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Effects of exercise training programmes on fasting gastrointestinal appetite hormones in adults with overweight and obesity: A systematic review and meta-analysis

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ABSTRACT

A systematic review and meta-analysis was performed to determine the effect of exercise training on fasting gastrointestinal appetite hormones in adults living with overweight and obesity. For eligibility, only randomised controlled trials (duration ≥ four weeks) examining the effect of exercise training interventions were considered. This review was registered in the International Prospective Register of Systematic Reviews (CRD42020218976). The searches were performed on five databases: MEDLINE, EMBASE, Cochrane Library, Web of Science, and Scopus. The initial search identified 13204 records. Nine studies, which include sixteen exercise interventions, met the criteria for inclusion. Meta-analysis was calculated as the standardised mean difference (Cohen's d). Exercise training had no effect on fasting concentrations of total ghrelin (d: 1.06, 95% CI -0.38 to 2.50, P = 0.15), acylated ghrelin (d: 0.08, 95% CI: −0.31 to 0.47, P = 0.68) and peptide YY (PYY) (d = −0.16, 95% CI: −0.62 to 0.31, P = 0.51) compared to the control group. Analysis of body mass index (BMI) (d: −0.31, 95% CI: −0.50 to −0.12, P < 0.01) and body mass (d: −0.22, 95% CI: −0.42 to −0.03, P = 0.03) found a significant reduction after exercise compared to controls. Overall, exercise interventions did not modify fasting concentrations of total ghrelin, acylated ghrelin, and PYY in individuals with overweight or obesity, although they reduced body mass and BMI. Thus, any upregulation of appetite and energy intake in individuals with overweight and obesity participating in exercise programmes is unlikely to be related to fasting concentrations of gastrointestinal appetite hormones.

1. Introduction

The World Health Organization (WHO) documented that more than 1.9 billion adults aged 18 years and over are living with overweight or obesity (BMI ≥25 kg/m^2; WHO, 2021). Body mass gain results from repeated episodes of increased energy intake and/or reduced accumulation of physical activity and exercise (Blundell et al., 2015; Hall et al., 2012; Spiegelman & Flier, 2001). Thus, participation in exercise programs has been advocated as a non-pharmacological and non-surgical approach to obesity prevention and treatment (Dorling et al., 2018). However, the effectiveness of exercise-induced body mass loss in the absence of caloric restriction is variable (Gibbons et al., 2017; Jackson et al., 2018; King et al., 2008; Manthou et al., 2010) and is attenuated by compensatory changes in appetite and energy intake (Blundell et al., 2015; King et al., 2008). Therefore, understanding how appetite regulatory mechanisms are altered by exercise in overweight and obese individuals is of great interest.

The regulation of appetite is controlled by a coordinated and complex system of central neurons and peripheral appetite hormones (Augustine et al., 2018). It is well established that gastrointestinal hormones such as anorexigenic peptide YY (PYY), glucagon-like peptide 1 (GLP-1), cholecystokinin (CCK) and orexigenic ghrelin are acutely altered in response to feeding (Suzuki et al., 2011). Despite the lack of a definitive consensus, several studies suggest that an acute bout of exercise

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suppresses levels of acylated ghrelin while simultaneously increasing PYY and GLP-1, and this has the potential to modify food and drink intake following exercise (Stensel., 2010; King et al., 2013, Schubert et al., 2014; Douglas et al., 2016; Ouerghi et al., 2021). Existing evidence also suggests that changes in gastrointestinal appetite hormone concentrations depend on the mode, intensity, and duration of acute exercise sessions, along with the body weight and nutritional status of investigated participants (Dorling et al., 2018; Zouhal et al., 2019).

The evidence regarding the effects of exercise training on gastrointestinal hormones has not been extensively synthesised. Previous narrative reviews suggest that chronic exercise has no influence on ghrelin concentrations independently of body mass loss and leads to increased fasting concentrations of PYY and GLP-1 (King et al., 2013; Martins et al., 2008; Stensel, 2010). In addition, a narrative review suggested that exercise training increases fasting hunger and postprandial satiety and improves the coupling between exergy expenditure and energy intake exergy expenditure in response to food intake (Dorling et al., 2018). These reviews, however, did not adhere to a rigorous systematic methodology to assess study selection, data extraction, and study quality. A more recent systematic review summarising evidence on total and acylated ghrelin responses to chronic exercise reports that data are inconsistent, with studies showing increased, decreased, or unchanged circulating concentrations of total ghrelin and acylated ghrelin (Ouerghi et al., 2021). The inconsistency of the data might be related to large differences between studies in terms of participant characteristics, particularly body mass status (Ouerghi et al., 2021). Adults living with overweight and obesity have altered concentrations of gastrointestinal hormones in response to exercise (Lean & Malkova, 2016; Zouhal et al., 2019), so research is needed with a specific focus on this population. Ouerghi et al. (2021) also included studies that did not apply a randomised control trial design and hence did not provide the most accurate estimate of the exercise training response. Therefore, this systematic review and meta-analysis aimed to fill the evidence-based gap by quantifying the effect of exercise training programs (duration $\geq$ four weeks) from randomised controlled studies on the fasting gastrointestinal appetite hormones of adults living with overweight and obesity.

2. Methods

The Preferred Reporting Items conducted this study for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page et al., 2021). The review is registered at PROSPERO 2020-CRD42020218976 (https://www.crd.york.ac.uk/prospero/).

2.1. Literature search

A systematic search strategy based on keywords related to exercise interventions and gastrointestinal appetite hormones was developed to identify relevant papers using MEDLINE, EMBASE, Cochrane Library, Web of Science, and Scopus databases (Supplementary material 1). Protocols and ongoing trials were identified through the International Standard Randomized Controlled Trial Number (ISRCTN) trials registry and ClinicalTrials.gov. The search was conducted from database inception up to November 25th, 2021. In addition, hand searches of reference lists of key reviews and retrieved full-text articles were conducted. Citation screening through Google Scholar was also performed for included full-text articles as a final check.

2.2. Eligibility criteria

Criteria for consideration in this systematic review included adults (aged $\geq$18 years) with overweight and obesity (BMI $\geq$25 kg/m^2), an exercise intervention ($\geq$4 weeks) that investigated the impact on at least one gastrointestinal appetite hormones (total ghrelin, acylated ghrelin, PYY, CCK, and GLP-1). The inclusion of exercise interventions with a minimum exercise duration of 4 weeks was based on the evidence that this duration achieves measurable body weight and body fat change (Jackson et al., 2018; Manthou et al., 2010). For studies that included adolescents and adults, at least 50% of the sample were required to be aged $\geq$18 years; further, at least 50% of participants in selected studies had to have a BMI $\geq$25 kg/m$^{2.}$ Studies were excluded if they were not published in English and did not apply a randomised control trial design since randomized controlled trials are considered the most reliable method for determining the effectiveness of interventions (Akobeng, 2005). The primary outcome of this review was to examine the differences in fasting gastrointestinal hormones between the exercise and control groups following interventions. The change in body mass and BMI after exercise training programs was also considered.

2.3. Selection process

The articles identified were electronically imported into Covidence software for screening (www.covidence.org) and duplicate studies were automatically removed. The screening of the title and abstracts was conducted by two independent reviewers (SA & TA). Potentially relevant articles were sourced, and the full-text articles were screened against the criteria above (TA & DM). Any disagreements on study selection were discussed and resolved by a consensus decision. Reliability between reviewers for the title and abstract screening and full-text screening were calculated in SPSS (version 27; SPSS IBM, New York, NY, USA) using Cohen's kappa scores, demonstrating almost perfect agreement and moderate agreement ($\kappa = 0.99$ and 0.65, for the title and abstract and full-text articles screening, respectively; Landis & Koch, 1977).

2.4. Data extraction

Two reviewers (TA & SW) independently conducted the data extraction from a pre-specified data extraction template using Microsoft Excel adapted from reviews (Harris et al., 2018; McGarty et al., 2018). The results were compared, and a consensus was agreed upon. Data extraction included study characteristics (e.g., the location and aim of the study), intervention components (e.g., frequency, intensity, type of exercise sessions, and the duration of the whole intervention), outcome measures (e.g., total ghrelin, acylated ghrelin, PYY, GLP-1, CCK, body mass and BMI), and results (e.g., post-intervention and control mean, standard deviation, and sample size).

2.5. Risk of bias

The Cochrane Collaborations tool version 2 (Higgins et al. 2011) was used to judge the risk of bias in included studies. The studies were judged as low, with some concerns or high risk of bias according to the following six domains: (1) the randomisation process; (2) deviations from the intended interventions (effect of assignment to intervention); (3) deviations from the intended interventions (effect of adhering to intervention); (4) missing outcome data; (5) measurement of the outcome; (6) selection of the reported result. Two researchers (TA & LH) independently conducted the risk of bias, and disagreement was resolved through discussion with a third reviewer (AM).

2.6. Data synthesis

Meta-analyses were conducted using Comprehensive Meta-Analysis (Version 3.0 for Windows: Biostat, Englewood, Colorado, USA). Effect sizes for each outcome were calculated as the standardized difference in means, expressed as Cohen's d (Cohen, 1988). Effects sizes were calculated based on imputed data (post-intervention and control mean, standard deviation, and sample size) and interpreted as small ($d = 0.20$), moderate ($d = 0.50$) or large ($d = 0.80$; Cohen, 1988). A random-effects model was used to compute effect sizes to account for true variation

between study effects, as well as a random error within a study (DerSimonian & Laird, 1986). Heterogeneity was assessed using Cochrane's Q statistic, with a significance level of $P < 0.05$ indicating evidence of statistical heterogeneity. The I^2 statistic was used to quantify the degree of heterogeneity, with $I^2 \geq 50\%$ indicating substantial heterogeneity (Higgins et al., 2003). Due to the small number of studies included in this systematic review, it was not possible to conduct any subgroup or moderator analysis to explore heterogeneity between studies or explore the relationship between changes in gastrointestinal hormones and changes in body weight/BMI (Higgins & Green, 2011). The limited number of studies also meant that there was not adequate power of reliability of tests to detect the presence of publication bias (Higgins & Green, 2011).

