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Highlights

- A single bout of exercise is likely to induce small to large increases in myokine expression immediately after and up to 60 min post-exercise, while myokine responses typically revert to baseline levels from 180 min to 24 h post-exercise.
- Both aerobic exercise and resistance exercise lead to notable changes in the expression of myokines; however, the magnitude of these changes varies according to the specific myokine type.
- This meta-analysis expands our knowledge of the overall effects of myokine expression in relation to exercise modes; however, substantial variation is evident, indicating that the response to exercise mode is myokine-specific.
- Some exercise modes and time points have not been investigated for certain myokines and, thus, should be considered for future research.

Review

Exercise training mode effects on myokine expression in healthy adults:

A systematic review with meta-analysis

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Running head: Exercise training mode effects on myokine expression

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Abstract

Background: The benefits of exercise are well known; however, many of the underlying molecular mechanisms are not fully understood. Skeletal muscle secretes myokines, which mediate muscle–organ crosstalk. Myokines regulate satellite-cell proliferation and migration, inflammatory cascade, insulin secretion, angiogenesis, fatty oxidation, and cancer suppression. To date, the effects of different exercise modes (namely, aerobic and resistance exercise) on myokine response remain to be elucidated. This is crucial considering the clinical implementation of exercise to enhance general health and wellbeing and as a medical treatment.

Methods: A systematic search was undertaken in PubMed, Medline, CINAHL, Embase, SPORTDiscus, and Web of Science in April 2023. Eligible studies examining the effects of a single bout of exercise on IL-15, irisin, SPARC, OSM, and decorin were included. A random-effects meta-analysis was also undertaken to quantify the magnitude of change.

Results: Sixty-two studies were included (n = 1193). Overall, exercise appeared to induce small to large increases in myokine expression, with effects observed immediately after to 60 min post-exercise, although these were mostly not statistically significant. Both aerobic and resistance exercise resulted in changes in myokine levels, without any significant difference between training modes, and with the magnitude of change differing across myokines. Myokine levels returned to baseline levels within 180 min to 24 h post-exercise. However, owing to potential sources of heterogeneity, most changes were not statistically significant, indicating that precise conclusions cannot be drawn.

Conclusion: Knowledge is limited but expanding with respect to the impact of overall and specific effects of exercise on myokine expression at different time points in the systemic circulation. Further research is required to investigate the effects of different exercise modes at multiple time points on myokine response.

Keywords

Myokine; Resistance exercise; Aerobic exercise; Cytokine; Systemic circulation

1. Introduction

The World Health Organization (WHO) defines physical activity as any bodily movement produced by skeletal muscles that requires energy expenditure.[1] The WHO expert panel recommends at least 150–300 or 75–150 min of moderate or vigorous aerobic physical activity, respectively, and strengthening exercises involving all major muscle groups at moderate or high intensity at least twice per week.[1] Exercise is a subset of physical activity that is planned, structured, and repetitive and aims to improve markers of fitness and health, including muscle strength, cardiorespiratory fitness, bone

density, body weight, reduced risk of depression, etc.[1] Additionally, exercise can prevent the possible onset of noncommunicable diseases, including cardiovascular diseases, chronic respiratory diseases, type 2 diabetes mellitus, and cancer.[1] For these reasons, there is a growing interest in exercise for general health and wellbeing and, most recently, as a medical treatment.[1,2]

Although the benefits of exercise are well known, not all the underlying molecular mechanisms are fully understood. Skeletal muscle, which accounts for approximately 40% of total body weight, is recognized as an endocrine organ.[3,4] Indeed, during muscular contractions, skeletal muscle cells secret cytokines called myokines into circulation to exert either paracrine, autocrine, or endocrine effects.[5-8] From a biological perspective, not only are myokines involved in the regulation of muscle metabolism, but they also mediate crosstalk between muscle and organs, including adipose tissue, bone, the liver, the gut, the pancreas, and the brain.[6,9–11] Myokines are implicated in several processes, including satellite-cell proliferation and migration, control of inflammatory cascade and insulin secretion, regulation of angiogenesis and fatty oxidation, and importantly, direct anti-cancer defense (e.g., reducing cancer cell growth).[12,13] As more than 600 myokines have been identified to date, and the role of most of them remains unknown,[6] this review will focus on exercise-induced myokines with established effects on the human body, including interleukin 15 (IL-15), secreted protein acidic and rich in cysteine (SPARC), irisin, oncostatin M (OSM), and decorin.

Briefly, exercise-induced myokine IL-15 contributes to the regulation of muscle mass with its anabolic effects; it is also capable of influencing adipogenesis, reducing adipocyte proliferation and differentiation, altering adipocyte size and number, and promoting apoptosis.[14,15] Additionally, the myokine irisin contributes to the browning of white adipose tissue and is essential for regulating glucose, lipid, and energy homeostasis.[16] Recently, it has been proposed that irisin may also have pro-myogenic effects in skeletal muscle.[17] SPARC is another myokine that plays a pivotal role in muscle metabolism, augmenting fatty acid oxidation and glucose uptake and stimulating insulin sensitivity.[18, 19] Similarly, exercise-induced OSM has also been proposed to mediate muscle hypertrophy, although further research is necessary.[20] Lastly, decorin is considered a candidate in inducing protein synthesis, which leads to muscle growth.[21,22] The role of these myokines in both the prevention and treatment of cancer is particularly interesting. SPARC, irisin, OSM, and decorin have been demonstrated to have potential direct cancer suppressive effects, while IL-15 appears to be an immunomodulator candidate for cancer.[13,23–25] Therefore, a better understanding of these myokines and how they respond to exercise appears to be an important line of investigation for both healthy individuals and for those suffering from disease.

From a physiological perspective, preliminary evidence shows that benefits driven by exercise-induced myokines are the result of an accumulation of single bouts of exercise rather than chronic exposure to exercise training programs.[26] Therefore, it seems logical to investigate the effects of a

single bout of exercise on myokine expression. Although it has been postulated that muscular contractions increase myokine levels in the bloodstream, contradictory results have been found, indicating that more research is necessary to clearly elucidate the effects of a single bout of exercise on myokine expression.[27] In addition, and of utmost importance, the effects of different exercise modes on myokine response remain to be clarified. Indeed, to date, 2 distinct modes are commonly used, namely aerobic exercise (AE) and resistance exercise (RE).[28] This is significant considering the clinical implementation of precise exercise prescription (i.e., AE or RE) to enhance general health and wellbeing and as a form of medical treatment (e.g., cancer-suppressive effects of exercise).[13]

To the best of our knowledge, no systematic reviews or meta-analyses have been conducted to explore either the effects of a single bout of exercise on IL-15, SPARC, OSM, and decorin expression nor the potential differential effects by exercise mode. Although recent reviews have been reported on the effects of a single bout of exercise on the acute irisin response (i.e., immediately after exercise),[29–31] our meta-analysis is the first to examine the effects of different exercise modes across different time points (i.e., up to 24 h after exercise). Thus, the aims of this systematic review with meta-analysis were 3-fold: (a) to examine the overall effects of a single bout of exercise on IL-15, irisin, SPARC, OSM, and decorin expression in healthy adults; (b) to determine the effects of different exercise modes (i.e., AE, RE, and combined) on myokine responses; and (c) to investigate changes in myokine expression at different time points (i.e., from immediately up to 24 h) after a single bout of exercise.

2. Methods

2.1. Search strategy and study selection procedure

All procedures were conducted in compliance with the guidelines outlined by the Cochrane Back Review Group,[32] adhering to the reporting standards established in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (Fig. 1),[33,34] and registered with the International Prospective Register of Systematic Reviews (PROSPERO: CRD42023414177). The search was conducted in Medline (via PubMed), CINAHL, Embase, SPORTDiscus (via EBSCOhost), and Web of Science in April 2023. A manual search was undertaken in the reference lists provided in all retrieved studies. Eligibility was assessed independently by 2 reviewers (FB and AMM) and evaluated by a third reviewer in case of disagreement (JSK). The search strategy is presented in the Supplementary File (Search terms).

2.2. Eligibility criteria

For the current review, we included randomized or non-randomized clinical trials, cross-over (>72 h wash-out period), and single-group studies investigating the effects of AE, RE or combined AE and RE on myokine expression. Primary outcomes were changes in the myokine expression (including IL-15, irisin, SPARC, OSM, and decorin) immediately after; 30 min, 60 min, 120 min, or 180 min; or 24 h after a single bout of AE, RE, or combined exercise. The inclusion criteria were sedentary, physically active, or trained adults (≥18 years) randomized or enrolled to perform a single bout of exercise. Exclusion criteria were: (a) studies involving participants with chronic conditions (e.g., type 2 diabetes, cancer, etc.); (b) body mass index (BMI) > 30 kg/m^2; (c) studies with no precise indications regarding volume and intensity and different exposure for each subject participating (e.g., marathon or football matches); (d) studies including any other intervention coupled with exercise (e.g., diet, cold or heat exposure); and (e) studies written in a language other than English.

