minutes of running and 20 minutes of resistance training 3-4 days/week
Cooke 2022[21]	n=34	Male/Female Overweight or obesity	16 weeks	**RT[a]: Parallel- arm Per protocol**	1. 5:2 (ad libitum) 2. Sprint interval training 3. 5:2 + sprint interval training	Sprint interval training 3 days/week 4 × 20 s work followed by 40 s of active rest
Headland 2019[19]	n=332 n=124 analyzed	Male/Female Overweight or obesity	52 weeks	**RT[a]: Parallel- arm**	1. 5:2: Fast day (F: 500, M:600 kcal) Feast day (ad libitum) 2. Week-on, week-off (F: 1000, M: 120 0kcal/d) Week-off (ad libitum) 3. CR[d] (-30% TEE[C])	All groups: Increase to 10,000 steps
Jospe 2020[20]	n=250 n=171 analyzed	Male/Female, Overweight or obesity	52 weeks	**Parallel- arm non-randomized Per protocol**	1. Mediterranean Diet 2. 5:2 3. Paleolithic Self-selected diet arm	Choice of standard physical activity recommendations OR home based HIIT[b]
Alternate day fasting						

Cho 2019[25,26]	n=100 n=31/33 analyzed	Male/Female Overweight or obesity	8 weeks	**RCT[e]: Parallel- arm**	1. ADF[f] +Exercise 2. ADF[f] 3. Ex 4. Control	Resistance and aerobic training 3 days/week. First week only supervised.
Bhutani 2013[23]	N=64	Male/Female Obesity	12 weeks	**RCT[e]: Parallel- arm**	1. ADF[f] +Exercise 2. ADF[f] 3. Exercise 4. Control	Aerobic activity 3 days/week, supervised
Ezpeleta 2023[24]	n=80	Male/Female Obesity non-alcoholic fatty liver disease	12 weeks	**RCT[e]: Parallel- arm**	1. ADF[f] 2. Exercise alone 3. ADF[f]+Exercise 4. Control	Aerobic activity 5 days/week, supervised
Time restricted eating						
Moro 2020[27]	n=16	Male elite cyclists	4 weeks	**RCT[e]: Parallel- arm**	1. TRE[g] (8h, 10am-6PM) 2. Normal Diet (12h) Isocaloric (7d diet plan) 3 meals + one snack	500 km/week over 6 sessions
Richardson 2023[28]	n=24 n=15 analyzed	Male endurance trained runners	4 weeks, 2-week washout	**RCT[e]: Crossover**	1. TRE[g] (8h, self-selected) 2. Normal Diet (12h) Isocaloric	Maintain current training
Correia 2023[29]	n= 18	Male healthy trained	30 days	**RCT[e]: Parallel- arm**	1. TRE[g] + resistance training 2. Normal diet (12h) + resistance training	Resistance training 3 days/week, 1 time/week supervised
Waldman 2023[30,43]	n=15 n=12 analyzed	Male cyclists	4 weeks	**Single arm**	1. TRE[g] (16h self-selected)	150 minutes per week
Haganes 2022[33]	n=131	Male/Female Overweight or Obesity	7 weeks	**RCT[e]: Parallel- arm**	1. TRE[g] 2. HIIT[g] 3. TRE[g] and HIIT[b] 4. Control	HIIT[b] (running) 3 days per week, supervised and wearable utilized
Moro 2016[31]	n=34	Male healthy trained	8 weeks	**RCT[e]: Parallel- arm**	1. TRE[g] (4h 4d/wk) + resistance training 2. Normal diet (12h) + resistance training Weight maintenance calorie goal	Resistance training 3 non-consecutive days/week
Moro 2021[42]	n=20	Male healthy	Follow-up at 52 weeks [31]	**RCT[e]: Parallel- arm**	1. TRE[g] (1-9PM) 2. Normal diet (12h)	Resistance training 3 non-consecutive days/week, supervised
Tinsley 2017[34]	n=18	Male healthy trained	8 weeks	**RCT[e]: Parallel- arm**	1. TRE[g] (1-8PM) + resistance training 2. Normal diet (12h) + resistance training Weight maintenance calorie goal	Resistance training 3 days/week on non-fasting days
Brady 2021[36]	n=23 n=17 analyzed	Male middle/ long distance runners	8 weeks	**RCT[e]: Parallel- arm**	1. TRE[g] (8h) 2. Control	Maintain habitual running, wearable utilized
Tinsley 2019[35]	n=40	Female Resistance trained	8 weeks	**RCT[e]: Placebo controlled**	1. TRE[g] (8h) + resistance training 2. TRE[g] (8h) + supplement + resistance training 3. Normal diet (12h) + resistance training	Resistance training 3 non-consecutive days/week, supervised and wearable utilized