3. Results

3.1. Study selection process

The electronic database searches identified a total of 13,204 records. Seven further studies were identified from hand searching of bibliographies of included studies. Duplicate studies were removed, and initial title and abstract screening were conducted for 9325 studies. Sixty-eight studies underwent full-text screening, and nine studies met the eligibility criteria (Fig. 1). The full list of excluded studies and the reasons for exclusion are presented in the supporting information (Supplementary Materials). The nine eligible studies are descriptively summarized in Table 1. Three studies did not provide sufficient data for appetite hormones and therefore were not included in the meta-analysis (Foster--Schubert et al., 2005; Mason et al., 2015; Shakiba et al., 2019). The outcome data from two studies were not reported in suitable units for the meta-analysis (Foster-Schubert et al., 2005; Mason et al., 2015), and one study did not report data for the control group to allow comparison with the intervention group (Shakiba et al., 2019).

3.2. Study characteristics

A summary of the study characteristics of included studies is presented in Table 1. Gastrointestinal appetite hormones were considered the primary outcome by eight studies (Ahmadi et al., 2019; Foster-Schubert et al., 2005; Guelfi et al., 2013; Kang et al., 2018; Mason et al., 2015; Rosenkilde et al., 2013; Shakiba et al., 2019; Sim et al., 2015), with one study considering this as a secondary outcome (Quist et al., 2019). Two studies were conducted in Australia (Guelfi et al., 2013; Sim et al., 2015), two in Denmark (Quist et al., 2019; Rosenkilde et al., 2013), two in Iran (Ahmadi et al., 2019; Shakiba et al., 2019), two in the United States (Foster-Schubert et al., 2005; Mason et al., 2015), and one in South Korea (Kang et al., 2018).

A total of 707 participants (259 men and 448 women) were recruited across the nine studies, with the number of participants included in the studies ranging from 26 to 186. Participants were physically inactive adults with a mean age range of 28–69 years and a mean BMI between 27.1 and 31.8 kg/m^2. Three studies recruited adults classified as living with overweight (Ahmadi et al., 2019; Rosenkilde et al., 2013; Sim et al., 2015), five recruited adults living with overweight and/or obesity (Foster-Schubert et al., 2005; Guelfi et al., 2013; Mason et al., 2015; Quist et al., 2019; Shakiba et al., 2019), and one study recruited only adults living with obesity (Kang et al., 2018). Five studies recruited male participants (Guelfi et al., 2013; Rosenkilde et al., 2013; Sim et al., 2015; Ahmadi et al., 2019; Shakiba et al., 2019), three only female participants (Foster-Schubert et al., 2005; Kang et al., 2018; Mason et al., 2015), and one study included both males and females (Quist et al., 2019). Participants were asked not to change their habitual diets during exercise training in all studies.

3.3. Exercise interventions

Sixteen exercise interventions were applied across nine studies, with five studies including more than one exercise intervention group (Guelfi et al., 2013; Quist et al., 2019; Rosenkilde et al., 2013; Shakiba et al., 2019; Sim et al., 2015). Exercise intervention designs varied across studies in terms of mode of intervention, duration, frequency, and exercise intensity. Twelve interventions were based on endurance training (Foster-Schubert et al., 2005; Guelfi et al., 2013; Rosenkilde et al., 2013; Mason et al., 2015; Sim et al., 2015; Ahmadi et al., 2019; Quist et al., 2019; Shakiba et al., 2019), two interventions were either resistance (Guelfi et al., 2013; Shakiba et al., 2019), or combined (endurance and resistance) exercise training (Kang et al., 2018; Shakiba et al., 2019).

The type of endurance training included walking (Foster-Schubert

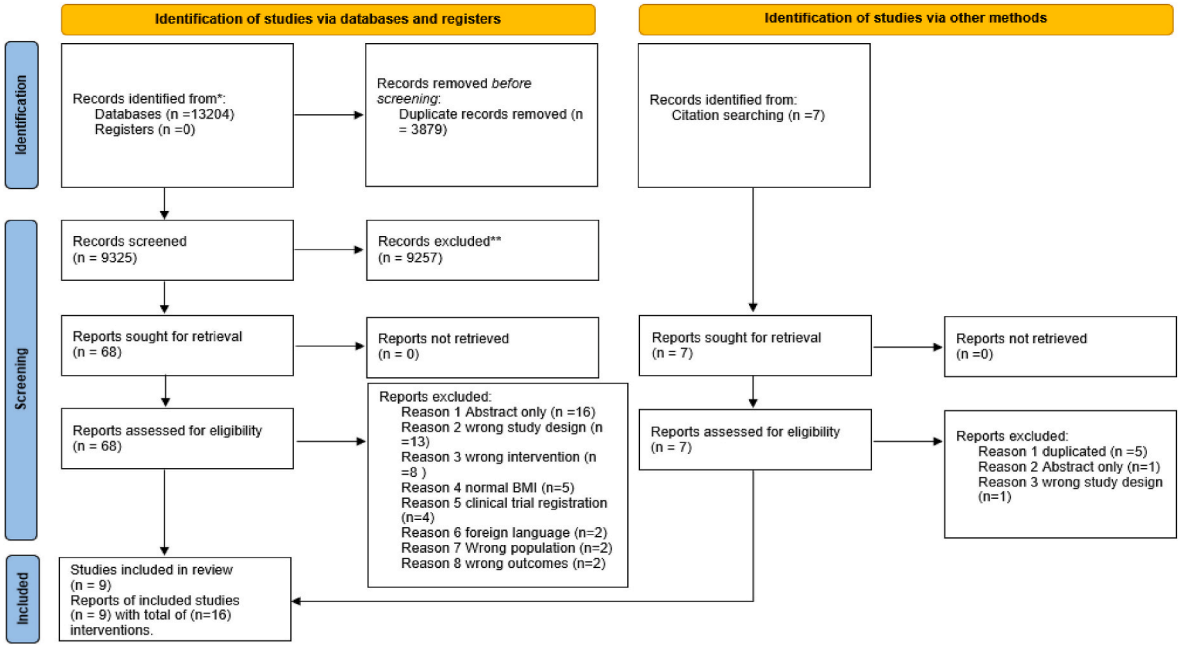

Fig. 1. Flow chart of the studies selection process.

Table 1
Key features of the included randomized controlled trials (RCT).

Study (country)	Study population (n; gender, age, BMI, weight)		Exercise Intervention	Study duration	Attrition	Total Ghrelin	Acylated ghrelin	Results				BMI
	Exercise	Control						PYY	GLP	CCK	Body weight	
Ahmadi et al. (2019) (Iran)	N = 15 men. Age: 60-70 BMI: 25-30 Weight: NR	N = 9 men. Age: 60-70 BMI: 25-30 Weight: NR	Mode: ET Frequency: 4/7. Intensity: 60–85% HRmax Duration: 20–45 min. Control group: NR	8 weeks	NR	Pre to post: Exercise groups: ↑Ghr Control group: ↔Ghr.	NR	NR	NR	NR	NR	Pre to post: AE group: ↓BMI Control group: ↔BMI.
Foster-Schubert et al. (2005) (USA)	N = 87 women. Age: 60.7 ± 6.7 BMI: 30.4 ± 4.1 Weight: 81.4 ± 14.1	N = 86 women. Age:60.6 ± 6.8 BMI: 30.5 ± 3.7 Weight: 81.4 ± 14.1	Mode: ET (walking bicycling and aerobic) Frequency: 5/7 Intensity: Gradual increase from 40% to 60–75% HR_{max} Duration: Gradual increase from 16 to 45min Control group once weekly 45 min stretching classes and no change in other exercise habits	12 months	2.9%	Pre to post: CE groups: ↑Ghr Control group: ↔Ghr.	NR	NR	NR	NR	Pre to post: AE group: ↓ BW ST group: ↔ BW	NR
Guelfi et al. (2013) (Australia)	AE N = 12 men. Age: 49 ± 7 BMI: 31.7 ± 3.5 Weight:102 ± 12.6 RE N = 13 men. Age: 49 ± 7 BMI: 30.3 ± 3.5 Weight:98.4.1 ± 12.1	N = 8 men. Age: 49 ± 7 BMI: 30.1 ± 6.1 Weight:93.9 ± 20.4	Mode: AR (stationary cycling with elliptical cross-training) Frequency: 3/7. Intensity: increased from 70%–75% of HR_{max} to 75%–80% HR_{max} by week 5. Duration: 60 min. Mode: RE (combination of pulley weight machines and free weight) Frequency: 3/7. Intensity: 3 sets of 10 repetitions at 75% of 1RM, with an increase to 4 sets of 8 repetitions at 85% 1RM by the end of the intervention Duration: NR Control group: Continued with their normal sedentary routine	12 weeks	NR	Pre to post: AE group: ↔ AG RE group: ↔ AG Control group: ↔ AC	Pre to post: AE group: ↔ PYY RE group: ↔ PYY Control group: ↔ PYY	NR	NR NR	Pre to post: AE group: ↓BW RE group: ↔ BW Control group: ↔ BW	Pre to post: AE group: ↓BMI RE group: ↔ BMI Control group: ↔ BMI	Guelfi et al. (2013) (Australia)
Kang et al. (2018) (Republic of Korea)	N = 13 women. Age: 50.1 ± 3.8 BMI: 31.8 ± 3.2 Weight: 82.7 ± 10.4	N = 13 women. Age: 49.8 ± 2.9 BMI: 30.4 ± 2.3. Weight: 77.2 ± 9.6	Mode: CT (consisted of walking and 5 types of weight-bearing) Frequency: 5/7 Intensity: 12–14 based on Borg rating of perceived exertion. Duration: 45 min. Control group: Maintain habitual physical activity	12 weeks	NR	Pre to post: CE groups: ↑Ghr Control group: ↓ Ghr.	NR	NR	NR	NR	Pre to post: CE group: ↓BW Control group: ↔BW	Pre to post: CE group: ↓BMI Control group: ↔BMI
Mason et al. (2015) (USA)	N = 106 women. Age: 57.7 4 ± 4.4 BMI: 30.7 ± 3.9 Weight:84.2 ± 12.5	N = 80 women. Age: 58.1 ± 5 BMI: 30.7 ± 3.7 Weight:83.7 ± 12.3	Mode: ET (walking, cycling or hiking) Frequency: 5/7 Intensity: 60–70% to 70–85% HR_{max} Duration: 45mins. Control group No-life change but four group nutrition classes and 8 weeks of facility exercise	12 months	9.4%	Pre to post: CE groups: ↑Ghr Control group: ↔Ghr.	NR	NR	NR	NR	Pre to post: HIIT group: ↓BW Control group: ↔ BW.	NR