2.3. Data extraction

Data extraction was performed by 2 independent authors (FB and AMM). Study information, including sample size, gender, physical status, age, BMI, study design, and training intervention were extracted along with the outcomes of interest. For the outcomes examined, baseline and post-intervention assessments were extracted in their absolute units, inclusive of mean and standard deviation (SD). When graphs were used instead of numerical data, we assessed graphs by analyzing their plots using a specific tool for data extraction (Version 4.7; WebPlotDigitizer, San Francisco, CA, USA).[35] As initially planned, the TESTEX scale was selected to assess the risk of bias.[36] It should be noted that the TESTEX scale is used to investigate items for chronic training interventions, including allocation concealment, blinding of participants and assessors, outcomes measured in 85% of subjects, between-group statistical comparison, monitoring of the control group, and constancy of exercise intensity during the interventions. However, the current review looks at studies examining a single bout of exercise (and often lacking a control group), meaning the majority of included studies adopted a single group assessment of within-group pre and post changes (Supplementary Table 1). Consequently, most of the items in the original TESTEX scale were inappropriate. Therefore, the authors decided not to use the risk of bias tool, which is in line with previous reviews investigating the effects of a single bout of exercise.[37–39] This highlights the fact that there is currently no validated scale for acute studies.

2.4. Statistical analysis

A 3-level mixed-effects meta-analysis with study included as a random effect was performed to examine the acute effects of a single bout of exercise on myokine response. A minimum of 2 studies

were required to run a meta-analysis for each myokine at a given time point. Given the availability of several dependent outcomes from the same study, a robust variance estimation approach was undertaken to account for the nested structure of the effect sizes calculated from the studies included (i.e., effects nested within categories nested within studies).[40] The pooled effect estimated from the outcomes of interest was obtained from within-group mean difference (MD) and expressed as the standardized mean difference (SMD). Cluster robust point estimates 95% confidence intervals (95%CIs) were reported, weighted by inverse sampling variance to account for the within- and between-study variance (τ^2). In addition, restricted maximal-likelihood estimation was used in all models. The criterion for statistical significance was set at $p < 0.05$. According to Hedges' g, SMD values of 0.00 to ≤0.50 indicate small, >0.50 to 0.79 moderate, and ≥0.80 large effects.[41]

Statistical heterogeneity was assessed using the Cochran Q test. A threshold p value of 0.1 and values greater than 50% in I^2 were considered indicative of high heterogeneity. Publication bias was explored by contour-enhanced funnel plots and Egger's test when more than 10 studies were available.[42] Subgroup analyses were provided for: (a) different exercise modes (i.e., AE, RE, and combined exercise); (b) different time points, from immediately after (i.e., within 10 min from blood collection) to 24 h after; and (c) different physical activity statuses (i.e., sedentary, physically active, trained) when available. A meta-regression was also undertaken to quantify the association of age with changes in outcomes of interest when more than 10 studies were available.[42]

Analyses were conducted using the package metafor and clubSandwich from R (R Core Team, Version, 4.0.3., 2020; R Foundation for Statistical Computing, Vienna, Austria).[43]

3. Results

A total of 6599 studies were retrieved from our search, with 3911 potential records retained for screening after duplicate removals. After excluding 2642 records due to their irrelevance to the research question, 1215 were considered eligible for full-text assessment (Fig. 1). A total of 62 articles investigating the effects of AE, RE, or combined exercise on IL-15, irisin, SPARC, OSM, or decorin expression at different time points were subsequently included in the meta-analyses.[44–105]

3.1. Participants and intervention characteristics

A total of 1193 healthy adults participated in the included studies; median age was 29.74 years (interquartile range: 22.3–29.9 years) and median BMI was 23.64 kg/m^2 (interquartile range: 22.1–24.8 kg/m^2). Among the participants, there were 676 men and 227 women, as well as 290 participants whose gender was not reported. From the 62 studies, a total of 240, 267, and 379 subjects were

classed as trained, physically active, and sedentary, respectively, while physical fitness status was not stated for 307 subjects. In regard to the exercise modes, a single bout of AE, RE, and combined exercise was used in 48, 17, and 2 interventions, respectively (Supplementary Table 1).[44–105]

For AE, which included running, cycling, and rowing, moderate intensity continuous aerobic exercise (MICAE) and high intensity aerobic exercise (HIAE; encompassing both incremental test to exhaustion and high intensity interval training) were used in 29 and 21 interventions, respectively.[44,46,47,51–61,64,66,68–71,73–86,89–94,96,97,100–105] Training duration (e.g., minutes) and intensity (e.g., maximal oxygen consumption (VO_{2max})) for AE was reported in 45 and 48 interventions, respectively. MICAE duration ranged from 20 to 180 min with an intensity set from 40% to 80% VO_{2max}, 60% to 110% maximal heart rate (HR_{max}), or 40% to 70% heart rate reserve ($HR_{reserve}$). For HIAE, the duration of the higher intensity bouts ranged from 20 sec to 5 min with an intensity from 57% to 64% HR_{max}, 70% to 75% $HR_{reserve}$, or maximal effort. Additionally, some interventions performed an incremental bout of HIAE to exhaustion without any bout at lower intensity.

For RE, 17 interventions utilized traditional RE, 2 used cluster sets and concentric RE separately, and there was 1 intervention each for eccentric and isometric RE.[45,48–50,58,63,65,67,70,72,83,87,88,95,98,99,102] Volume in terms of sets and repetitions ranged from 1 to 5 sets and from 5 to 30 repetitions with intensity from 30% to 100% of 1-repetition maximum (1RM); apart from 2 interventions where RE to volitional exhaustion was adopted. The number of exercises ranged from 1 to 10 across all interventions.

Regarding combined AE and RE, 2 interventions were found including RE (i.e., 3 sets of 12 repetitions at 65% 1RM), AE (i.e., 30 min at 65% VO_{2max}), and multimodal exercise (i.e., jogging, gymnastics, and sprints).[62, 83]

In the following sub-headings, we reported the overall effects of a single bout of exercise and, when available, the effects of a single bout of AE, RE, or combined exercise. Similarly, when available, we recorded each time point from immediately after up to 24 h after the single bout of exercise. Additionally, it should be noted that the number of studies and effect sizes for each exercise mode may differentiate from the overall effect. This comes from the fact that meta-analyses were performed only if sufficient data for each exercise mode were available.

3.2. IL-15

3.2.1. Main model effects, sensitivity analysis, and subgroup analysis

Main model. Twenty studies and 74 effect sizes were undertaken for the IL-15 model[45, 48, 50, 52, 58, 61, 63, 64, 66, 72, 74, 77, 80, 90, 92, 93, 95, 97-99] (Table 1). When examining the main model effect, a non-significant large increase was found (SMD = 0.95; 95%CI: –0.23 to 2.13; $p = 0.11$). The heterogeneity I^2 was 46.70%

with an effect of publication bias (t = 5.3; p < 0.001). No statistically significant differences between AE and RE (p = 0.10) (Supplementary Table 2) or by different physical activity status (SMD = 0.07–1.28; p = 0.22–0.48) (Supplementary Table 3) were observed. In addition, age was not significantly associated with changes in IL-15 (β = –0.008 ± 0.02; p = 0.73) (Supplementary Fig. 1).

Immediately after. Twenty studies and 34 effect sizes were undertaken for IL-15 expression immediately after a single bout of exercise compared to baseline[45,48,50,52,58,61,63,64,66,72,74,77,80,90,92,93,95,97–99] (Table 1 and Fig. 2). When examining the overall effect, a non-significant large increase was found (SMD = 1.14; 95%CI: –0.21 to 2.49; p = 0.09). For AE a non-significant small increase was found (SMD = 0.17; 95%CI: –0.27 to 0.60; p = 0.41) while for RE a non-significant large increase was found (SMD = 2.66; 95%CI: –0.67 to 5.99; p = 0.10). No statistically significant differences between AE and RE were observed (p = 0.08) (Supplementary Table 2).

30 min after. Four studies and 8 effect sizes were undertaken for IL-15 expression 30 min after a single bout of exercise compared to baseline[58,63,95,99] (Table 1). When examining the overall effect, a non-significant large increase was found (SMD = 1.64; 95%CI: –2.92 to 6.20; p = 0.33). For RE, a non-significant large increase was found (SMD = 1.48; 95%CI: –3.30 to 6.26; p = 0.40). The other effect sizes were composed by AE from the same study, preventing meta-analysis from being performed.

60 min after. Ten studies and 15 effect sizes were undertaken for IL-15 expression 60 min after a single bout of exercise compared to baseline[48,61,63,66,80,90,93,95,98,99] (Table 1). When examining the overall effect, a non-significant large increase was found (SMD = 1.49; 95%CI: –0.85 to 3.83; p = 0.18). For AE there was no effect (SMD = 0.01; 95%CI: –0.23 to 0.22; p = 0.95) while for RE a non-significant large increase was found (SMD = 3.11; 95%CI: –2.47 to 8.69; p = 0.20). No statistically significant differences between AE and RE were observed (p = 0.12) (Supplementary Table 2).

120 min after. Two studies and 2 effect sizes were undertaken for IL-15 expression 120 min after a single bout of exercise compared to baseline[93,95] (Table 1). When examining the overall effect, a non-significant large increase was found (SMD = 3.69; 95%CI: –40.72 to 48.10; p = 0.48). The effect sizes were composed by 1 AE and 1 RE.

180 min after. Four studies and 4 effect sizes were undertaken for IL-15 expression 180 min after a single bout of exercise compared to baseline[74,77,80,93] (Table 1). When examining the overall effect, a non-significant change was found (SMD = 0.00; 95%CI: –0.32 to 0.32; p = 0.98). As the studies only included AE, results are the same when subgrouping by exercise mode.