Kotarsky 2021[37]	n=28 n=21 analyzed	Male/Female Overweight or obesity	8 weeks	**RCT[e]: Parallel- arm**	1. TRE[g] (12- 8PM, ad libitum) 2. Control (normal eating)	300 minutes of moderate or 150 vigorous aerobic and resistance training per week, resistance training supervised, wearable utilized
Isenmann 2021[38]	n=35	Male/Female Overweight or obesity	2 weeks familiarization 8 weeks intervention	**RT[a] : Parallel- arm** **Per protocol**	1. TRE[g] (12-8PM, ad libitum but macronutrient goal breakdown given) 2. MBD[h] (80% unprocessed, 20% could be processed, chose foods based on the Nutri-score scale)	Two group training sessions per week, unsupervised, gym attendance checked
Martínez-Rodríguez 2021[39]	n=14	Female active normal weight	16 weeks	**RT[a] : Crossover**	1. TRE[g] + HIIT[b] 2. HIIT[b]	HIIT[b] 3 days /week (40 minutes) 3 × 10 repetitions of 30 s of aerobic exercises all out alternated with 30 s of passive recovery, supervised

[a]RT: Randomized trial, [b]HIIT: high intensity interval training, [c]TEE: total energy expenditure, [d]CR: Calorie restriction, [e]RCT: Randomized controlled trial, [f]ADF: Alternate day fasting, [g]TRE: time restricted eating, [h]MBD: macronutrient-based diet

Table 2. Results: Effects of intermittent fasting combined with exercise on body weight, body composition, cardiometabolic markers and muscular strength and cardiorespiratory fitness.