(*continued on next page*)

Table 1 (*continued*)

Study (country)	Study population (n; gender, age, BMI, weight)		Exercise Intervention	Study duration	Attrition	Total Ghrelin	Acylated ghrelin	Results				BMI
	Exercise	Control						PYY	GLP	CCK	Body weight	
			training with individualized were offered by the end of the trail.									
Quist et al. (2019) **(Denmark)**	BIKE N = 22 (10 men and 12 women). Age: 35 ± 7 BMI: 30.1 ± 3.3 Weight: 90.2 ± 12.5 MOD N = 33 (17men and 16women). Age: 33 ± 7 BMI: 29.2 ± 1.9 Weight: 89.5 ± 11.1 VIG N = 25 (12men and 13women). Age: 37 ± 7 BMI: 30 ± 2.4 Weight: 92.4 ± 14.1	N = 16 (9men and 7women) Age: 35 ± 7 BMI: 30.1 ± 2.3 Weight: 93.2 ± 11.8	Mode: ET (Active commuting by bike) Frequency: 7/7 Intensity: 60% of VO_{2peak}, with an average speed of 17 km/h and 20 km/h for women and men, respectively. Distance: women: 9–15 km/day and men 11–17 km/day. Mode: ET (walking, cycling, running, or rowing) Frequency: 5/7 Intensity: 50% VO_2 peak Energy expenditure: at least 150 min/wk. Mode: ET(walking, cycling, running, or rowing) Frequency: 5/7 Intensity: 70% VO_2 peak Duration to expend: 320 kcal/day for women and 420 kcal/day for men. This corresponded to 1600 kcal/wk for women and 2100 kcal/wk for men. Control group: Habitual lifestyle and offered individualized lifestyle advice with emphasis on physical activity and a 1-year membership to a fitness center after study completion	6 months	BIKE: 30% MOD: 58% VIG: 84%	NR	Pre to post: BIKE group: ↔ AG MOD group: ↔ AG VIG group: ↔ AG Control group: ↔ AC	Pre to post: BIKE group: ↔ PYY MOD group: ↔ PYY VIG group: ↔ PYY Control group: ↔ PYY	Pre to post: BIKE group: ↔ GLP-1 MOD group: ↔ GLP-1 VIG group: ↔ GLP-1 Control group: ↔ GLP-1	Pre to post: BIKE group: ↔ CCK MOD group: ↔ CCK VIG group: ↔ CCK Control group: ↔ CCK	Pre to post: BIKE group: ↔BW MOD group: ↔ BW VIG group: ↓BW Control group: ↔ BW.	Pre to post: BIKE group: ↔BMI MOD group: ↔ BMI VIG group: ↓BMI Control group: ↔ BMI
Rosenkilde et al. (2013) **(Denmark)**	MOD N = 18 men. Age: 30 ± 7 BMI: 28.6 ± 1.8 Weight: 93.2 ± 8.1 HIGH N = 18 men. Age: 27.6 ± 1.4 BMI: 31.8 ± 3.2 Weight: 91.3 ± 7.2	N = 17 men. Age: 31 ± 6 BMI: 28 ± 2.3 Weight:92.8 ± 8.5	Mode: ET (running and cycling (TrEE of 300 kcal/day) Frequency:7/7 Intensity: 3 sessions at ≥ 70% of $\dot{V}O_{2\ max}$ and the intensity of the remaining sessions were chosen by participants Duration: 30min/day. Mode: ET running and cycling (TrEE of 600 kcal/day) Frequency: 7/7 Intensity: 3 sessions at ≥ 70% of $\dot{V}O_{2max}$ and the intensity of the remaining sessions were chosen by participants Duration: 60mins/day Control group: Maintained a sedentary lifestyle and were offered consultations regarding healthy lifestyle changes after completion of the study.	12 weeks	MOD: 17% HIGH: 22%	Pre to post: MOD groups: ↔Ghr HIGH group: ↔Ghr. Control Group: ↔Ghr	NR	Pre to post: MOD group: ↔ PYY HIGH group: ↔ PYY Control group: ↔ PYY	NR	NR	Pre to post: MOD group: ↓BW HIGH group: ↓BW Control group: ↔ BW.	Pre to post: MOD group: ↓BMI HIGH group:↓ BMI Control group: ↔ BMI
Shakiba et al. (2019) **(Iran)**	RT N = 11 men Age: students BMI: 28.59 ± 1.61 Weight: 89.36 ±	N = 11 men Age: NR (student) BMI: 30.1 ± 2.3	Mode: RT (7 resistance movement) Frequency: 3/7 Intensity: 7 resistance movements in 4 sets of 8 repetitions with 80% of 1RM. The rest intervals between sets and movements were	12 weeks	NR	NR	Pre to post: RT group: ↓ AG ET group:	Pre to post: RT group: ↑ PYY	Pre to post: RT group: ↔ GLP	NR	Pre to post: RT group: ↓BW	Pre to post: RT group: ↓BMI ET group: ↓BMI

(*continued on next page*)

Table 1 (*continued*)

Study (country)	Study population (n; gender, age, BMI, weight)		Exercise Intervention	Study duration	Attrition	Total Ghrelin	Acylated ghrelin	Results				BMI
	Exercise	Control						PYY	GLP	CCK	Body weight	
	7.67 ET N = 11 men Age: students BMI: 27.96 ± 1.32 Weight: 87.43 ± 9.69 CT N = 11 men Age: students BMI: 30.35 ± 3.60 Weight: 93.55 ± 10.20	Weight: 29.80 ± 2.99	1 and 2 min, respectively. Duration: 60 min Mode: ET (running) Frequency: 3/7 Intensity: 3 sets of 10 min of running at 80–90% HR_{max} with 5 min of slow walk between sets. Duration: 60 min (10 min to warm up, 45 min for main training phase, and 5 min for cool down Mode: CT (RT and ET in the same session) Frequency: 3/7 Intensity: a combination of endurance and resistance training protocols similar to ET and RT groups. Duration: 60 min. Control group: No regular training program was assigned during the trial period.				↓ AG CT group: ↓ AG Control group: ↔ AC	ET group: ↑ PYY CT group: ↑PYY Control group: ↑ PYY	ET group: ↔ GLP CT group: ↔ GLP Control group: ↔ GLP		ET group: ↓ BW CT group: ↓BW Control group: ↔ BW.	CT group: ↓BMI Control group: ↔ BMI
Sim et al. (2015) **(Australia)**	HIIT group N = 10 men. Age: 31 ± 8 BMI: 27.2 ± 1.3 Weight: 87.4 ± 7.7 ICT group N = 10 men. Age: 31 ± 8 BMI: 27.2 ± 1.3 Weight: 86.5 ± 8.6	N = 10 men. Age: 31 ± 8 BMI: 27.2 ± 1.3 Weight: 85.6 ± 6.4	Mode: ET (calibrated front access air-braked cycle ergometers). Frequency: 3/7 Intensity: 15-s at a power output equivalent to ~170% $\dot{V}O_2$Peak with an active recovery period (60-s at a power output ~32% $\dot{V}O_2$Peak) between efforts Duration: 30–45 min. Mode: ET (calibrated front access air-braked cycle ergometers) Frequency: 3/7 Intensity: 60% VO_2 peak Duration: 30–45 min Control group: NR	12 weeks	NR	NR	Pre to post: HIIT group: ↔ AG MICT group: ↔ AG Control group: ↔ AC	Pre to post: HIIT group: ↔ PYY MICT group: ↔ PYY Control group: ↔ PYY	NR	NR	Pre to post: HIIT group: ↔BW MICT group: ↔ BW Control group: ↔ BW.	Pre to post: HIIT group: ↔BMI MICT group: ↔ BMI Control group: ↑BMI

Note: ET: endurance training. RT: resistance exercise, CT: combined training, BIKE: active community by bike, MOD, moderate-intensity exercise, VIG: vigorous-intensity exercise, HIGH, high dose exercise, HIIT: high-intensity intermittent exercise training, MICT: moderate-intensity continuous exercise training, ST: stretchers,TrEE: training energy expenditure, Age in years, BMI in Kg/m^2, Weight: Kg, $\dot{V}$ O2max. maximal rate of oxygen consumption, HR_{max}: maximum heart rate, BW: body weight, Ghr: Total ghrelin, AG: acylated ghrelin, BMI: body mass index.

et al., 2005; Mason et al., 2015; Quist et al., 2019), running (Quist et al., 2019; Rosenkilde et al., 2013; Shakiba et al., 2019), cycling (Foster-Schubert et al., 2005; Guelfi et al., 2013; Rosenkilde et al., 2013; Mason et al., 2015; Sim et al., 2015; Quist et al., 2019), cross-training (Guelfi et al., 2013; Quist et al., 2019), aerobic-based home exercise (Foster-Schubert et al., 2005), and rowing (Quist et al., 2019). Only one study did not specify the mode of endurance exercise (Ahmadi et al., 2019). The resistance training prescribed in all studies focused on all major muscle groups (e.g., chest press, shoulder or military press, leg press, bicep curl, and triceps extension) (Guelfi et al., 2013; Kang et al., 2018; Shakiba et al., 2019).