24 h after. Seven studies and 11 effect sizes were undertaken for IL-15 expression 24 h after a single bout of exercise compared to baseline[63,72,74,93,95,98,99] (Table 1). When examining the overall effect, a non-significant large increase was found (SMD = 1.35; 95%CI: –1.29 to 3.98; p = 0.26). For AE a

non-significant small increase was found (SMD = 0.34; 95%CI: –3.46 to 4.14; $p = 0.46$) while for RE a non-significant large increase was found (SMD = 1.72; 95%CI: –2.66 to 6.10; $p = 0.34$). No statistically significant differences between AE and RE were observed ($p = 0.39$) (Supplementary Table 2).

3.3. Irisin

3.3.1. Main model effects, sensitivity analysis, and subgroup analysis

Main model. Thirty-six studies and 110 effect sizes were undertaken for the irisin model[44,46,47,49,54–57,59,60,62,65,67–71,73,76,78,81–86,88,89,91,94,96,100–103,105] (Table 2). When examining the main model effect, a non-significant small increase was found (SMD = 0.44; 95%CI: –0.04 to 0.91; $p = 0.07$). The heterogeneity I^2 was 40.20% with no effect of publication bias ($t = –0.1$; $p = 0.92$). No statistically significant differences between AE and RE ($p = 0.38$) (Supplementary Table 2) or by different physical activity status (SMD = 0.24–1.24; $p = 0.23$–0.30) (Supplementary Table 3) were observed. In addition, age was not significantly associated with changes in irisin ($\beta = 0.01 \pm 0.01$; $p = 0.57$) (Supplementary Fig. 2).

Immediately after. Thirty-four studies and 58 effect sizes were undertaken for irisin expression immediately after a single bout of exercise compared to baseline[44,46,47,49,54–57,59,60,62,65,67–71,73,76,78,81–86,88,89,91,94,100–103] (Table 2 and Fig. 3). When examining the overall effect, a non-significant small increase was found (SMD = 0.50; 95%CI: –0.22 to 1.22; $p = 0.17$). For AE a non-significant moderate increase was found (SMD = 0.63; 95%CI: –0.30 to 1.56; $p = 0.18$) while for RE a non-significant small increase was found (SMD = 0.10; 95%CI: –0.29 to 0.48; $p = 0.55$). When examining the effect of combined exercise, a non-significant small increase was found (SMD = 0.26; 95%CI: –0.42 to 0.94; $p = 0.13$). No statistically significant differences between AE and RE were observed ($p = 0.39$) (Supplementary Table 2).

30 min after. Eleven studies and 17 effect sizes were undertaken for irisin expression 30 min after a single bout of exercise compared to baseline[55,56,62,65,76,83,86,94,96,102,105] (Table 2). When examining the overall effect, a non-significant moderate increase was found (SMD = 0.81; 95%CI: –0.35 to 1.98; $p = 0.15$). For AE a non-significant large increase was found (SMD = 1.18; 95%CI: –0.52 to 2.87; $p = 0.14$) while for RE a non-significant small increase was found (SMD = 0.02; 95%CI: –0.31 to 0.35; $p = 0.81$). When investigating the effect of combined exercise, a non-significant small increase was found (SMD = 0.13; 95%CI: –4.71 to 4.97; $p = 0.79$). No statistically significant differences between AE and RE were observed ($p = 0.26$) (Supplementary Table 2).

60 min after. Seven studies and 12 effect sizes were undertaken for irisin expression 60 min after a single bout of exercise compared to baseline[65,70,83,84,86,89,102] (Table 2). When examining the overall

effect, a significant small increase was found (SMD = 0.38; 95%CI: 0.05–0.71; p = 0.03). For AE a significant small increase was found (SMD = 0.40; 95%CI: –0.01 to 0.81; p = 0.05); similarly, for RE a non-significant small increase was found (SMD = 0.32; 95%CI: –1.21 to 1.85; p = 0.47). No statistically significant differences between AE and RE were observed (p = 0.83) (Supplementary Table 2).

120 min after. Five studies and 8 effect sizes were undertaken for irisin expression 120 min after a single bout of exercise compared to baseline[65,69,70,83,84] (Table 2). When examining the overall effect, a non-significant small increase was found (SMD = 0.09; 95%CI: –0.21 to 0.39; p = 0.40). For AE there was no effect (SMD = 0.01; 95%CI: –0.33 to 0.34; p = 0.94); similarly, for RE a non-significant small increase was found (SMD = 0.09; 95%CI: –0.71 to 0.88; p = 0.69). No statistically significant differences between AE and RE were observed (p = 0.71) (Supplementary Table 2).

180 min after. Six studies and 11 effect sizes were undertaken for irisin expression 180 min after a single bout of exercise compared to baseline[46,57,73,82–84] (Table 2). When examining the overall effect, a non-significant small decrease was found (SMD = –0.14; 95%CI: –0.75 to 0.46; p = 0.55). For AE a non-significant small decrease was found (SMD = –0.26; 95%CI: –0.76 to 0.24; p = 0.23). The other effect sizes were composed by RE from the same study, preventing meta-analysis from being performed.

24 h after. Two studies and 4 effect sizes were undertaken for irisin expression 24 h after a single bout of exercise compared to baseline[70,86] (Table 2). When examining the overall effect, there was no effect (SMD = 0.05; 95%CI: –0.80 to 0.89; p = 0.61). For AE there was no effect (SMD = –0.01; 95%CI: –2.25 to 2.24; p = 0.97). The other effect sizes were composed by RE from the same study, preventing meta-analysis from being performed.

3.4. SPARC

3.4.1. Main model effects, sensitivity analysis, and subgroup analysis

Main model. Seven studies and 16 effect sizes were undertaken for the SPARC model[50,52,53,75,79,93,104] (Table 3). When examining the main model effect, a non-significant small increase was found (SMD = 0.32; 95%CI: –0.06 to 0.69; p = 0.08) and the heterogeneity I^2 was 0%.

Immediately after. Seven studies and 9 effect sizes were undertaken for SPARC expression immediately after a single bout of exercise compared to baseline[50,52,53,75,79,93,104] (Table 3 and Fig. 4). When examining the overall effect, a significant small increase was found (SMD = 0.50; 95%CI: 0.01–0.99; p = 0.05). For AE a significant moderate increase was found (SMD = 0.66; 95%CI: 0.24–

1.07; p = 0.01). The other effect sizes were composed by RE from the same study, preventing meta-analysis from being performed.

60 min after. Two studies and 2 effect sizes were undertaken for SPARC expression 60 min after a single bout of exercise compared to baseline[79,93] (Table 3). When examining the overall effect, there was no effect (SMD = –0.04; 95%CI: –0.17 to 0.08; p = 0.14). As the studies only included AE, results are the same when subgrouping by exercise mode.

180 min after. Two studies and 2 effect sizes were undertaken for SPARC expression 180 min after a single bout of exercise compared to baseline[93,104] (Table 3). When examining the overall effect, a non-significant small increase was found (SMD = 0.12; 95%CI: –5.30 to 5.54; p = 0.82). As the studies only included AE, results are the same when subgrouping by exercise mode.

24 h after. Two studies and 2 effect sizes were undertaken for SPARC expression 24 h after a single bout of exercise compared to baseline[93,104] (Table 3). When examining the overall effect, a non-significant small decrease was found (SMD = –0.26; 95%CI: –6.85 to 6.32; p = 0.70). As the studies only included AE, results are the same when subgrouping by exercise mode.

3.5. OSM

3.5.1. Main model effects, sensitivity analysis, and subgroup analysis

Main model. Three studies and 11 effect sizes were undertaken for the OSM model[51–53] (Table 3). When examining the main model effect, a non-significant small increase was found (SMD = 0.08; 95%CI: –2.40 to 2.56; p = 0.90) and the heterogeneity I^2 was 32.50%.

Immediately after. Three studies and 7 effect sizes were undertaken for OSM expression immediately after a single bout of exercise compared to baseline[51–53] (Table 3 and Fig. 5). When examining the overall effect, a non-significant small increase was found (SMD = 0.33; 95%CI = –1.23 to 1.88; p = 0.43). As the studies only included AE, results are the same when subgrouping by exercise mode.

3.6. Decorin

3.6.1. Main model effects, sensitivity analysis, and subgroup analysis

Main model. Two studies and 13 effect sizes were undertaken for the decorin model[87,98] (Table 3). When examining the main model effect, a non-significant large increase was found (SMD = 0.99; 95%CI = –11.14 to 13.12; p = 0.49) and the heterogeneity I^2 was 39%.

24 h after. Two studies and 5 effect sizes were undertaken for decorin expression 24 h after a single bout of exercise compared to baseline[87,98] (Table 3). When examining the overall effect, a non-significant large increase was found (SMD = 1.11; 95%CI: –14.04 to 16.26; p = 0.52). As the studies only included RE, results are the same when subgrouping by exercise mode.

4. Discussion

To the best of our knowledge this is the first systematic review and meta-analysis examining the overall and specific effects of different exercise modes after a single bout of exercise on the expression of IL-15, irisin, SPARC, OSM, and decorin in healthy adults at different time points post-exercise. There are 3 important findings. First, a single bout of exercise appeared to induce small to large increases in myokine expression, especially when blood was collected immediately after and up to 60 min post-exercise, although due to the large variation in response, the changes were, for the most part, not statistically significant. Second, AE and RE induce alterations in myokine expression with the magnitude of change differing across myokines, although no statistically significant difference was observed between training modes. Third, myokine responses from 180 min to 24 h post-exercise reverted to baseline levels. However, as noted above, most changes were not statistically significant, and so precise conclusions cannot be drawn. Nevertheless, the findings from the current study provide insights into the impact of a single bout of exercise on myokine expression at different time points and emphasize the need for further research to clearly elucidate the effects of a single bout of exercise on myokine response.