Reference	Participants	Diet length	Intervention Groups	Body weight	Body composition			Blood pressure	Plasma lipids			Glucoregulatory factors			Performance/ Strength
					FM[a]	FFM[b]	VF[c]		LDL[d]	HDL[e]	TG[f]	Fasting Glucose	Fasting Insulin	IR[g]/IS[h] /A1c[i]	
5:2 Diet															
Batitucci 2022[16]	n=36	8-week	1. 5:2 2. 5:2 + Ex[j] 3. Ex[j]	1. ∅ 2. ↓2% 3. ∅	1. ∅ 2. ↓ 3. ↓	1. ∅ 2. ↑ 3. ↑	1. ∅ 2. 3. ↓	--	--	--	--	--	--	--	1. ∅ 2. ↑ walking, strength, HRmax[k], V02peak[l] 3. ↑ walking, strength, HRmax[k], V02peak[l]
Keenan 2021, 2022[15,22]	n=44 n=34 analyzed	12-week	1. 5:2 + Ex[j] 2. CR[m] + Ex[j]	1. ↓4% 2. ↓5%	1. ↓ 2. ↓	1. ↑ 2. ↑	--	--	1. ↓† 2. ↓	1. ↓ 2. ↓	1. ∅ 2. ∅	1. ∅ 2. ∅	1. ∅ 2. ∅	1. ∅ 2. ∅ -	1. ↑ upper and lower body strength 2. ↑ muscle surface area, upper and lower body strength
Kang 2022[17]	n= 131	12-week	1. 5:2 2. CR[m] 3. High protein meal replacement	1. ↓9%† 2. ↓5% 3. ↓9%†	1. ↓ 2. ↓ 3. ↓	1. ↑ 2. ↑ 3. ↑	--	--	--	--	--	--	--	--	--
Hottenrott 2020[18]	n=80 n=68 analyzed	12-week	1. 5:2 + Alkaline supplement 2. 5:2 Placebo 3. Ad Lib[n] Alkaline Supplement 4. Ad lib[n] Placebo	1.↓8kg† 2.↓6kg 3.↓6kg 4.↓3kg	1. ↓† 2. ↓ 3. ↓ 4. ↓	--	1. ↓† 2. ↓ 3. ↓ 4. ↓	--	--	--	--	--	--	--	1. ↑† running velocity 2. ∅ 3. ∅ 4. ∅
Cooke 2022[21]	n=34	16-week	1. 5:2 2. SIT[o] 3. 5:2 + SIT[o]	1. ↓† 2. ∅ 3. ↓†	1. ↓† 2. ∅ 3. ↓†	1. ↓ 2. ↓ 3. ↓	1. ↓ 2. ↓ 3. ↓ WC[p]	1. ∅ 2. ∅ 3. ∅	1. ∅ 2. ∅ 3. ∅	1. ∅ 2. ∅ 3. ∅	1. ∅ 2. ∅ 3. ∅	1. ∅ 2. ∅ 3. ∅	1. ∅ 2. ∅ 3. ∅	1. ∅ IR[g] 2. ∅ IR[g] 3. ∅ IR[g]	1. ∅ 2. ↑^† V02peak[l] 3. ↑† V02peak[l]
Headland 2019[19]	n=332 n=124 analyzed	52 weeks	1. 5:2 2. Week-on, week-off 3. CR[m]	1. ↓6% 2. ↓6% 3. ↓8%	1. ↓ 2. ↓ 3. ↓	1. ↓ 2. ↓ 3. ↓	--	--	1. ∅ 2. ∅ 3. ∅	1. ↑ 2. ↑ 3. ↑	1. ↓ 2. ↓ 3. ↓	1. ∅ 2. ∅ 3. ∅	--	--	--
Jospe 2020[20]	n=250	52 weeks	1. Mediterranean	1. ↓ 3% 2. ↓4%	1. ↓ 2. ↓	--	1. ↓ 2. ↓	1. ↓SBP[q] ↓ DBP[r]	1. ↓ 2. ∅	1. ∅ 2. ↑	1. ∅ 2. ∅	--	--	1. ↓A1c^[i] 2. ∅	--