The duration of the exercise sessions was between 45 and 60 min including a 5–10 min warm-up and cool down. The frequency of exercise sessions varied between studies with three (Guelfi et al., 2013; Shakiba et al., 2019; Sim et al., 2015), four (Ahmadi et al., 2019), five (Foster-Schubert et al., 2005; Kang et al., 2018; Mason et al., 2015; Quist et al., 2019), and seven (Quist et al., 2019; Rosenkilde et al., 2013) sessions per week. The intensity of endurance exercise sessions varied across studies from 50 to 70% oxygen uptake peak/max (VO_2 peak/-max) (Quist et al., 2019; Rosenkilde et al., 2013; Sim et al., 2015) and 60–90% heart rate (HR) max (Ahmadi et al., 2019; Foster-Schubert et al., 2005; Guelfi et al., 2013; Mason et al., 2015; Shakiba et al., 2019). The resistance training intensity was four sets of eight repetitions at 80% of one-repetition maximum (1RM) in the study by Shakiba et al. (2019), and participants progressed from 75% to 85% 1RM in the study by Guelfi et al. (2013). One of the studies using combined exercise (endurance and resistance) intervention prescribed intensity based on the ratings of perceived exertion scale at 12–14 points (somewhat hard) (Kang et al., 2018).

The total duration of the studies ranged from 8 to 52 weeks. In most studies, a 12-week intervention was conducted (Guelfi et al., 2013; Rosenkilde et al., 2013; Sim et al., 2015; Kang et al., 2018; Shakiba et al., 2019) while in other studies 8(Ahmadi et al., 2019), 31 (Quist et al., 2019), and 52 (Foster-Schubert et al., 2005; Mason et al., 2015) week interventions were applied.

3.4. Outcome measures

Total ghrelin concentration was measured by radioimmunoassay (RIA) (Foster-Schubert et al., 2005; Rosenkilde et al., 2013) or enzyme-linked immunosorbent assay (ELISA) (Ahmadi et al., 2019). The method used to measure total ghrelin in the study of Kang et al. (2018) was not described. The concentrations of acylated ghrelin were measured by RIA (Quist et al., 2019), Milliplex Human Gut Hormone Panel (Guelfi et al., 2013), Milliplex Map Human Metabolic Hormone Magnetic Bead Panel (Sim et al., 2015) and ELISA method (Shakiba et al., 2019). PYY concentrations were measured using Milliplex Human Gut Hormone Panel (Guelfi et al., 2013), Milliplex Map Human Metabolic Hormone Magnetic Bead Panel (Sim et al., 2015), ELISA (Shakiba et al., 2019) and RIA (Quist et al., 2019). GLP-1 was measured using the ELISA (Shakiba et al., 2019) and RIA (Quist et al., 2019) methods. CCK was measured by RIA (Quist et al., 2019).

Body mass and height were measured to the nearest 0.1 kg and 0.1 cm, respectively. Several standardised methods were used, including beam scale and stadiometer (Foster-Schubert et al., 2005; Mason et al., 2015), automatic extensometer (Kang et al., 2018), and electronic scales (Quist et al., 2019; Rosenkilde et al., 2013). Body weight and height were used to calculate BMI (kg/m^2).

3.5. Adherence to the interventions

Adherence to training sessions was reported by six studies (Foster-Schubert et al., 2005; Guelfi et al., 2013; Mason et al., 2015; Quist et al., 2019; Rosenkilde et al., 2013; Sim et al., 2015). Adherence to the exercise intervention sessions was high, ranging from 82 to 99%. In the study, conducted by Foster-Schubert et al. (2005), there was similar adherence to supervised and home-based exercise sessions, which accounted for 82% and 87%, respectively. In the study by Guelfi et al. (2013) adherence at 92% did not differ between endurance and resistance training groups. The intensity of exercise sessions also had no effect on training adherence in the study by Sim et al. (2015), in which the high-intensity intermittent exercise group and the moderate-intensity continuous group achieved adherence of 98% and 97%, respectively. Quist et al. (2019) found that women and men similarly adhered to the intervention sessions. For men and women, adherence to cycle training was 91% and 100%, respectively. The adherence was similar for moderate-intensity exercises (men: 100%, women: 99%) and vigorous-intensity exercises (men: 95%, women: 90%).

3.6. Attrition

Five studies presented data for participants who completed the study and did not report any participants dropping out of the study (Ahmadi et al., 2019; Guelfi et al., 2013; Kang et al., 2018; Shakiba et al., 2019; Sim et al., 2015). Four studies reported participants who dropped out from the interventions (Foster-Schubert et al., 2005; Mason et al., 2015; Quist et al., 2019; Rosenkilde et al., 2013), with attrition rates ranging from 2.9% to 7.5%. In the study by Foster-Schubert et al. (2005), four participants (4.5%) dropped out of the exercise and one (1.2%) of the control group. In the study by Quist et al. (2019), the interventions were completed by 87 out of 130 participants, resulting in an overall attrition rate of 33% (11% control group; 46% bike group; 23% moderate-intensity exercise group, and 24% vigorous-intensity exercise group). Only one study reported reasons for dropping out from the exercise intervention and identified that a participant in the high-intensity exercise group dropped out due to the recurrence of a previously experienced injury (Rosenkilde et al., 2013).

3.7. Assessment of risk of bias

Eight studies were judged to be at high risk of bias, with one study considered some concern of risk of bias (Mason et al., 2015). This was due mainly to a lack of reporting across domains. The risk of bias for each domain is presented in the supporting information (Table S1, Supplementary material). Five studies were assessed as low risk of bias for the randomisation process as they reported appropriate methods for sequence generation and allocation concealment; for example, computerised program, block randomisation, and random number generator software (Foster-Schubert et al., 2005; Mason et al., 2015; Quist et al., 2019; Rosenkilde et al., 2013; Sim et al., 2015). Four studies were judged as some concern because although they reported the participants were randomised, they did not provide any details of the methodologies used (Ahmadi et al., 2019; Guelfi et al., 2013; Kang et al., 2018; Quist et al., 2019).

The effect of the intervention assignment was judged as some concern. This was mainly because of the nature of the physical activity interventions making blinding participants and researchers challenging. Information was also not reported regarding deviation arising because of the trial context. Only two studies specified adhering to intention-to-treat analysis (Quist et al., 2019; Rosenkilde et al., 2013). The risk of bias in relation to the effect of adherence to the intervention was high, again due to the lack of blinding of participants and personnel. There was also a lack of information on protocol interventions balanced across intervention groups and inappropriate analysis to estimate the effect of adherence.

The risk of bias for missing outcomes was judged as low for most of the studies and as high for only one study (Quist et al., 2019), which had a high number of dropouts (>20%) and, therefore, missing data on the outcome measures. It was assumed that outcome assessments were not blinded. Selection bias was assessed as low risk of bias in four studies as they reported having a published protocol with a pre-specified statistical analysis plan (Foster-Schubert et al., 2005; Mason et al., 2015; Quist

et al., 2019; Rosenkilde et al., 2013). Five studies were assessed as some concern as it was not reported whether they followed a pre-specified plan (Mason et al., 2015; Guelfi et al., 2013; Kang et al., 2018; Ahmadi et al., 2019; Quist et al., 2019).

3.8. Power and sample size

Only one study reported sample size calculation for appetite hormone outcomes (Shakiba et al., 2019). Four studies conducted sample size calculations for primary outcomes; however, these were not related to appetite hormones (Foster-Schubert et al., 2005; Rosenkilde et al., 2013; Mason et al., 2015; Quist et al., 2019). Four studies did not report sample size calculation; therefore, it is uncertain whether these studies were adequately powered to detect a significant difference in outcome measures.

3.9. Effects of the interventions on gastrointestinal appetite hormones

3.9.1. Total ghrelin

Three studies (four interventions) which measured total ghrelin were included in the meta-analysis (Fig. 2). The pooled effect size illustrated that exercise intervention had no impact on fasting total ghrelin concentration (d: 1.06, 95% CI -0.38 to 2.50, P = 0.15). There was substantial heterogeneity between studies [Q-statistic = 31.50, df = 3, (P = 0.001; I^2 = 90.5%).

Two studies did not provide sufficient data to be included in the meta-analysis (Foster-Schubert et al., 2005; Mason et al., 2015). According to one of these studies, a significant (P = 0.03) increase in fasting total ghrelin concentration was found following endurance exercise training at 75% HR max for 12 months (Foster-Schubert et al., 2005), whereas no change (P = 0.53) in fasting total ghrelin was found in another study that applied 12 months of exercise intervention (Mason et al., 2015).

3.9.2. Acylated ghrelin

Three studies were included in the meta-analysis. Altogether, the three studies included seven exercise interventions (Fig. 3). The pooled effect size illustrated no significant effect on fasting concentration of acylated ghrelin between exercise interventions and control groups (d: 0.08, 95% CI: −0.31 to 0.47, P = 0.68). There was no evidence of statistical heterogeneity between studies [Q-statistic = 3.11, df = 6, (P = 0.795); I^2 = 0%].

One study did not provide sufficient data to be included in the meta-analysis for acylated ghrelin. This study reported a significant decrease of acylated ghrelin concentration in the resistance (P < 0.001), a combined (resistance and endurance) (P < 0.001) and endurance training (P < 0.05) groups after 12 weeks in men with overweight (Shakiba et al., 2019, Table 1).

3.9.3. PYY

PYY levels were reported in four studies. Three out of four studies (seven intervention groups) were included in the meta-analysis. A pooled effect size (Fig. 4) indicated that there was no significant difference in fasting PYY concentration between the exercise and control interventions (d = −0.16, 95% CI: −0.62 to 0.31, P = 0.51). There was substantial heterogeneity between studies [Q-statistic = 8.30, df = 6, (P = 0.22); I^2 = 27.68%].

Two studies were not included in the meta-analysis due to insufficient data (Rosenkilde et al., 2013; Shakiba et al., 2019). In one of these studies, the fasting concentration of PYY was significantly increased due to 12 weeks of resistance (P = 0.03), combined (endurance and resistance) (P = 0.04), and endurance (P = 0.04) training (Shakiba et al., 2019). Another study found that an increase in the fasting PYY concentration tended (P = 0.07) to be higher in the high-dose endurance exercise training group compared to the control group (Rosenkilde et al., 2013).