4.1. IL-15

Collectively, we examined the exercise effects on IL-15 in healthy individuals and found evidence that a single bout of exercise is likely effective in inducing increases in IL-15 responses from immediately post-exercise up to 24 h post-exercise. However, caution should be taken as some effect sizes showed large variations in CIs, which partially explains the lack of statistically significant difference as well as the wide response after exercise (Table 1). When data were available, the sub-group analyses revealed that RE appeared to elicit higher IL-15 expression compared to AE, and this was observed immediately after and 60 min post-exercise. The underlying reasons are not readily apparent; however, it should be noted that some studies adopted HIAE with low total volume (i.e., 10 min)[58] while in other studies MICAE lasted only 30 min, which may be below the stimulus threshold to drive substantial changes in IL-15 expression (Supplementary Table 1).[61,64,80] To further support this, He et al.[106] did not report significant differences when comparing a single bout of RE *vs.* HIAE performed for 45–50 min at different time points (i.e., from immediately after up to 72 h post-exercise). Taken together, the volume and intensity adopted for some AE bouts may have skewed the

results and, consequently, limited physiological modifications to occur. In contrast, it should be noted that the exercise prescriptions for RE in most of the studies included[45,48,72,98] were in line with the current guidelines,[107] increasing confidence in the findings reported. Additionally, we observed a relatively high heterogeneity (I^2 up to 49.70%), which may have accounted for exercise mode differences. Overall, although no significant differences were observed at any time point, it appears that a single bout of exercise, especially when RE is performed, may represent an exercise mode capable of inducing changes in IL-15 levels at different time points.

4.2. Irisin

It appears that irisin expression increases up to 60 min after a single bout of exercise, which was statistically significant, with a gradual decline to baseline levels over the subsequent 24-h period (Table 2). Although a direct comparison could not be performed and no statistically significant difference was observed, it appears that larger effects were observed when subjects performed a single bout of AE compared to RE, especially up to 60 min post-exercise, even though relatively high heterogeneity was found I^2 = 42.70%–46.50%. Interestingly, such differences in irisin levels after AE *vs.* RE were not observed at the other time points. In this regard, it should be acknowledged that the low to moderate intensity (i.e., 40%–60% 1RM) and the number of exercises performed (i.e., only 1 exercise per session) in some RE interventions may have impeded substantial change (Supplementary Table 1).[65,67,88,102] In contrast, higher volume (i.e., up to 120 min) and intensity (i.e., 60%–80% VO_{2max} or 70% $HR_{reserve}$) performed as MICAE or HIAE likely elicited more substantial increases in irisin.[46,55, 56,59,69,70,73,76,81,83,84,89] Furthermore, the number of studies using RE were substantially lower than those using AE; therefore, caution should be taken when comparing these exercise modes for irisin.

Our results are also in line with those of Fox et al.,[29] who found clinically significant increases in irisin expression by 15% immediately after a single bout of exercise without subgrouping by exercise mode. In contrast, our meta-analysis did not reveal statistically significant changes; however, our inclusion criteria differed from the study done by Fox et al.,[29] which included obese subjects with or without metabolic conditions. This may have altered the results as different responses were found when investigating the effects of a single bout of exercise on irisin expression in lean *vs.* obese subjects,[62] highlighting the influence of excessive adipose tissue and low skeletal muscle mass on myokine expression.[93,108] In agreement with our findings, a review by Kazeminasab et al.[31] reported that a single bout of exercise increased irisin expression in healthy individuals (although it was not statistically significant), with AE inducing larger responses compared to RE. However, we examined multiple time points up to 24 h post-exercise, whereas Kazeminasab et al.[31] included blood collected from immediately after up to 54 min after exercise in the same analysis. Such an approach might have

introduced potential variations into the outcome, considering the potential of different effects at these time points.[109] Similarly, researchers recently investigated the effects of AE on irisin expression, observing significant increases after a single bout of exercise.[30] However, it should be noted that the authors included cross-over trials with only a 48-h wash-out period.[110] Although evidence is still sparse, it has been assumed that myokines are elevated immediately after exercise followed by a rapid decrease to baseline levels (i.e., from a few hours to more than 24 h).[111] Therefore, including cross-over trials with less than 72 h of total rest may have influenced the results. Taken together, the multiple time point assessments and the robust inclusion criteria in our analysis allow for a more nuanced understanding of irisin expression, enabling insights into the specific response after a single bout of exercise. In summary, although significant differences were few, irisin appears to be elevated by AE up to 60 min after a single bout of exercise.

4.3. SPARC

A single bout of exercise induced significant SPARC elevation immediately post-exercise and a return to initial baseline values thereafter, even though no statistically significant difference was observed at 60 and 180 min after exercise (Table 3). Interestingly, only 1 study adopting RE was included in our review,[50] which impeded sub-group analysis and the comparison with AE. Regarding AE, most of the studies included had an exercise duration of 30–60 min with intensity from 50% to 70% VO_{2max} or 60% $HR_{reserve}$ using MICAE (Supplementary Table 1),[52,53,75,79,93,104] which appears sufficient to drive alterations in SPARC levels. Furthermore, the very low heterogeneity observed (i.e., I^2 = 0%) increases confidence in the findings. However, given the scarcity of studies, further research is required to explore the impact of different exercise modes at different time intervals on SPARC levels, precluding any additional assumptions about RE at distinct time points. Overall, a single bout of exercise significantly increases SPARC immediately after exercise and returning to baseline levels thereafter.

4.4. OSM

The effects of a single bout of exercise may drive small increases in OSM expression immediately after exercise (Table 3). We report only 3 studies investigating OSM, and as highlighted above for SPARC, they included only AE. There was no statistically significant difference; however, in regard to the exercise prescription for AE, even though the heterogeneity among studies was low (i.e., I^2 = 11.00%), it should be noted that in the study by Humińska-Lisowska et al.[51] subjects performed only a 30-s maximal effort with resistive load on a cycle ergometer (Supplementary Table 1), which may not be sufficient to stimulate OSM responses. Furthermore, no studies have investigated the effects of RE

on OSM expression in healthy adults, indicating that future investigations are required. In addition, to detect the changes of OSM in the systemic circulation, more studies collecting blood at different time points are required. In summary, although exercise may have a positive effect on OSM expression, more research is needed to clearly elucidate the effects of different exercise modes at different time points.

4.5. Decorin

When investigating the effects of a single bout of exercise on decorin expression, it appears that large increases can be observed 24 h post-exercise (Table 3). It should be noted that large variations in CIs may have accounted for the lack of statistically significant difference, as was the case for IL-15. As mentioned above with respect to SPARC and OSM, our review included studies performing RE only. In this instance, the training dosage for RE included low- and high-intensity RE (i.e., 50%–80% 1RM, respectively) until volitional failure (Supplementary Table 1).[87] Moreover, Bugera et al.[98] used traditional RE as well as blood flow restriction RE (i.e., 4 sets of 15 to 30 repetitions at 30%–80% 1RM). Although a statistically significant difference was not observed, it should be noted the adoption of an alternative RE method (e.g., blood flow restriction) may guide future investigations of exercise prescriptions to induce myokine changes. However, the relatively high heterogeneity (i.e., I^2 = 41.90%) should be taken into account as well. In summary, due to the paucity of studies, no definitive conclusions can be drawn, highlighting the need for further investigations to comprehensively understand how different exercise modes at different time intervals impact decorin responses.

4.6. Limitations

There are a few limitations in this review which are worthy of comment. First, the population included sedentary, physically active, and trained adult populations. Furthermore, gender, age, and BMI of participants varied among studies, increasing the heterogeneity of this current review. Secondly, there is no consensus about the study design procedures to be adopted when measuring changes in myokine expression before and after a single bout of exercise. Indeed, time of assessment (i.e., a.m. *vs.* p.m.) and difference in hours spent fasting (e.g., 1 h *vs.* 3 h) may have influenced the results.[112] Lastly, there remains a distinct lack of studies investigating myokine expression at different time points, especially 60 min after a single exercise bout.

4.7. Directions for future research

Based on our findings, it appears of utmost importance to investigate the effects of different exercise modes to precisely determine whether or not a single bout of AE or RE drives different responses in myokine expression. It should be noted that there was a paucity of studies investigating RE for SPARC and OSM as well as those examining a single bout of AE for decorin. Additionally, and in line with this suggestion, very few studies explored the effects of a combined approach (i.e., AE + RE) for most of the myokines included. Furthermore, subsequent investigations employing alternative training methods (e.g., blood flow restriction, cluster set, or accentuated eccentric training[113–115]) may shed further light on exercise-induced myokine expression. Since myokines are released in response to muscular contractions and exert their actions on different organs,[6,9–11] targeting of exercise prescription may facilitate clinical implementation of exercise for health, well-being, and disease treatment (e.g., cancer).[12,13] Moreover, blood collection at multiple time points may further elucidate the unique response of myokines to exercise across time. Finally, it is still unknown what are the training parameters to induce substantial myokine responses. Future research should aim to investigate the minimal dosage in terms of volume and/or intensity for both AE and RE, as well as the participant characteristics (e.g., training status) required to drive alterations in myokine expression, therefore elucidating the impact of training parameters on myokine responses.