	n=171 analyzed		Diet 2. 5:2 3. Paleolithic	3. ∅	3. ∅		3. ∅	2. ↓ SBP[q] ↓ DBP[r] 3. ∅ SBP[q] ↓ DBP[r]	3. ↓	3. ∅	3. ∅			3. ∅	
Alternate Day Fasting															
Cho 2019[25,26]	n=100 n=31/33 analyzed	8 weeks	1. ADF[s] + Ex[j] 2. ADF[s] 3. Ex[j] 4. Control	1. ↓4%† 2. ↓3%† 3. ∅ 4. ∅	1. ↓† 2. ↓† 3. ↓ 4. ↓	1.↓ 2. ∅ 3. ∅ 4. ∅	1. ↓ 2. ↓ 3. ↓ 4. ∅	--	1. ∅ 2. ∅ 3. ↑ 4. ∅	1. ↑ 2. ∅ 3. ↑ 4. ↑	1. ↓ 2. ↑† 3. ↓† 4. ↑†	1. ↓ 2. ↓ 3. ∅ 4. ∅	1. ∅ 2. ∅ 3. ∅ 4. ↑	1. ∅ IR[o] 2. ∅ IR[o] 3. ∅ IR[o] 4. ↑ IR[o]	1. ↑ V02peak[l] , ↑ Mets min/wk, muscle strength (chest press, shoulder press, lat pull) 2. ↓ Chest press 3. ↑ Muscle strength (chest press, shoulder press, lat pull) 4. ∅
Bhutani 2013[23]	N=64	12 weeks	1. ADF[s] + Ex[j] 2. ADF[s] 3. Ex[j] 4. Control	1. ↓7%† 2. ↓3% 3. 1% ↓ 4. ∅	1. ↓† 2. ↓ 3. ∅ 4. ∅	1. ∅ 2. ↓ 3. ∅ 4. ∅	1. ↓† 2. ↓ 3. ↓ 4. ∅	1. ∅ 2. ↓ SBP[q] ↓ DBP[r] 3. ∅ 4. ∅	1. ↓ 2. ∅ 3. ∅ 4. ∅	1. ↑† 2. ∅ 3. ∅ 4. ∅	1. ∅ 2. ∅ 3. ∅ 4. ∅	1. ∅ 2. ∅ 3. ∅ 4. ∅	1. ∅ 2. ∅ 3. ∅ 4. ∅	1. ∅ IR[o] 2. ∅ IR[o] 3. ∅ IR[o] 4. ∅ IR[o]	--
Ezpeleta 2023[24]	n=80	12 weeks	1. ADF[s] 2. Ex[j] 3. ADF[s] +Ex[g] 4. Control	1. ↓5% 2. ↓2% 3. 5% ↓† 4. ∅	1. ↓ 2. ↓ 3. ↓† 4. ∅	1. ↓ 2. ↓ 3. ↓† 4. ∅	1. ↓ 2. ∅ 3. ↓† 4. ∅	1. ∅ 2. ∅ 3. ∅ SBP[q] ↓ DBP[r] 4. ∅	1. ∅ 2. ∅ 3. ∅ 4. ∅	1. ∅ 2. ∅ 3. ∅ 4. ∅	1. ↓ 2. ∅ 3. ∅ 4. ∅	1. ∅ 2. ∅ 3. ∅ 4. ∅	1. ↓ 2. ∅ 3. ↓† 4. ∅	1. ↑ IS[h] ↓ IR[o] 2.↑ IS[h] 3. ↑† IS[h] ↓IR[o] 4. ∅ ∅ A1c[a]	--
Time Restricted Eating															
Moro 2020 [27]	n=16	4 weeks	1. TRE[t] 2. ND[u]	1. 2%↓† 2. Ø	1. ↓^ 2. Ø	1. Ø 2. Ø	--	--	--	--	1. Ø 2. Ø	1. Ø 2. Ø	1. Ø 2. Ø	--	1. Ø differences between performance tests, ↑ peak power/BW[v] 2. Ø
Richardson 2023[28]	n=24 n=15 analyzed	4 weeks	1. TRE[t] 2. ND[u]	1. Ø 2. Ø	1. ↓ 2. Ø	1. Ø 2. Ø	--	1. Ø 2. Ø SBP[q] / DBP[r]	1. Ø 2. Ø	1. Ø 2. Ø	1. Ø 2. Ø	1. Ø 2. Ø	1. Ø 2. Ø	1. Ø IR[o], IS 2. Ø IR[o], IS[h]	--
Correia 2023[29]	n= 18	4 weeks	1. TRE[t] + RT[w] 2. ND[u] + RT[w]	1. Ø 2. Ø	1. ↓ 2. ↓	1. Ø 2. Ø	--	--	--	--	--	--	--	--	1. ↑ explosive upper body strength, ↑†bench press throw peak force & bench