3.9.4. GLP-1

Two studies measured the effects of exercise training on GLP-1 (Quist et al., 2019; Shakiba et al., 2019). One study investigated the impact of the 6-month endurance training programme with the intensity of exercise sessions corresponding to 70% of $\dot{V}O_2$ peak and it found that after six months, fasting GLP-1 concentration in the exercise group was significantly higher than in the control group (P = 0.04) (Quist et al., 2019). In the study by Shakiba et al. (2019), fasting GLP-1 concentration was not affected by exercise regimens (resistance, endurance, and combined training) after 12 weeks (P > 0.05).

3.9.5. CCK

Only one study investigated the effect of exercise on fasting plasma level of CCK and found that after six months of exercise intervention, fasting CCK concentration did not change (P ≥ 0.5) in any endurance exercise training group (moderate intensity leisure, vigorous-intensity leisure or active commuting by bike) compared with the control group (Quist et al., 2019).

3.9.6. Body mass and BMI

Overall, based on results from seven selected studies, the meta-analysis showed a significant reduction in body mass (d: −0.22, 95% CI: −0.42 to −0.03, P = 0.03). A BMI analysis was conducted based on eight studies and found a significant reduction (d: −0.31, 95% CI: −0.50 to −0.12, P = 0.001) after exercise interventions in comparison to

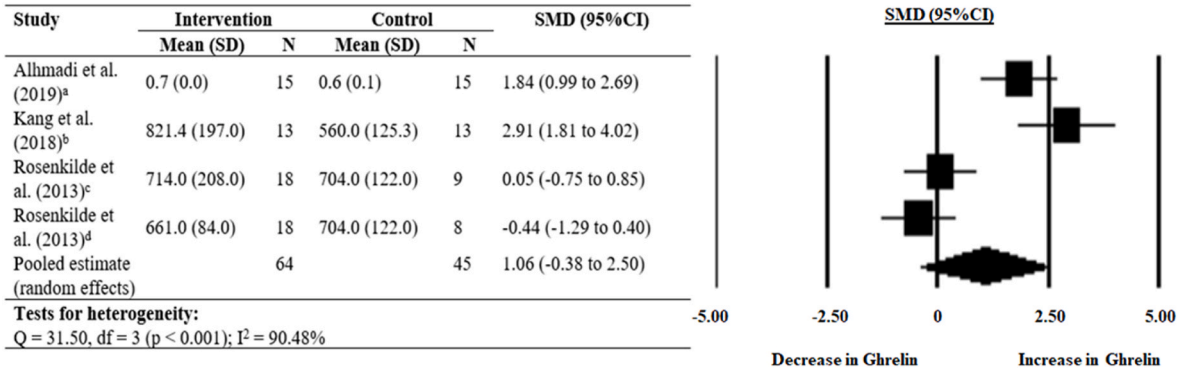

Fig. 2. Forest plot of randomised controlled trials comparing the impact on ghrelin of interventions involving exercise training with non-exercise control group comparators. Effects of trials are presented as means and SDs at the end of the interventions and SMD (95% CI). a, endurance training; b, combined (aerobic and resistance) training; c, endurance training (moderate intensity); d, endurance training (high intensity); DF, degrees of freedom; SMD, standardised mean difference; CI, confidence interval; Q, heterogeneity statistic to test homogeneity; I^2, index of heterogeneity beyond within-study sampling error. In the study of Ahmadi et al. (2019) ghrelin concentration was measured in ng/ml.

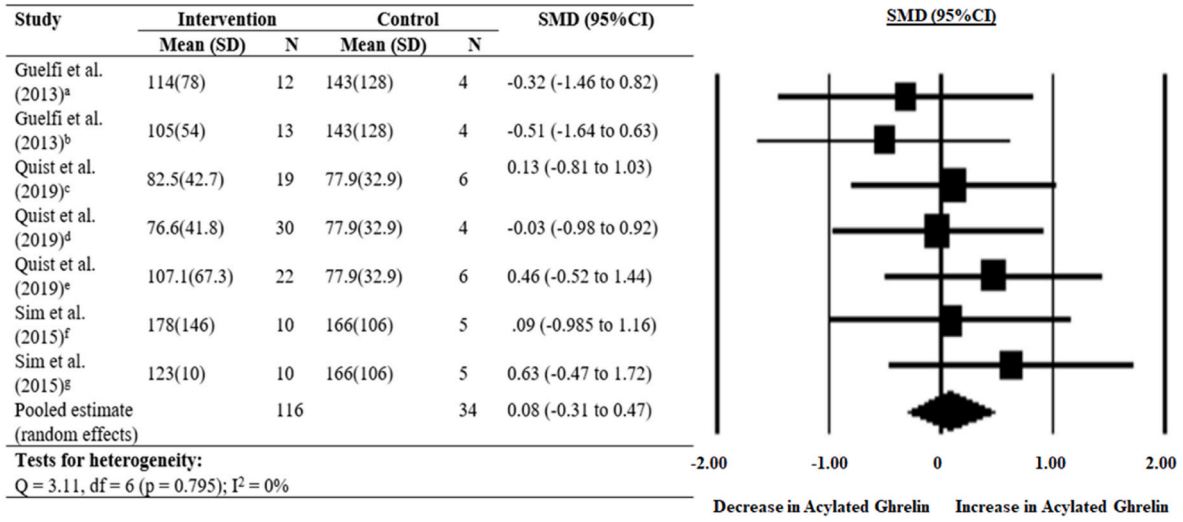

Fig. 3. Forest plot of randomised controlled trials comparing the impact on acylated ghrelin of interventions involving exercise training with non-exercise control group comparators. Effects of trials are presented as means and SDs at the end of the interventions and SMD (95% CI). a, endurance training; b, resistance training program; c, endurance training program (moderate intensity leisure); d, endurance training (vigorous-intensity leisure); e, endurance training (active commuting by bike); f, endurance training (high intensity intermitted exercise training); g, endurance training (continuous moderate intensity training); DF, degrees of freedom; SMD, standardised mean difference; CI, confidence interval; Q, heterogeneity statistic to test homogeneity; I2, index of heterogeneity beyond within-study sampling error.

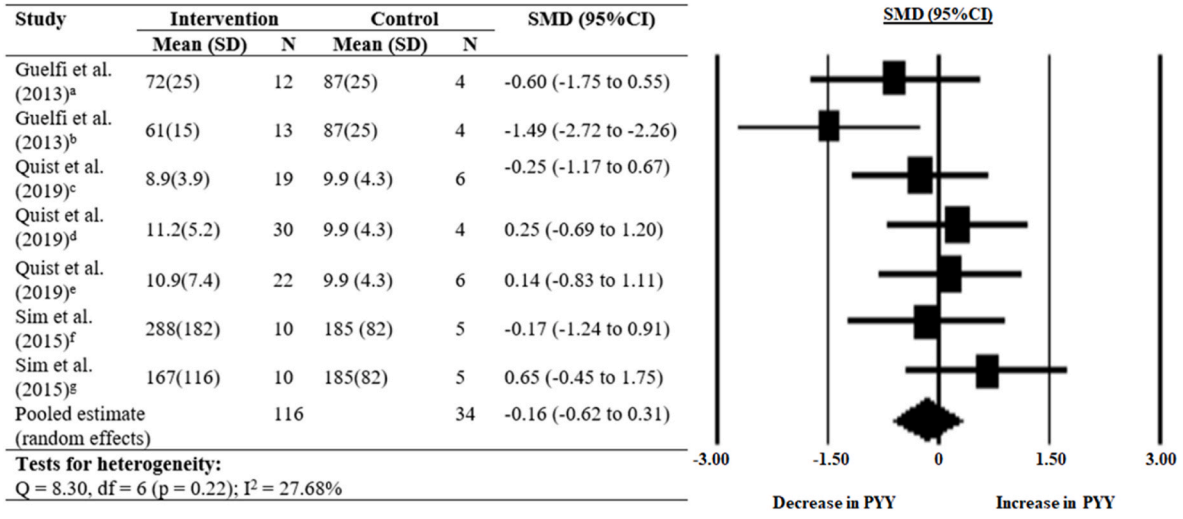

Fig. 4. Forest plot of randomised controlled trials comparing the impact on PYY of interventions involving exercise training with non-exercise control group comparators. a, endurance training; b, resistance training; c, endurance training (moderate intensity leisure); d, endurance training (vigorous-intensity leisure); e, endurance training (active commuting by bike); f, endurance training (continuous moderate-intensity training); g, endurance training (high intensity intermitted exercise training); DF, degrees of freedom; SMD, standardised mean difference; CI, confidence interval; Q, heterogeneity statistic to test homogeneity; I2, index of heterogeneity beyond within-study sampling error.

control (Figs. 5 and 6). In both cases, there was no evidence of statistical heterogeneity between studies for body mass [Q-statistic = 6.16, df = 13, (P = 0.94); I2 = 0%] and BMI [Q-statistics = 10.21, df = 14(P = 0.47); $I^2 = 0\%$]. Two studies had insufficient results to be included in the meta-analysis (Foster-Schubert et al., 2005; Ahmadi et al., 2019). These studies reported significantly reduced body mass and BMI due to 12 months of endurance training (Foster-Schubert et al., 2005) and significantly reduced BMI due to 8 weeks of endurance training (Ahmadi et al., 2019).

3.9.7. Correlation between body mass and appetite hormone changes

Three studies analysed the correlation between body mass and appetite hormones (Foster-Schubert et al., 2005; Mason et al., 2015; Shakiba et al., 2019) and found that weight loss ($P < 0.05$) and reduction in BMI ($P < 0.05$) that occurred with exercise was positively associated with an increase in plasma concentration of total ghrelin ($P < 0.05$) (Foster-Schubert et al., 2005). Increased ghrelin concentrations were also linked to more advanced body weight loss ($P < 0.0001$), and BMI reduction ($P < 0.0001$) in the study by Mason et al. (2015). In the study of Shakiba et al. (2019) body mass loss and BMI reduction were positively correlated with a reduction in acylated ghrelin ($P = 0.003$, $P = 0.009$, respectively) and negatively correlated with an increase in plasma PYY concentration ($P = 0.003$, $P = 0.03$, respectively).