5. Conclusion

In this systematic review and meta-analysis, we examined the overall and specific effects of a single bout of exercise on myokine expression in healthy adults at different time points post-exercise. It appears that small to large increases can be induced by exercise measured immediately after and up to 60 min following exercise while myokine responses revert toward baseline from 180 min to 24 h post-exercise. Furthermore, both AE and RE induce alterations in myokine expression, although the extent of these changes varies depending on the specific myokines. However, owing to the large variations observed, most of the changes were not statistically significant, indicating that precise conclusions cannot be drawn. Nevertheless, through this research we have expanded our knowledge of the impact of overall effects as well as the effects of different exercise modes on myokine expression. Further research is required to investigate the effects of different exercise modes, volume and intensity at multiple time points on myokine responses.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Authors' contributions

FB conceived the study design, searched studies in the databases, extracted data, run statistical analysis, elaborated results and drafted the manuscript; PL run statistical analysis; AMM, VN searched studies in the databases and extracted data; DRT, DAG, CB, JSK, and RUN edited and revised the manuscript. All authors have read and approved the final version of the manuscript, and agree with the order of presentation of the authors.

Competing interests

The authors declare that they have no competing interests.

References

1. Bull FC, Al-Ansari SS, Biddle S, et al. World health organization 2020 guidelines on physical activity and sedentary behaviour. *Br J Sports Med* 2020;**54**:1451-62.
2. Thompson WR, Sallis R, Joy E, Jaworski CA, Stuhr RM, Trilk JL. Exercise is medicine. *Am J Lifestyle Med* 2020;**14**:511-23.
3. Hoffmann C, Weigert C. Skeletal muscle as an endocrine organ: The role of myokines in exercise adaptations. *Cold Spring Harb Perspect Med* 2017;**7**:a029793. doi: 10.1101/cshperspect.a029793.
4. Iizuka K, Machida T, Hirafuji M. Skeletal muscle is an endocrine organ. *J Pharmacol Sci* 2014;**125**:125-31.
5. Son JS, Chae SA, Testroet ED, Du M, Jun HP. Exercise-induced myokines: A brief review of controversial issues of this decade. *Expert Rev Endocrinol Metab* 2018;**13**:51-8.
6. Lee JH, Jun HS. Role of myokines in regulating skeletal muscle mass and function. *Front Physiol* 2019;**10**:42. doi: 10.3389/fphys.2019.00042.
7. Pedersen BK, Akerström TC, Nielsen AR, Fischer CP. Role of myokines in exercise and metabolism. *J Appl Physiol (1985)* 2007;**103**:1093-8.
8. Pedersen BK. From the discovery of myokines to exercise as medicine. *Dan Med J* 2023;70:A12220766.
9. Severinsen MCK, Pedersen BK. Muscle-organ crosstalk: The emerging roles of myokines. *Endocr Rev* 2020;**41**:594-609.
10. Pedersen BK, Febbraio MA. Muscles, exercise and obesity: Skeletal muscle as a secretory organ. *Nat Rev Endocrinol* 2012;**8**:457-65.
11. Pedersen BK. Physical activity and muscle–brain crosstalk. *Nat Rev Endocrinol* 2019;**15**:383-92.
12. Khan SU, Ghafoor S. Myokines: Discovery challenges and therapeutic impediments. *J Pak Med Assoc* 2019;**69**:1014-7.
13. Bettariga F, Taaffe DR, Galvão DA, Bishop C, Kim J-S, Newton RU. Suppressive effects of exercise-conditioned serum on cancer cells: A narrative review of the influence of exercise mode, volume, and intensity. *J Sport Health Sci* 2023. doi: 10.1016/j.jshs.2023.12.001.
14. Carbó N, López-Soriano J, Costelli P, et al. Interleukin-15 mediates reciprocal regulation of adipose and muscle mass: A potential role in body weight control. *Biochim Biophys Acta* 2001;**1526**:17-24.
15. Fuster G, Almendro V, Fontes-Oliveira CC, et al. Interleukin-15 affects differentiation and apoptosis in adipocytes: Implications in obesity. *Lipids* 2011;**46**:1033-42.
16. Arhire LI, Mihalache L, Covasa M. Irisin: A hope in understanding and managing obesity and metabolic syndrome. *Front Endocrinol (Lausanne)* 2019;**10**:524. doi: 10.3389/fendo.2019.00524.

17. Reza MM, Subramaniyam N, Sim CM, et al. Irisin is a pro-myogenic factor that induces skeletal muscle hypertrophy and rescues denervation-induced atrophy. *Nat Commun* 2017;**8**:1104. doi: 10.1038/s41467-017-01131-0.
18. Song H, Guan Y, Zhang L, Li K, Dong C. Sparc interacts with ampk and regulates glut4 expression. *Biochem Biophys Res Commun* 2010;**396**:961-6.
19. Petersson SJ, Jørgensen LH, Andersen DC, Nørgaard RC, Jensen CH, Schrøder HD. Sparc is up-regulated during skeletal muscle regeneration and inhibits myoblast differentiation. *Histol Histopathol* 2013;**28**:1451-60.
20. Cornish SM, Bugera EM, Duhamel TA, Peeler JD, Anderson JE. A focused review of myokines as a potential contributor to muscle hypertrophy from resistance-based exercise. *Eur J Appl Physiol* 2020;**120**:941-59.
21. Kishioka Y, Thomas M, Wakamatsu J, et al. Decorin enhances the proliferation and differentiation of myogenic cells through suppressing myostatin activity. *J Cell Physiol* 2008;**215**:856-67.
22. Miura T, Kishioka Y, Wakamatsu J, et al. Decorin binds myostatin and modulates its activity to muscle cells. *Biochem Biophys Res Commun* 2006;**340**:675-80.
23. Steel JC, Waldmann TA, Morris JC. Interleukin-15 biology and its therapeutic implications in cancer. *Trends Pharmacol Sci* 2012;**33**:35-41.
24. Park SY, Hwang BO, Song NY. The role of myokines in cancer: Crosstalk between skeletal muscle and tumor. *BMB Rep* 2023;**56**:365-73.
25. Kim JS, Galvão DA, Newton RU, Gray E, Taaffe DR. Exercise-induced myokines and their effect on prostate cancer. *Nat Rev Urol* 2021;**18**:519-42.
26. Dethlefsen C, Lillelund C, Midtgaard J, et al. Exercise regulates breast cancer cell viability: Systemic training adaptations versus acute exercise responses. *Breast Cancer Res Treat* 2016;**159**:469-79.
27. Domin R, Dadej D, Pytka M, Zybek-Kocik A, Ruchała M, Guzik P. Effect of various exercise regimens on selected exercise-induced cytokines in healthy people. *Int J Environ Res Public Health* 2021;**18**:1261. doi: 10.3390/ijerph18031261.
28. Kraemer WJ, Adams K, Cafarelli E, et al. American College of Sports Medicine position stand. Progression models in resistance training for healthy adults. *Med Sci Sports Exerc* 2002;**34**:364-80.
29. Fox J, Rioux BV, Goulet EDB, et al. Effect of an acute exercise bout on immediate post-exercise irisin concentration in adults: A meta-analysis. *Scand J Med Sci Sports* 2018;**28**:16-28.
30. Cosio PL, Pelaez M, Cadefau JA, Farran-Codina A. Systematic review and meta-analysis of circulating irisin levels following endurance training: Results of continuous and interval training. *Biol Res Nurs* 2023;**25**:367-81.
31. Kazeminasab F, Sadeghi E, Afshari-Safavi A. Comparative impact of various exercises on circulating irisin in healthy subjects: A systematic review and network meta-analysis. *Oxid Med Cell Longev* 2022;**2022**:8235809. doi: 10.1155/2022/8235809.
32. Furlan AD, Pennick V, Bombardier C, van Tulder M. 2009 updated method guidelines for systematic reviews in the cochrane back review group. *Spine (Phila Pa 1976)* 2009;**34**:1929-41.
33. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: Explanation and elaboration. *BMJ* 2009;**339**:b2700. doi: 10.1136/bmj.b2700.
34. Page MJ, McKenzie JE, Bossuyt PM, et al. Mapping of reporting guidance for systematic reviews and meta-analyses generated a comprehensive item bank for future reporting guidelines. *J Clin Epidemiol* 2020;**118**:60-8.
35. Drevon D, Fursa SR, Malcolm AL. Intercoder reliability and validity of webplotdigitizer in extracting graphed data. *Behav Modif* 2017;**41**:323-39.
36. Smart NA, Waldron M, Ismail H, et al. Validation of a new tool for the assessment of study quality and reporting in exercise training studies: TESTEX. *Int J Evid Based Healthc* 2015;**13**:9-18.