															press throw dynamic index 2. ↑ explosive upper body strength, ↑† lower and upper body muscle strength
Waldman 2023[30]	n=15 n=12 analyzed	4 weeks	1. TRE[t]	1. ↓3%	1. ↓	1. ∅	--	--	1. ∅	1. ↑	1. ∅	1. ↓	1. ∅	∅	∅
Haganes 2022[33]	n=131	7 weeks	1. TRE[t] 2. HIIT[x] 3. TRE[t] and HIIT[x] 4. Control	1.↓2%† 2. ↓2%† 3. ↓4%† 4. ∅	1.↓† 2. ↓† 3. ↓† 4. ∅	1. ↓† 2. ∅ 3. ∅ 4. ∅	1.↓† 2. ↓† 3. ↓† 4. ∅	1. ∅ 2. ∅ 3. ∅ 4. ∅	1. ∅ 2. ∅ 3. ∅ 4. ∅	1. ∅ 2. ∅ 3. ↓† 4. ∅	1. ∅ 2. ∅ 3. ∅ 4. ∅	1. ∅ 2. ∅ 3. ∅ 4. ∅	1. ∅ 2. ∅ 3. ∅ 4. ∅	1. ∅ A1c[a], IR[o] 2. ∅ A1c[a], IR[o] 3. ↓ A1c[a], ∅IR[o] 4. ∅ A1c[a], IR[o]	1.∅ 2. ↑ V02peak[l] 3. ↑ V02peak[l] 4. ∅
Moro 2016[31]	n=34	8 weeks	1. TRE[t] + RT[w] 2. ND[u] + RT[w]	1. Ø 2. Ø	1.↓† 2. Ø	1. Ø 2. Ø	--	--	1. Ø 2. Ø	1.↑ 2. Ø	1.↓† 2. Ø	1.↓ 2. Ø	1.↓ 2. Ø	1.↓ IR[o] 2. Ø	1. ↑ Leg press, hip sled 2. ↑ Leg press, hip sled
Moro 2021[42]	n=20	52-week follow-up	1. TRE[t] 2. ND[u]	1. ↓3%† 2. ↑3%	1. ↓† 2. Ø	1. Ø 2. ↑†	1. Ø 2. Ø		1. ↓ 2. ∅	1.↑† 2. Ø	1. ↓ † 2. ∅	1. ↓ † 2. ∅	1. ↓ † 2. ∅	1. ↓† IR[o] 2. ∅ IR[o]	1. ↓†Thigh and arm circumference, ↑Bench and leg press 2. ↑Bench and leg press
Tinsley 2017[34]	n=18	8 weeks	1. TRE[t] + RT[w] 2. ND[u] + RT[w]	1. Ø 2. Ø	1. Ø 2. Ø	1. Ø 2. Ø	1. Ø 2. Ø	--	--	--	1. Ø 2. Ø	1. Ø 2. Ø	1. Ø 2. Ø	1. Ø IR[o] 2. Ø IR[o]	1. ↑ Bench press, hip sled, hip sled endurance 2. ↑ Bench press, hip sled, hip sled endurance
Brady 2021[36]	n=23 n=17 analyzed	8 weeks	1. TRE[t] 2. Control	1.↓2%† 2. Ø	1. Ø 2. Ø	1. Ø 2. Ø	--	--	--	--	1. Ø 2. Ø	1. Ø 2. Ø	1. Ø 2. Ø	1. Ø IR[o] 2. Ø IR[o]	1 Ø V02peak[l], FBLC[y], HR at FBLC[y], %HRmax[k] 2. Ø
Tinsley 2019[35]	n=40	8 weeks	1. TRE[t] + RT[w] 2. TRE[t] + supplement + RT[w] 3. Control Diet + RT[w]	1. 1%↑ 2. 1%↑ 3. 2%↑	1. ↓ 2. ↓ 3. ↓	1. ↑ 2. ↑ 3. ↑	--	1. ↓ DBP[r] 2. ↓ DBP[r] 3. ↓ DBP[r]	1. Ø 2. Ø 3. Ø	1. Ø 2. Ø 3. Ø	1. Ø 2. Ø 3. Ø	1. Ø 2. Ø 3. Ø	1. Ø 2. Ø 3. Ø	--	1. ↑ Max[z] strength and muscular performance 2. ↑ Max[z] strength and muscular performance 3. ↑ Max[z] strength and muscular performance

Kotarsky 2021[37]	n=28 n=21 analyzed	8 weeks	1. TRE[t] 2. Control	1. ↓4%† 2. Ø	1. ↓† 2. Ø	1. ↑ 2. ↑	1. ↓ 2. ↓ WC[p]	1. Ø 2. Ø	--	1. Ø 2. Ø	--	--	1. Ø 2. Ø	1. Ø 2. Ø A1c[a]	1. ↑ knee flexion strength peak torque and endurance total work, dorsiflexion strength peak torque and endurance total work 2. ↑ knee flexion strength peak torque and endurance total work, dorsiflexion strength peak torque and endurance total work
Isenmann 2021[38]	n=35	8 weeks	1. TRE[t] 2. MBD[aa]	1.↓5% 2.↓5%	1.↓ 2.↓	1. Ø 2. Ø	1.↓ 2.↓ WC[p]	--	--	--	--	--	--	--	--
Martínez-Rodríguez 2021[39]	n=14	16 weeks	1. TRE[t] + HIIT[x] 2. HIIT[x]	1. Ø 2. Ø	1. ↓† 2. Ø	1. Ø 2. Ø	--	--	--	--	--	--	--	--	1. ↑ counter-movement jump, relative mean power† 2. Ø