4. Discussion

To the best of our knowledge, this is the first systematic review with meta-analysis to investigate the effect of exercise training programs with

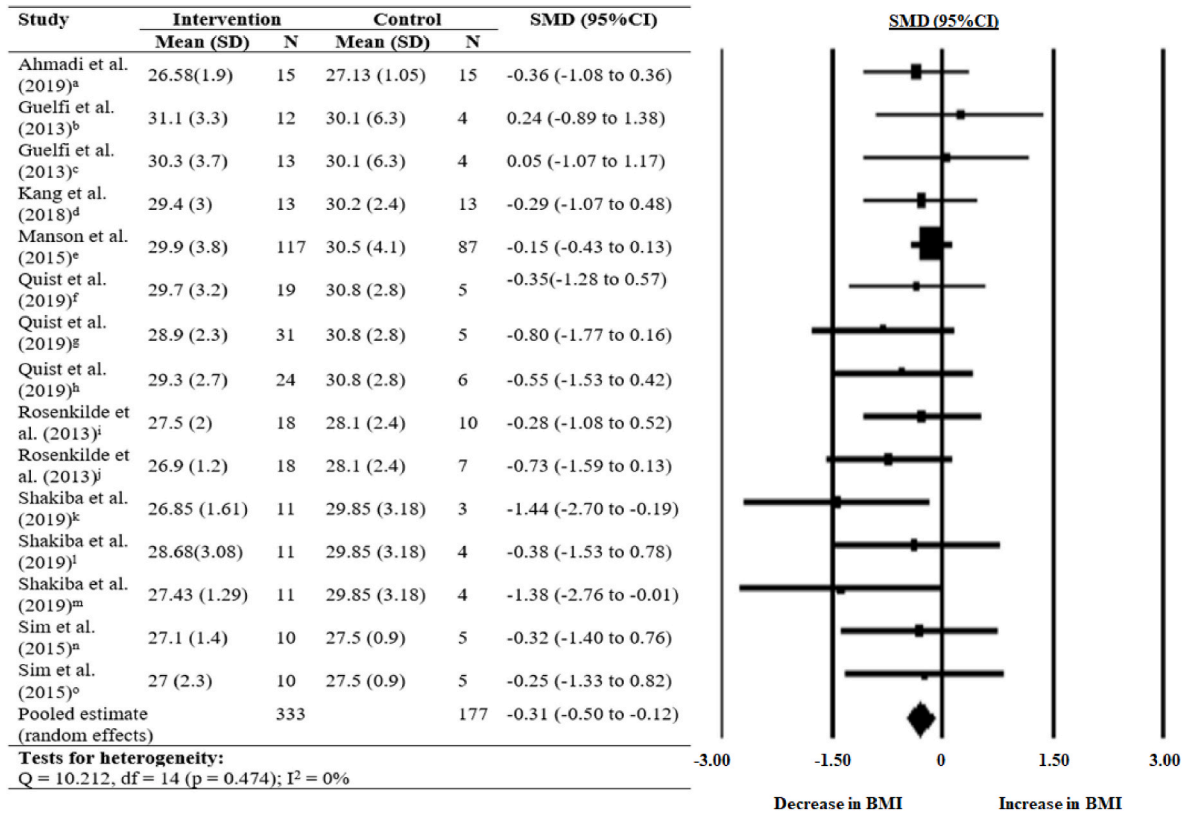

Fig. 5. Forest plot of randomised controlled trials comparing the impact on BMI of interventions involving exercise training with non-exercise control group comparators. a, endurance training; b, endurance training(cycling); c, resistance training; d, combined training; e, endurance training (moderate to vigorous-intensity exercise); f, endurance training (moderate intensity leisure); g, endurance training (vigorous-intensity leisure); h, endurance (active commuting by bike); i, endurance training (moderate-intensity exercise); j, endurance training (high-intensity exercise); k, resistance training; l, endurance training (running); m, combined training; n, endurance training (continuous moderate-intensity training); o, endurance training (high intensity intermitted exercise training); DF = degrees of freedom; SMD = standardised mean difference; CI = confidence interval; Q = heterogeneity statistic to test homogeneity; I2 = index of heterogeneity beyond within-study sampling error.

a duration of at least four weeks on fasting concentrations of gastrointestinal appetite hormones in healthy adults with overweight and obesity. The principal findings of this systematic review and meta-analysis were that exercise training programmes had no impact on fasting concentrations of gastrointestinal appetite hormones such as total ghrelin, acylated ghrelin and PYY in comparison to the control group. We also found that exercise training decreased body mass and BMI in comparison to the control group, though the relation between changes in body mass or BMI and fasting appetite hormones could not be fully explored due to the small number of studies included in this review. The results obtained should be interpreted with caution since our review identified only a few studies, and these were underpowered and carried a high risk of bias. Thus, this systematic review highlights the need for more well-reported RCTs.

Although our systematic review obtained only a few studies in individuals living with overweight and obesity, many studies examining the influence of acute and chronic exercise on appetite regulation have assessed ghrelin, given its relatively unique status as an identified orexigenic hormone (Dorling et al., 2018). Our results indicate that exercise training did not alter fasting concentrations of total ghrelin or acylated ghrelin in individuals with overweight and obesity. The acylated ghrelin results support a recent review showing that, despite some variability, exercise training does not influence acylated ghrelin in most settings (Ouerghi et al., 2021). Nonetheless, in contrast to our results, the same review also demonstrated that exercise increased total ghrelin compared to the control (Ouerghi et al., 2021). It is possible that differences in the populations studied are the reason for these variations. Indeed, the systematic review of Ouerghi et al. (2021) included studies which involved participants with diverse characteristics (e.g., sex, age, body mass and body composition, physical fitness, and health status) while participants of the studies considered in our systematic review were physically inactive adults of ≥18 years and a BMI ranging between 27.1 and 31.8 kg/m^2. In addition, the systematic review of Ouerghi et al. (2021) applied physical exercise intervention alone or combined with other interventions.

Further to ghrelin, numerous anorexigenic hormones have been implicated in appetite regulation in humans (Karra & Batterham., 2010). In this regard, our meta-analysis found no overall effect on fasting concentrations of PYY, with very low substantial heterogeneity between studies that included seven exercise interventions. Though we could not perform a meta-analysis on other anorexigenic hormones, one study that examined CCK concentrations in response to exercise training in individuals living with overweight and obesity found no changes (Quist et al., 2019), and the studies that assessed GLP-1 yielded mixed findings, with one study finding an increase (Quist et al., 2019) and one study finding no change with exercise (Shakiba et al., 2019). Thus, the effect of exercise training on these gastrointestinal satiety hormones clearly requires further investigation in individuals living with overweight and obesity.

Evidence from single-arm exercise intervention studies indicates that training reduces the postprandial suppression of acylated ghrelin and exerts little influence on postprandial PYY, GLP-1 and CCK concentrations (Martins et al., 2010, 2013); yet there are relatively few randomised controlled trials applying exercise training that have assessed gastrointestinal hormones in the postprandial state (Dorling et al., 2018). As a result of this and evidence indicating that exercise training

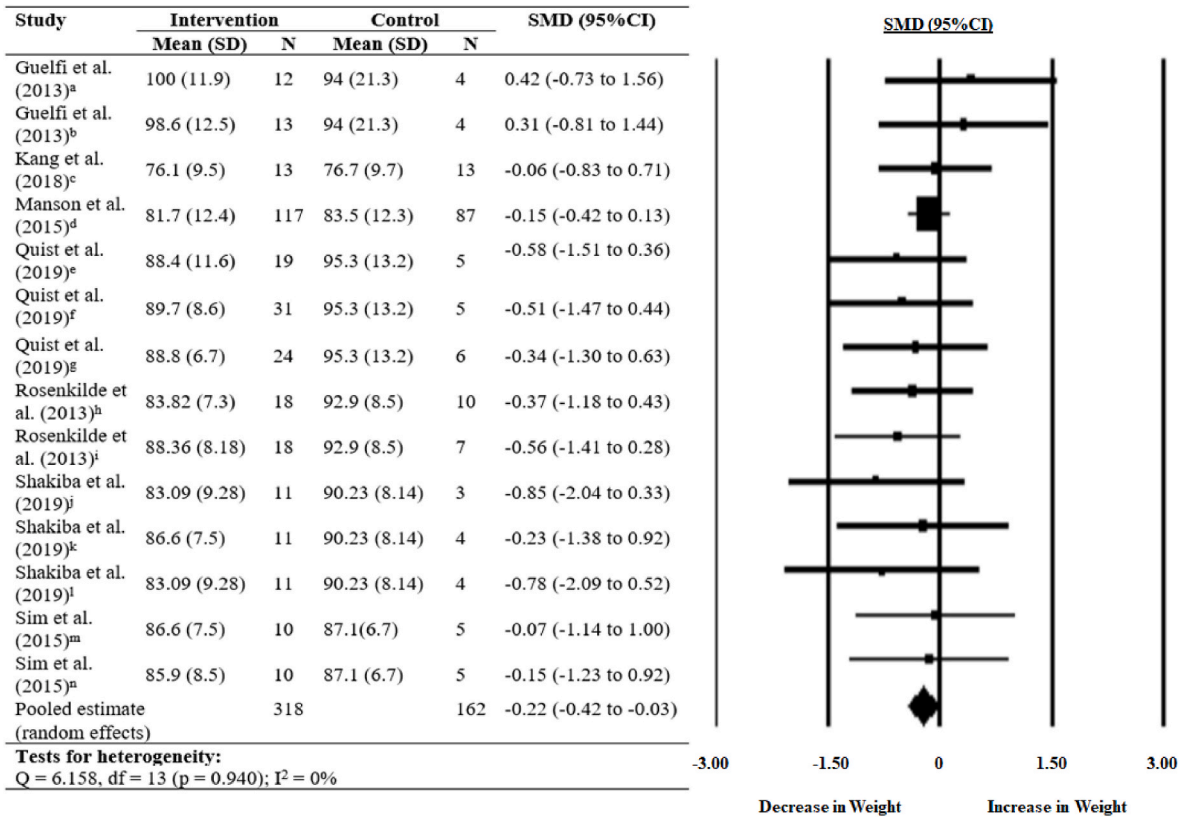

Fig. 6. Forest plot of randomised controlled trials comparing the impact on the weight of interventions involving exercise training with non-exercise control group comparators. a, endurance training (cycling); b, resistance training; c, combined training; d, endurance training (moderate to vigorous intensity); e, endurance training (moderate intensity leisure); f, endurance training (vigorous-intensity leisure); g, endurance training (active commuting by bike); h, endurance training (moderate-intensity exercise); i, endurance training (high-intensity exercise); j, resistance training; k, endurance training; l, combined training; m, endurance training (continuous moderate-intensity training); n, endurance training (high intensity intermitted exercise training); DF = degrees of freedom; SMD = standardised mean difference; CI = confidence interval; Q = heterogeneity statistic to test homogeneity; I2 = index of heterogeneity beyond within-study sampling error.