37. Loy BD, O'Connor PJ, Dishman RK. Effect of acute exercise on fatigue in people with ME/CFS/SEID: A meta-analysis. *Med Sci Sports Exerc* 2016;**48**:2003-12.
38. Siedlik JA, Benedict SH, Landes EJ, Weir JP, Vardiman JP, Gallagher PM. Acute bouts of exercise induce a suppressive effect on lymphocyte proliferation in human subjects: A meta-analysis. *Brain Behav Immun* 2016;**56**:343-51.
39. Naugle KM, Fillingim RB, Riley 3rd JL. A meta-analytic review of the hypoalgesic effects of exercise. *J Pain* 2012;**13**:1139-50.
40. Cheung MW. Modeling dependent effect sizes with three-level meta-analyses: A structural equation modeling approach. *Psychol Methods* 2014;**19**:211-29.
41. Cohen J. Statistical power analysis. *Curr Dir Psychol Sci* 1992;**1**:98-101.
42. Peters JL, Sutton AJ, Jones DR, Abrams KR, Rushton L. Contour-enhanced meta-analysis funnel plots help distinguish publication bias from other causes of asymmetry. *J Clin Epidemiol* 2008;**61**:991-6.
43. Viechtbauer W. Conducting meta-analyses in R with the metafor package. *J Stat Softw* 2010;**36**:1-48. doi: 10.18637/jss.v036.i03.
44. Algul S, Ozdenk C, Ozcelik O. Variations in leptin, nesfatin-1 and irisin levels induced by aerobic exercise in young trained and untrained male subjects. *Biol Sport* 2017;**34**:339-44.
45. Bazgir B, Salesi M, Koushki M, Amirghofran Z. Effects of eccentric and concentric emphasized resistance exercise on IL-15 serum levels and its relation to inflammatory markers in athletes and non-athletes. *Asian J Sports Med* 2015;**6**:e27980. doi: 10.5812/asjsm.27980.
46. Bubak MP, Heesch MWS, Shute RJ, et al. Irisin and fibronectin type iii domain-containing 5 responses to exercise in different environmental conditions. *Int J Exerc Sci* 2017;**10**:666-80.
47. Eken Ö, Kafkas ME. Effects of low and high intensity interval training exercises on vo(2max) and components of neuromuscular and vascular system in male volunteers. *J Musculoskelet Neuronal Interact* 2022;**22**:352-63.
48. Eskandari A, Fashi M, Saeidi A, et al. Resistance exercise in a hot environment alters serum markers in untrained males. *Front Physiol* 2020;**11**:597. doi: 10.3389/fphys.2020.00597.
49. Fernandez del Valle M, Short M, Chung E, et al. Effects of high-intensity resistance training on circulating levels of irisin in healthy adults: A randomized controlled trial. *Asian J Sports Med* 2018;**9**:e1305. doi:10.5812/ASJSM.13025.
50. Fortunato AK, Pontes WM, De Souza DMS, et al. Strength training session induces important changes on physiological, immunological, and inflammatory biomarkers. *J Immunol Res* 2018;**2018**:9675216. doi: 10.1155/2018/9675216.
51. Humińska-Lisowska K, Mieszkowski J, Kochanowicz A, et al. Implications of adipose tissue content for changes in serum levels of exercise-induced adipokines: A quasi-experimental study. *Int J Environ Res Public Health* 2022;**19**:8782. doi: 10.3390/ijerph19148782.
52. Hutchinson KA, Mohammad S, Garneau L, McInnis K, Aguer C, Adamo KB. Examination of the myokine response in pregnant and non-pregnant women following an acute bout of moderate-intensity walking. *Front Physiol* 2019;**10**:1188. doi: 10.3389/fphys.2019.01188.
53. Hwang J, McGovern J, Minett G, et al. Mobilizing serum factors and immune cells through exercise to counteract age-related changes in cancer risk. *Exerc Immunol Rev* 2020;**26**:80-99.
54. Joro R, Korkmaz A, Lakka TA, Uusitalo ALT, Atalay M. Plasma irisin and its associations with oxidative stress in athletes suffering from overtraining syndrome. *Physiol Int* 2020;**107**:513-26.
55. Jürimäe J, Purge P, Tillmann V. Serum sclerostin and cytokine responses to prolonged sculling exercise in highly-trained male rowers. *J Sports Sci* 2021;**39**:591-7.
56. Jürimäe J, Vaiksaar S, Purge P, Tillmann V. Irisin, fibroplast growth factor-21, and follistatin responses to endurance rowing training session in female rowers. *Front Physiol* 2021;**12**:689696. doi: 10.3389/fphys.2021.689696.
57. Kabak B, Belviranli M, Okudan N. Irisin and myostatin responses to acute high-intensity interval exercise in humans. *Horm Mol Biol Clin Investig* 2018;**35**:/j/hmbci.2018.35.issue-3/hmbci-2018-0008/hmbci-2018-0008.xml. doi: 10.1515/hmbci-2018-0008.
58. Kapilevich LV, Zakharova AN, Kabachkova AV, Kironenko TA, Orlov SN. Dynamic and static exercises differentially affect plasma cytokine content in elite endurance- and strength-

trained athletes and untrained volunteers. *Front Physiol* 2017;**8**:35. doi: 10.3389/fphys.2017.00035.

59. Kraemer RR, Shockett P, Webb ND, Shah U, Castracane VD. A transient elevated irisin blood concentration in response to prolonged, moderate aerobic exercise in young men and women. *Horm Metab Res* 2014;**46**:150-4.
60. Lagzdina R, Rumaka M, Gersone G, Tretjakovs P. Circulating irisin in healthy adults: Changes after acute exercise, correlation with body composition, and energy expenditure parameters in cross-sectional study. *Medicina (Kaunas)* 2020;**56**:274. doi: 10.3390/medicina56060274.
61. Li H, Li F, Zhou R, Gao K, Liang L, Zhang X. Aerobic exercise increases tear secretion and decreases inflammatory cytokines in healthy subjects. *Asia Pac J Ophthalmol (Phila)* 2020;**9**:404-11.
62. Löffler D, Müller U, Scheuermann K, et al. Serum irisin levels are regulated by acute strenuous exercise. *J Clin Endocrinol Metab* 2015;**100**:1289-99.
63. Luk HY, Jones MT, Vingren JL. Effect of rest period configurations on systemic inflammatory response in resistance-trained women. *J Sports Sci* 2021;**39**:1504-11.
64. MacNeil LG, Tarnopolsky MA, Crane JD. Acute, exercise-induced alterations in cytokines and chemokines in the blood distinguish physically active and sedentary aging. *J Gerontol A Biol Sci Med Sci* 2021;**76**:811-8.
65. Mendez-Gutierrez A, Aguilera CM, Osuna-Prieto FJ, et al. Exercise-induced changes on exerkines that might influence brown adipose tissue metabolism in young sedentary adults. *Eur J Sport Sci* 2023;**23**:625-36.
66. Minuzzi LG, Chupel MU, Rama L, et al. Lifelong exercise practice and immunosenescence: Master athletes cytokine response to acute exercise. *Cytokine* 2019;**115**:1-7.
67. Moienneia N, Attarzadeh Hosseini SR. Acute and chronic responses of metabolic myokine to different intensities of exercise in sedentary young women. *Obes Med* 2016;**1**:15-20.
68. Naghavi N, Yokoyama H, Yamashina Y, et al. Elevation in serum irisin levels after a single bout of exercise do not modulate resting energy expenditure and diet-induced thermogenesis in healthy young adults. *Osaka City Med J* 2017;**63**:93-104.
69. Norheim F, Langleite TM, Hjorth M, et al. The effects of acute and chronic exercise on pgc-1α, irisin and browning of subcutaneous adipose tissue in humans. *FEBS J* 2014;**281**:739-49.
70. Nygaard H, Slettaløkken G, Vegge G, et al. Irisin in blood increases transiently after single sessions of intense endurance exercise and heavy strength training. *PLoS One* 2015;**10**:e0121367. doi: 10.1371/journal.pone.0121367.
71. Ozbay S, Ulupınar S, Şebin E, Altınkaynak K. Acute and chronic effects of aerobic exercise on serum irisin, adropin, and cholesterol levels in the winter season: Indoor training versus outdoor training. *Chin J Physiol* 2020;**63**:21-6.
72. Prestes J, Shiguemoto G, Botero JP, et al. Effects of resistance training on resistin, leptin, cytokines, and muscle force in elderly post-menopausal women. *J Sports Sci* 2009;**27**:1607-15.
73. Qiu S, Bosnyák E, Treff G, et al. Acute exercise-induced irisin release in healthy adults: Associations with training status and exercise mode. *Eur J Sport Sci* 2018;**18**:1226-33.
74. Reichel T, Boßlau TK, Palmowski J, et al. Reliability and suitability of physiological exercise response and recovery markers. *Sci Rep* 2020;**10**:11924. doi: 10.1038/s41598-020-69280-9.
75. Reichel T, Held S, Schwarz A, et al. Acute response of biomarkers in plasma from capillary blood after a strenuous endurance exercise bout. *Eur J Appl Physiol* 2023;**123**:179-89.
76. Reycraft JT, Islam H, Townsend LK, Hayward GC, Hazell TJ, Macpherson REK. Exercise intensity and recovery on circulating brain-derived neurotrophic factor. *Med Sci Sports Exerc* 2020;**52**:1210-7.
77. Rinnov A, Yfanti C, Nielsen S, et al. Endurance training enhances skeletal muscle interleukin-15 in human male subjects. *Endocrine* 2014;**45**:271-8.
78. Rodziewicz E, Król-Zielińska M, Zieliński J, Kusy K, Ziemann E. Plasma concentration of irisin and brain-derived-neurotrophic factor and their association with the level of erythrocyte adenine nucleotides in response to long-term endurance training at rest and after a single bout of exercise. *Front Physiol* 2020;**11**:923. doi: 10.3389/fphys.2020.00923.