^ P < 0.05, Significantly different between groups (between group effect).
† P < 0.05, Significant time by diet interaction.
[a]FM: Fat mass, [b]FFM: Fat free mass, [c]VF: Visceral fat mass, [d]LDL: Low density lipoprotein cholesterol, [e]HDL: High density lipoprotein cholesterol, [f]TG: Triglycerides, [g]IR: Insulin resistance, [h]IS: insulin sensitivity, [i]A1c: hemoglobin, [j]Ex: exercise, [k]HRmax: heart rate maximum, [l]V02peak: volume of oxygen peak, [m]CR: Calorie restriction, [n]Ad lib: Ad libitum energy intake, [o]SIT: sprint interval training, [p]WC: waist circumference, [q]SBP: Systolic blood pressure, , [r]DBP: Diastolic blood pressure, [s]ADF: Alternate day fasting, [t]TRE: Time restricted eating, [u]ND: normal diet, [v]BW: body weight, [w]RT: Resistance training, [x]HIIT: high intensity interval training, [y]FBLC:fixed blood lactate concentration, [z]Max: maximum, [aa]MBD: macronutrient-based diet

Table 3. Inclusion criteria (including sex, BMI, age, and training status), exercise modality, and adherence monitoring for the review of trials combining intermittent fasting with exercise.

	Sex		BMI[a]			Age			Training status		Exercise			Adherence	
	M[b]	F[c]	<25	25-29.9	>30	18-45	45-65	>65	Trained	Untrained	AT[d]	RT[e]	HIIT[f]	Supervised	Wearable
5:2															
Batitucci 2022[16]		●			●	●			--	--			●	●	
Keenan 2021, 2022[15,22]	●	●	●	●	●	●	●	●		●		●		2 d/wk	
Kang 2022[17]	●	●		●	●	●	●	●	--	--	●				
Hottenrott 2020[18]	●	●		●	●	●	●		●		●				
Cooke 2022[21]	●	●		●	●	●				●	●	●		●	
Headland 2019[19]	●	●		●	●	●	●	●	--	--	●		●		
Jospe 2020[20]	●	●		●	●	●	●	●	--	--	●	●	●		●
ADF[g]															
Cho 2019[25,26]	●	●		●	●	●	●		--	--	●	●		first week	
Bhutani 2013[23]	●	●			●	●	●	●		●	●			●	
Ezpeleta 2023[24]	●	●			●	●	●	●		●	●			●	
TRE[h]															
Moro 2020[27]	●		●			●			●		●				
Richardson 2023[28]	●		●			●			●		●				
Correia 2023[29]	●		●			●			●			●		1 d/wk	
Waldman 2023[30,43]	●		●				●	●	●		●				
Haganes 2022[33]	●	●		●	●	●				●			●	●	●
Moro 2016[31]	●		●						●			●		●	
Moro 2021[42]	●		●						●			●			
Tinsley 2017[34]	●		●						●			●			
Brady 2021[36]	●		●			●			●		●				●
Tinsley 2019[35]		●	●			●			●			●		●	●
Kotarsky 2021[37]	●	●		●	●	●	●			●	●	●		●	●
Isenmann 2021[38]	●	●		●	●	●			●		●	●			
Martínez-Rodríguez 2021[39]		●	●			●			●				●	●	

[a]BMI: Body Mass Index, [b]M: Male, [c]F: Female, [d]AT: Aerobic training, [e]RT: Resistance training, [f]HIIT: High intensity interval training, [g]ADF: Alternate day Fasting, [h]TRE: Time restricted eating