enhances the coupling between energy intake and exergy expenditure after food consumption (Blundell et al., 2015), additional controlled studies are needed to test how postprandial concentrations of gastrointestinal hormones are influenced by exercise training in individuals with overweight and obesity. Regardless, our systematic review suggests that any compensatory increase in energy intake due to exercise training is unlikely to be related to fasting gastrointestinal appetite hormone changes. At the same time, it is well established that during diet-induced weight loss, these hormones change the direction to favour increased appetite, energy intake and weight regain (Lean & Malkova, 2016; Thom et al., 2020). Thus, findings from this systematic review, combined with the evidence from body weight loss studies applying caloric restrictions, suggest that in individuals living with overweight and obesity sustainability of the achieved negative energy balance might be less challenging during exercise training than applications of caloric restriction.

It is possible that the collective tendency for studies to show non-significant average changes in appetite-related hormones is due to the small exercise-induced body mass loss observed in individuals with overweight and obesity. In line with most studies (Swift et al., 2014), we observed a small decrease in body mass and BMI in response to exercise, and while we could not explore the relationship between appetite-related hormones and body mass, previous studies have indicated that body mass and adiposity significantly influence appetite-related hormones (Lean & Malkova., 2016). Some studies included in this systematic review showed that greater exercise-induced body mass loss increased total ghrelin (Ahmadi et al., 2019; Foster--Schubert et al., 2005; Kang et al., 2018; Mason et al., 2015), though Shakiba et al. (2019) revealed that body mass was positively associated with circulating acylated ghrelin. Thus, further confirmatory work needs to test if greater body mass loss with exercise increases gastrointestinal hormone concentrations.

The finding of no impact of exercise training on mean changes of gastrointestinal appetite hormones and energy intake found in our systematic review might mask the presence of inter-individual variability. Heterogeneity in acylated ghrelin and PYY levels in response to acute exercise bouts has been reported (Goltz et al., 2019) and inter-individual variability in subjective appetite, energy intake and weight change with exercise training is well established (King et al., 2008). In addition, failure to find changes in gastrointestinal appetite hormones may be related to variations in methodological procedures, including differences in food intake during days leading to blood collection (Beaulieu et al., 2017), participant acclimatization to blood sampling procedures and differences in blood collection and processing methods (Chandarana et al., 2009). Given these methodological factors have a significant influence on fasting gastrointestinal hormone concentrations (Chandarana et al., 2009), standardized methodologies in the field should be devised and followed by exercise training studies in individuals with overweight and obesity to facilitate between-study comparisons (Dorling et al., 2018). Efforts could additionally be made to enhance the robustness of study designs by blinding researchers during sample processing and analysis where possible.

A key strength of this systematic review is that a comprehensive literature search strategy was used to identify all relevant research. This systematic review applied rigorous methodology in accordance with PRISMA guidelines (Page et al., 2021), including double screening of studies, data extraction, and assessment of the risk of bias. Further, the inclusion of data from randomised controlled trials provided a true estimate of intervention effects, and we investigated the impact of exercise

on a variety of appetite hormones in this review, rather than just focusing on one hormone. However, only a small number of studies (n = 9) met the inclusion criteria and the number of studies and interventions measuring appetite hormones other than acylated ghrelin was low. Therefore, neither a moderator nor a subgroup (e.g., sex, habitual physical activity, adiposity level, habitual diet) analysis could be conducted to examine the current study's data or assess the heterogeneity between effect estimates between the studies. Such analyses are important because inter-individual variations in gastrointestinal appetite hormones are evident and exploratory analyses have indicated that there are predictors of energy intake and body mass change during exercise training (Dorling et al., 2021; Hö;chsmann et al., 2020). Similarly, the numbers of participants in most studies and interventions were small, which suggests that these studies might be underpowered primarily to detect a significant difference between the groups. The restriction to the English language may be considered a limitation in this review.

In conclusion, this systematic review and meta-analysis indicates that exercise training programmes in individuals living with overweight and obesity have no impact on fasting concentrations of total and acylated ghrelin, PYY, GLP-1 and CCK, which suggests that any upregulation of appetite and energy intake, which is common during participation in exercise training, would be related to factors different from changes in fasting concentrations of gastrointestinal appetite hormones. While the low average body mass loss induced by exercise training may play a role in these findings, there were limited interventions of a high standard as well as inter-individual variability. As a result, further studies that test the influence of exercise training on appetite-related hormones, including responses in the postprandial state, are needed in individuals living with overweight and obesity.

Authors' contribution

Conceived and designed study: DM, LH, TA, CE. Conducted the initial and updated literature search and screening data extraction and risk of bias: TB, SA, LH, TA, AM, SW. Conducted meta-analysis: AM, LH. Wrote the manuscript: TA, DM, LH, JD. All authors performed critical analysis, revision of the manuscript and approved the final version.

Ethics

This manuscript is a systematic review and metanalysis and thus does not require to be approved by independent ethics committed.

Declaration of competing interest

The authors report no conflict of interest.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.appet.2022.106424.

References

Ahmadi, S. M., Fathi, M., RashidLamir, A., & Aminian, F. (2019). Effects of 8 Weeks aerobic training on plasma ghrelin level and ghrelin lymphocyte gene expression in elderly men. *Iranian Journal of Ageing, 13*(4), 494–505. https://doi.org/10.32598/SIJA.13.4.494

Akobeng, A. K. (2005). Understanding randomised controlled trials. *Archives of Disease in Childhood, 90*(8), 840–844. https://doi.org/10.1136/adc.2004.058222

Augustine, V., Gokce, S. K., & Oka, Y. (2018). Peripheral and central nutrient sensing underlying appetite regulation. *Trends in Neurosciences, 41*(8), 526–539. https://doi.org/10.1016/j.tins.2018.05.003

Beaulieu, K., Hopkins, M., Blundell, J., & Finlayson, G. (2017). Impact of physical activity level and dietary fat content on passive overconsumption of energy in non-obese adults. *International Journal of Behavioral Nutrition and Physical Activity, 14*(1), 14. https://doi.org/10.1186/s12966-017-0473-3

Blundell, J. E., Gibbons, C., Caudwell, P., Finlayson, G., & Hopkins, M. (2015). Appetite control and energy balance: Impact of exercise. *Obesity Reviews, 16*, 67–76. https://doi.org/10.1111/obr.12257

Chandarana, K., Drew, M. E., Emmanuel, J., Karra, E., Gelegen, C., Chan, P., Cron, N. J., & Batterham, R. L. (2009). Subject standardization, acclimatization, and sample processing affect gut hormone levels and appetite in humans. *Gastroenterology, 136*(7), 2115–2126. https://doi.org/10.1053/j.gastro.2009.02.047

Cohen, J. (1988). Set correlation and contingency tables. *Applied Psychological Measurement, 12*(4), 425–434. https://doi.org/10.1177/014662168801200410

DerSimonian, R., & Laird, N. (1986). Meta-analysis in clinical trials. *Controlled Clinical Trials, 7*(3), 177–188. https://doi.org/10.1016/0197-2456(86)90046-2

Dorling, J., Broom, D. R., Burns, S. F., Clayton, D. J., Deighton, K., James, L. J., King, J. A., Miyashita, M., Thackray, A. E., Batterham, R. L., & Stensel, D. J. (2018). Acute and chronic effects of exercise on appetite, energy intake, and appetite-related hormones: The modulating effect of adiposity, sex, and habitual physical activity. *Nutrients, 10*(9), 1140. https://doi.org/10.3390/nu10091140

Dorling, J. L., Höchsmann, C., Fearnbach, S. N., Apolzan, J. W., Hsia, D. S., Johannsen, N. M., … Martin, C. K. (2021). Initial weight change and long-term changes in weight and compensation during supervised exercise training. *Medicine & Science in Sports & Exercise, 53*(8), 1675–1684. https://doi.org/10.1249/MSS.0000000000002633

Douglas, J. A., Deighton, K., Atkinson, J. M., Sari-Sarraf, V., Stensel, D. J., & Atkinson, G. (2016). Acute exercise and appetite-regulating hormones in overweight and obese individuals: A meta-analysis. *Journal of Obesity*, 8. https://doi.org/10.1155/2016/2643625. Article ID 2643625.