79. Songsorn P, Ruffino J, Vollaard NB. No effect of acute and chronic supramaximal exercise on circulating levels of the myokine sparc. *Eur J Sport Sci* 2017;**17**:447-52.
80. Tamura Y, Watanabe K, Kantani T, Hayashi J, Ishida N, Kaneki M. Upregulation of circulating IL-15 by treadmill running in healthy individuals: Is IL-15 an endocrine mediator of the beneficial effects of endurance exercise? *Endocr J* 2011;**58**:211-5.
81. Tsai CL, Pan CY, Tseng YT, Chen FC, Chang YC, Wang TC. Acute effects of high-intensity interval training and moderate-intensity continuous exercise on bdnf and irisin levels and neurocognitive performance in late middle-aged and older adults. *Behav Brain Res* 2021;**413**:113472. doi: 10.1016/j.bbr.2021.113472.
82. Tsuchiya Y, Ando D, Goto K, Kiuchi M, Yamakita M, Koyama K. High-intensity exercise causes greater irisin response compared with low-intensity exercise under similar energy consumption. *Tohoku J Exp Med* 2014;**233**:135-40.
83. Tsuchiya Y, Ando D, Takamatsu K, Goto K. Resistance exercise induces a greater irisin response than endurance exercise. *Metabolism* 2015;**64**:1042-50.
84. Tsuchiya Y, Goto K. Myokine secretion following moderate-intensity endurance exercise under different environmental temperatures. *Cytokine* 2021;**144**:155553. doi: 10.1016/j.cyto.2021.155553.
85. Ugras S, Algul S, Ozdenk C. Comparatively evaluating the effects of exercising at the anaerobic threshold on oxidative stress and serum levels of leptin, nesfatin-1 and irisin in sedentary male and females. *Prog Nutr* 2022;**24**:e2022022.
86. Wiecek M, Szymura J, Maciejczyk M, Kantorowicz M, Szygula Z. Acute anaerobic exercise affects the secretion of asprosin, irisin, and other cytokines–A comparison between sexes. *Front Physiol* 2018;**9**:1782. doi: 10.3389/fphys.2018.01782.
87. Willoughby DS, Cardaci TD, Machek SB, Wilburn DT, Heileson JL. Resistance exercise-induced increases in muscle myostatin mrna and protein expression are subsequently decreased in circulation in the presence of increased levels of the extracellular matrix stabilizing protein decorin. *J Sports Sci Med* 2022;**21**:616-24.
88. Kara ÖS, Ercan A, Çelebier M, Kaplan O, Öncül S, Korkusuz F. Plasma irisin and metabolomic response differ between concentric and isometric exercise. *Sci Sport* 2022;**37**:610-7.
89. Dror N, Carbone J, Haddad F, Falk B, Klentrou P, Radom-Aizik S. Sclerostin and bone turnover markers response to cycling and running at the same moderate-to-vigorous exercise intensity in healthy men. *J Endocrinol Invest* 2022;**45**:391-7.
90. Dos Santos Quaresma MVL, Campos R, Tavares-Silva E, Marques CG, Thomatieli-Santos RV. Effect of acute caffeine supplementation before intermittent high-intensity exercise on cytokine levels and psychobiological parameters: A randomized, cross-over, placebo-controlled trial. *Cytokine* 2021;**144**:155583. doi: 10.1016/j.cyto.2021.155583.
91. Bizjak DA, Zügel M, Schumann U, et al. Do skeletal muscle composition and gene expression as well as acute exercise-induced serum adaptations in older adults depend on fitness status? *BMC Geriatrics* 2021;**21**:697. doi: 10.1186/s12877-021-02666-0.
92. Paula Silva Azevedo A, Nóbrega C, Darck Carola Correia Lima J, et al. Immediate effects of a real moderate interval-running training session on inflammatory profile. *Cytokine* 2020;**133**:155150. doi: 10.1016/j.cyto.2020.155150.
93. Garneau L, Parsons SA, Smith SR, Mulvihill EE, Sparks LM, Aguer C. Plasma myokine concentrations after acute exercise in non-obese and obese sedentary women. *Front Physiol* 2020;**11**:18. doi: 10.3389/fphys.2020.00018.
94. Bilski J, Mazur-Bialy AI, Surmiak M, et al. Effect of acute sprint exercise on myokines and food intake hormones in young healthy men. *Int J Mol Sci* 2020;**21**:8848. doi: 10.3390/ijms21228848.
95. Pérez-López A, McKendry J, Martin-Rincon M, et al. Skeletal muscle IL-15/IL-15Rα and myofibrillar protein synthesis after resistance exercise. *Scand J Med Sci Sports* 2018;**28**:116-25.
96. Kim J-H, Kim D-Y. Aquarobic exercises improve the serum blood irisin and brain-derived neurotrophic factor levels in elderly women. *Exp Gerontol* 2018;**104**:60-5.

97. Duzova H, Gullu E, Cicek G, et al. The effect of exercise induced weight-loss on myokines and adipokines in overweight sedentary females: Steps-aerobics *vs*. Jogging-walking exercises. *J Sports Med Phys Fitness* 2018;**58**:295-308.
98. Bugera EM, Duhamel TA, Peeler JD, Cornish SM. The systemic myokine response of decorin, interleukin-6 (IL-6) and interleukin-15 (IL-15) to an acute bout of blood flow restricted exercise. *Eur J Appl Physiol* 2018;**118**:2679-86.
99. Oliver JM, Jenke SC, Mata JD, Kreutzer A, Jones MT. Acute effect of cluster and traditional set configurations on myokines associated with hypertrophy. *Int J Sports Med* 2016;**37**:1019-24.
100. Murawska-Cialowicz E, Wojna J, Zuwala-Jagiello J. Crossfit training changes brain-derived neurotrophic factor and irisin levels at rest, after wingate and progressive tests, and improves aerobic capacity and body composition of young physically active men and women. *J Physiol Pharmacol* 2015;**66**:811-21.
101. Anastasilakis AD, Polyzos SA, Saridakis ZG, et al. Circulating irisin in healthy, young individuals: Day-night rhythm, effects of food intake and exercise, and associations with gender, physical activity, diet, and body composition. *J Clin Endocrinol Metab* 2014;**99**:3247-55.
102. Pekkala S, Wiklund PK, Hulmi JJ, et al. Are skeletal muscle FNDC5 gene expression and irisin release regulated by exercise and related to health? *J Physiol* 2013;**591**:5393-400.
103. Aydin S, Aydin S, Kuloglu T, et al. Alterations of irisin concentrations in saliva and serum of obese and normal-weight subjects, before and after 45 min of a turkish bath or running. *Peptides* 2013;**50**:13-8.
104. Aoi W, Naito Y, Takagi T, et al. A novel myokine, secreted protein acidic and rich in cysteine (SPARC), suppresses colon tumorigenesis via regular exercise. *Gut* 2013;**62**:882-9.
105. Huh JY, Panagiotou G, Mougios V, et al. FNDC5 and irisin in humans: I. Predictors of circulating concentrations in serum and plasma and II. mRNA expression and circulating concentrations in response to weight loss and exercise. *Metabolism* 2012;**61**:1725-38.
106. He Z, Tian Y, Valenzuela PL, et al. Myokine response to high-intensity interval *vs.* Resistance exercise: An individual approach. *Front Physiol* 2018;**9**:1735. doi: 10.3389/fphys.2018.01735.
107. Garber CE, Blissmer B, Deschenes MR, et al. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: Guidance for prescribing exercise. *Med Sci Sports Exerc* 2011;**43**:1334-59.
108. Graf C, Ferrari N. Metabolic health-the role of adipo-myokines. *Int J Mol Sci* 2019;**20**:6159. doi: 10.3390/ijms20246159.
109. Tsiani E, Tsakiridis N, Kouvelioti R, Jaglanian A, Klentrou P. Current evidence of the role of the myokine irisin in cancer. *Cancers* 2021;**13**:2628. doi: 10.3390/cancers13112628.
110. Daskalopoulou SS, Cooke AB, Gomez YH, et al. Plasma irisin levels progressively increase in response to increasing exercise workloads in young, healthy, active subjects. *Eur J Endocrinol* 2014;**171**:343-52.
111. Pedersen BK, Febbraio MA. Muscle as an endocrine organ: Focus on muscle-derived interleukin-6. *Physiol Rev* 2008;**88**:1379-406.
112. Rose G, Farley M, Flemming N, Skinner T, Schaumberg M. Between-day reliability of cytokines and adipokines for application in research and practice. *Front Physiol* 2022;**13**:967169. doi: 10.3389/fphys.2022.967169.
113. Bettariga F, Bishop C, Taaffe DR, Galvão DA, Maestroni L, Newton RU. Time to consider the potential role of alternative resistance training methods in cancer management? *J Sport Health Sci* 2023;**12**:715-25.
114. Latella C, Peddle-McIntyre C, Marcotte L, Steele J, Kendall K, Fairman CM. Strengthening the case for cluster set resistance training in aged and clinical settings: Emerging evidence, proposed benefits and suggestions. *Sports Med* 2021;**51**:1335-51.
115. Miller BC, Tirko AW, Shipe JM, Sumeriski OR, Moran K. The systemic effects of blood flow restriction training: A systematic review. *Int J Sports Phys Ther* 2021;**16**:978-90.

Table 1. Effects of single bouts of exercise on IL-15 expression.