Foster-Schubert, K. E., McTiernan, A., Frayo, R. S., Schwartz, R. S., Rajan, K. B., Yasui, Y., Tworoger, S. S., & Cummings, D. E. (2005). Human plasma ghrelin levels increase during a one-year exercise program. *Journal of Clinical Endocrinology and Metabolism, 90*(2), 820–825. https://doi.org/10.1210/jc.2004-2081

Gibbons, C., Blundell, J. E., Caudwell, P., Webb, D. L., Hellström, P. M., Näslund, E., & Finlayson, G. (2017). The role of episodic postprandial peptides in exercise-induced compensatory eating. *Journal of Clinical Endocrinology and Metabolism, 102*(11), 4051–4059. https://doi.org/10.1210/jc.2017-00817

Goltz, F. R., Thackray, A. E., Atkinson, G., Lolli, L., King, J. A., Dorling, J. L., … Stensel, D. J. (2019). True interindividual variability exists in postprandial appetite responses in healthy men but is not moderated by the FTO genotype. *Journal of Nutrition, 149*(7), 1159–1169. https://doi.org/10.1093/jn/nxz062

Guelfi, K. J., Donges, C. E., & Duffield, R. (2013). Beneficial effects of 12 weeks of aerobic compared with resistance exercise training on perceived appetite in previously sedentary overweight and obese men. *Metabolism, 62*(2), 235–243. https://doi.org/10.1016/j.metabol.2012.08.002

Hall, K. D., Heymsfield, S. B., Kemnitz, J. W., Klein, S., Schoeller, D. A., & Speakman, J. R. (2012). Energy balance and its components: Implications for body weight regulation. *The American Journal of Clinical Nutrition, 95*(4), 989–994. https://doi.org/10.3945/ajcn.112.036350

Harris, L., McGarty, A., Hutchison, L., Ells, L., & Hankey, C. (2018). Short-term intermittent energy restriction interventions for weight management: A systematic review and meta-analysis. *Obesity Reviews, 19*(1), 1–13. https://doi.org/10.1111/obr.12593

Higgins, J. P., Altman, D. G., Gøtzsche, P. C., Jüni, P., Moher, D., Oxman, A. D., Savovic, J., Schulz, K. F., Weeks, L., Sterne, J. A., & Cochrane Bias Methods Group; Cochrane Statistical Methods Group. (2011). The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *British Medical Journal, 18*(343), d5928. https://doi.org/10.1136/bmj.d5928

Higgins, J. P. T., & Green, S. (Eds.). (2011). *Cochrane Handbook for systematic reviews of interventions*. The Cochrane Collaboration. https://doi.org/10.1002/9780470712184 Version 5.1.0. .

Higgins, J. P., Thompson, S. G., Deeks, J. J., & Altman, D. G. (2003). Measuring inconsistency in meta-analyses. *British Medical Journal, 327*(7414), 557–560. https://doi.org/10.1136/bmj.327.7414.557

Höchsmann, C., Dorling, J. L., Apolzan, J. W., Johannsen, N. M., Hsia, D. S., & Martin, C. K. (2020). Baseline habitual physical activity predicts weight loss, weight compensation, and energy intake during aerobic exercise. *Obesity, 28*(5), 882–892. https://doi.org/10.1002/oby.22766

Jackson, M., Fatahi, F., Alabduljader, K., Jelleyman, C., Moore, J. P., & Kubis, H. P. (2018). Exercise training and weight loss, not always a happy marriage: Single-blind exercise trials in females with diverse BMI. *Applied Physiology Nutrition and Metabolism, 43*(4), 363–370. https://doi.org/10.1139/apnm-2017-0577

Kang, S. J., Kim, J. H., Gang, Z., Yook, Y. S., Yoon, J. R., Ha, G. C., & Ko, K. J. (2018). Effects of 12-week circuit exercise program on obesity index, appetite regulating hormones, and insulin resistance in middle-aged obese females. *Journal of Physical Therapy Science, 30*(1), 169–173. https://doi.org/10.1589/jpts.30.169

Karra, E., & Batterham, R. L. (2010). The role of gut hormones in the regulation of body weight and energy homeostasis. *Molecular and Cellular Endocrinology, 316*(2), 120–128. https://doi.org/10.1016/j.mce.2009.06.010

King, N. A., Hopkins, M., Caudwell, P., Stubbs, R. J., & Blundell, J. E. (2008). Individual variability following 12 weeks of supervised exercise: Identification and characterization of compensation for exercise-induced weight loss. *International Journal of Obesity, 32*(1), 177–184. https://doi.org/10.1038/sj.ijo.0803712

King, J. A., Wasse, L. K., Stensel, D. J., & Nimmo, M. A. (2013). Exercise and ghrelin. A narrative overview of research. *Appetite, 68*, 83–91. https://doi.org/10.1016/j.appet.2013.04.018

Landis, J. R., & Koch, G. G. (1977). The measurement of observer agreement for categorical data. *Biometrics, 33*(1), 159–174. https://doi.org/10.2307/2529310

Lean, M. E. J., & Malkova, D. (2016). Altered gut and adipose tissue hormones in overweight and obese individuals: Cause or consequence? *International Journal of Obesity, 40*(4), 622–632. https://doi.org/10.1038/ijo.2015.220

Manthou, E., Gill, J. M. R., Wright, A., & Malkova, D. (2010). Behavioral compensatory adjustments to exercise training in overweight women. *Medicine & Science in Sports & Exercise, 42*(6), 1121–1128. https://doi.org/10.1249/MSS.0b013e3181c524b7

Martins, C., Kulseng, B., King, N. A., Holst, J. J., & Blundell, J. E. (2010). The effects of exercise-induced weight loss on appetite-related peptides and motivation to eat. *Journal of Clinical Endocrinology and Metabolism, 95*(4), 1609–1616. https://doi.org/10.1210/jc.2009-2082

Martins, C., Kulseng, B., Rehfeld, J., King, N., & Blundell, J. (2013). Effect of chronic exercise on appetite control in overweight and obese individuals. *Medicine & Science in Sports & Exercise, 45*(5), 805–812. https://doi.org/10.1249/MSS.0b013e31827d1618

Martins, C., Morgan, L., & Truby, H. (2008). A review of the effects of exercise on appetite regulation: An obesity perspective. *International Journal of Obesity, 32*(9), 1337–1347. https://doi.org/10.1038/ijo.2008.98

Mason, C., Xiao, L., Imayama, I., Duggan, C. R., Campbell, K. L., Kong, A., Wang, C. Y., Alfano, C. M., Blackburn, G. L., Foster-Schubert, K. E., & McTiernan, A. (2015). The effects of separate and combined dietary weight loss and exercise on fasting ghrelin concentrations in overweight and obese women: A randomized controlled trial. *Clinical Endocrinology, 82*(3), 369–376. https://doi.org/10.1111/cen.12483

McGarty, A. M., Downs, S. J., Melville, C. A., & Harris, L. (2018). A systematic review and meta-analysis of interventions to increase physical activity in children and adolescents with intellectual disabilities. *Journal of Intellectual Disability Research, 62*(4), 312–329. https://doi.org/10.1111/jir.12467

Ouerghi, N., Feki, M., Bragazzi, N. L., Knechtle, B., Hill, L., Nikolaidis, P. T., & Bouassida, A. (2021). Ghrelin response to acute and chronic exercise: Insights and implications from a systematic review of the literature. *Sports Medicine, 51*(11), 2389–2410. https://doi.org/10.1007/s40279-021-01518-6

Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., & Chou, R. (2021). The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ*. https://doi.org/10.1186/s13643-021-01626-4, 372n71.

Quist, J. S., Blond, M. B., Gram, A. S., Steenholt, C. B., Janus, C., Holst, J. J., Rehfeld, J. F., Sjödin, A., Stallknecht, B., & Rosenkilde, M. (2019). Effects of active commuting and leisure-time exercise on appetite in individuals with overweight and obesity. *Journal of Applied Physiology, 126*(4), 941–951. https://doi.org/10.1152/japplphysiol.00239.2018

Rosenkilde, M., Reichkendler, M. H., Auerbach, P., Toräng, S., Gram, A. S., Ploug, T., Holst, J. J., Sjödin, A., & Stallknecht, B. (2013). Appetite regulation in overweight, sedentary men after different amounts of endurance exercise: A randomized controlled trial. *Journal of Applied Physiology, 115*(11), 1599–1609. https://doi.org/10.1152/japplphysiol.00680.2013

Schubert, M. M., Sabapathy, S., Leveritt, M., & Desbrow, B. (2014). Acute exercise and hormones related to appetite regulation: A meta-analysis. *Sports Medicine, 44*(3), 387–403. https://doi.org/10.1007/s40279-013-0120-3

Shakiba, E., Sheikholeslami-Vatani, D., Rostamzadeh, N., & Karim, H. (2019). The type of training program affects appetite-regulating hormones and body weight in overweight sedentary men. *Applied Physiology Nutrition and Metabolism, 44*(3), 282–287. https://doi.org/10.1139/apnm-2018-0197

Sim, A. Y., Wallman, K. E., Fairchild, T. J., & Guelfi, K. J. (2015). Effects of high-intensity intermittent exercise training on appetite regulation. *Medicine & Science in Sports & Exercise, 47*(11), 2441–2449. https://doi.org/10.1249/MSS.0000000000000687

Spiegelman, B. M., & Flier, J. S. (2001). Obesity and the regulation of energy balance. *Cell, 104*(4), 531–543. https://doi.org/10.1016/S0092-8674(01)00240-9

Stensel, D. (2010). Exercise, appetite and appetite-regulating hormones: Implications for food intake and weight control. *Annals of Nutrition and Metabolism, 57*(Suppl. 2), 36–42.

Suzuki, K., Jayasena, C. N., & Bloom, S. R. (2011). The gut hormones in appetite regulation. *Journal of Obesity*. , Article 528401. https://doi.org/10.1159/000322702, 2011.

Swift, D. L., Johannsen, N. M., Lavie, C. J., Earnest, C. P., & Church, T. S. (2014). The role of exercise and physical activity in weight loss and maintenance. *Progress in Cardiovascular Diseases, 56*(4), 441–447. https://doi.org/10.1016/j.pcad.2013.09.012

Thom, G., Dombrowski, S. U., Brosnahan, N., Algindan, Y. Y., Rosario Lopez-Gonzalez, M., Roditi, G., Lean, M. E. J., & Malkova, D. (2020). The role of appetite-related hormones, adaptive thermogenesis, perceived hunger and stress in long-term weight-loss maintenance: A mixed-methods study. *European Journal of Clinical Nutrition, 74*(4), 622–632. https://doi: 10.1038/s41430-020-0568-9.

World health Organization International. (2021). Obesity and overweight. Available at: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight.

Zouhal, H., Sellami, M., Saeidi, A., Slimani, M., Abbassi-Daloii, A., Khodamoradi, A., El Hage, R., Hackney, A. C., & Ben Abderrahman, A. (2019). Effect of physical exercise and training on gastrointestinal hormones in populations with different weight statuses. *Nutrition Reviews, 77*(7), 455–477. https://doi.org/10.1093/nutrit/nuz005