				Random-effect meta-analysis			Heterogeneity		
		K	**Number of ES**	**ES**	**95% CI**	***p***	***Q***	I^2	***p***
Main model	Main model effect	20	74	0.95	–0.23 to 2.13	0.11	399.10	46.70	0.001
Time points Immediately after									
	Overall effect	20	34	1.14	–0.21 to 2.49	0.09	162.90	47.40	0.001
	Aerobic exercise	12	17	0.17	–0.27 to 0.60	0.41	17.40	13.20	0.360
	Resistance exercise	9	17	2.66	–0.67 to 5.99	0.10	134.90	48.80	0.001
	Aerobic + Resistance exercise	NA							
30 min									
	Overall effect	4	8	1.64	–2.92 to 6.20	0.33	39.10	47.20	0.001
	Aerobic exercise	NA							
	Resistance exercise	4	6	1.48	–3.30 to 6.26	0.40	37	47.40	0.001
	Aerobic + Resistance exercise	NA							
60 min									
	Overall effect	10	15	1.49	–0.85 to 3.83	0.18	96.50	47.70	0.001
	Aerobic exercise	5	6	0.01	–0.23 to 0.22	0.95	2.60	0	0.760
	Resistance exercise	5	9	3.11	–2.47 to 8.69	0.20	91	49.70	0.001
	Aerobic + Resistance exercise	NA							
120 min									
	Overall effect	2	2	3.69	–40.72 to 48.10	0.48	28.10	48.20	0.001
	Aerobic exercise	NA							
	Resistance exercise	NA							
	Aerobic + Resistance exercise	NA							
180 min									
	Overall effect	4	4	0	–0.32 to 0.32	0.98	0.50	0	0.920
	Aerobic exercise	4	4	0	–0.32 to 0.32	0.98	0.50	0	0.920

	Resistance exercise	NA							
	Aerobic + Resistance exercise	NA							
24 h									
	Overall effect	7	11	1.35	–1.29 to 3.98	0.26	55.10	47.60	0.001
	Aerobic exercise	2	2	0.34	–3.46 to 4.14	0.46	0.60	0	0.420
	Resistance exercise	5	9	1.72	–2.66 to 6.10	0.34	54.40	48.30	0.001
	Aerobic + Resistance exercise	NA							

Abbreviations: 95%CI = 95% confidence interval; ES = effect size; I^2 = percentage of variation across studies that is due to heterogeneity; K = number of studies; NA = not available; Q = Cochran's Q test of heterogeneity.

Table 2. Effects of single bouts of exercise on irisin expression.

				Random-effect meta-analysis			Heterogeneity		
		K	**Number of ES**	**ES**	**95%CI**	***p***	***Q***	***I*²**	***p***
Main model	Main model effect	36	110	0.44	–0.04 to 0.91	0.07	279.10	40.20	0.001
Time points									
Immediately after	Overall effect	34	58	0.50	–0.22 to 1.22	0.17	200.90	45.20	0.001
	Aerobic exercise	28	46	0.63	–0.30 to 1.56	0.18	197.40	46.50	0.001
	Resistance exercise	7	9	0.10	–0.29 to 0.48	0.55	2.00	0	0.98
	Aerobic + Resistance exercise	2	3	0.26	–0.42 to 0.94	0.13	0.10	0	0.94
30 min									
	Overall effect	11	17	0.81	–0.35 to 1.98	0.15	61.40	42.70	0.001
	Aerobic exercise	8	11	1.18	–0.52 to 2.87	0.14	56.10	44.60	0.001
	Resistance exercise	3	3	0.02	–0.31 to 0.35	0.81	0.10	0	0.96
	Aerobic + Resistance exercise	2	3	0.13	–4.71 to 4.97	0.79	0.90	0	0.65

60 min									
	Overall effect	7	12	0.38	0.05 to 0.71	0.03	3.10	0	0.99
	Aerobic exercise	6	8	0.40	–0.01 to 0.81	0.05	1.50	0	0.98
	Resistance exercise	3	3	0.32	–1.21 to 1.85	0.47	1.60	0	0.45
	Aerobic + Resistance exercise	NA							
120 min									
	Overall effect	5	8	0.09	–0.21 to 0.39	0.40	1.30	0	0.99
	Aerobic exercise	4	4	0.01	–0.33 to 0.34	0.94	0.40	0	0.95
	Resistance exercise	3	3	0.09	–0.71 to 0.88	0.69	0.50	0	0.79
	Aerobic + Resistance exercise	NA							
180 min									
	Overall effect	6	11	–0.14	–0.75 to 0.46	0.55	4.20	1.90	0.94
	Aerobic exercise	6	9	–0.26	–0.76 to 0.24	0.23	2.70	0	0.95
	Resistance exercise	NA							
	Aerobic + Resistance exercise	NA							
24 h									
	Overall effect	2	4	0.05	–0.80 to 0.89	0.61	0.40	0	0.94
	Aerobic exercise	2	3	–0.01	–2.25 to 2.24	0.97	0.30	0	0.86
	Resistance exercise	NA							
	Aerobic + Resistance exercise	NA							

Abbreviations: 95%CI = 95% confidence interval; ES = effect size; I^2 = percentage of variation across studies that is due to heterogeneity; K = number of studies; NA = not available; Q = Cochran's Q test of heterogeneity.

Table 3. Effects of single bouts of exercise on SPARC, OSM, and Decorin expression.

				Random-effect meta-analysis			Heterogeneity		
		K	**Number of ES**	**ES**	**95%CI**	***p***	***Q***	I^2	***p***
SPARC									
Main model	Main model effect	7	16	0.32	–0.06 to 0.69	0.08	9.40	0	0.85
Time points									
Immediately after									
	Overall effect	7	9	0.50	0.01 to 0.99	0.05	5.10	0	0.75
	Aerobic exercise	6	7	0.66	0.24 to 1.07	0.01	1.40	0	0.96
	Resistance exercise	NA							
	Aerobic + resistance exercise	NA							
60 min									
	Overall effect	2	2	–0.04	–0.17 to 0.08	0.14	0	0	0.98
	Aerobic exercise	2	2	–0.04	–0.17 to 0.08	0.14	0	0	0.98
	Resistance exercise	NA							
	Aerobic + Resistance exercise	NA							
180 min									
	Overall effect	2	2	0.12	–5.30 to 5.54	0.82	0.70	0	0.40
	Aerobic exercise	2	2	0.12	–5.30 to 5.54	0.82	0.70	0	0.40
	Resistance exercise	NA							
	Aerobic + Resistance exercise	NA							
24 h									
	Overall effect	2	2	–0.26	–6.85 to 6.32	0.70	1.00	0	0.32
	Aerobic exercise	2	2	–0.26	–6.85 to 6.32	0.70	1.00	0	0.32
	Resistance exercise	NA							
	Aerobic + Resistance exercise	NA							
OSM									
Main model	Main model effect	3	11	0.08	–2.4 to 2.56	0.90	29.60	32.50	0.001

Time points Immediately after									
	Overall effect	3	7	0.33	–1.23 to 1.88	0.43	3.10	11	0.79
	Aerobic exercise	3	7	0.33	–1.23 to 1.88	0.43	3.10	11	0.79
	Resistance exercise	NA							
	Aerobic + Resistance exercise	NA							
Decorin									
Main model	Main model effect	2	13	0.99	–11.14 to 13.12	0.49	21.10	39	0.05
Time points 24 h									
	Overall effect	2	5	1.11	–14.04 to 16.26	0.52	13.30	41.90	0.01
	Aerobic exercise	NA							
	Resistance exercise	2	5	1.11	–14.04 to 16.26	0.52	13.30	41.90	0.01
	Aerobic + Resistance exercise	NA							

Abbreviations: 95%CI = 95% confidence interval; ES = effect size; I^2 = percentage of variation across studies that is due to heterogeneity; K = number of studies; NA = not available; Q = Cochran's Q test of heterogeneity.

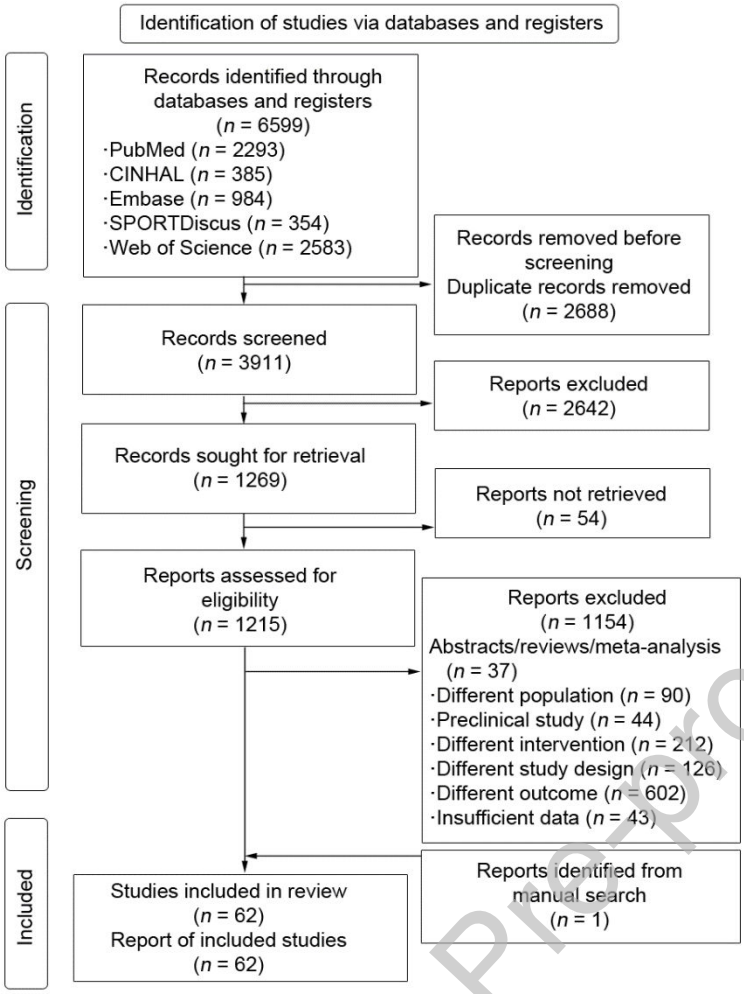

Fig. 1. Flow chart of study selection process.

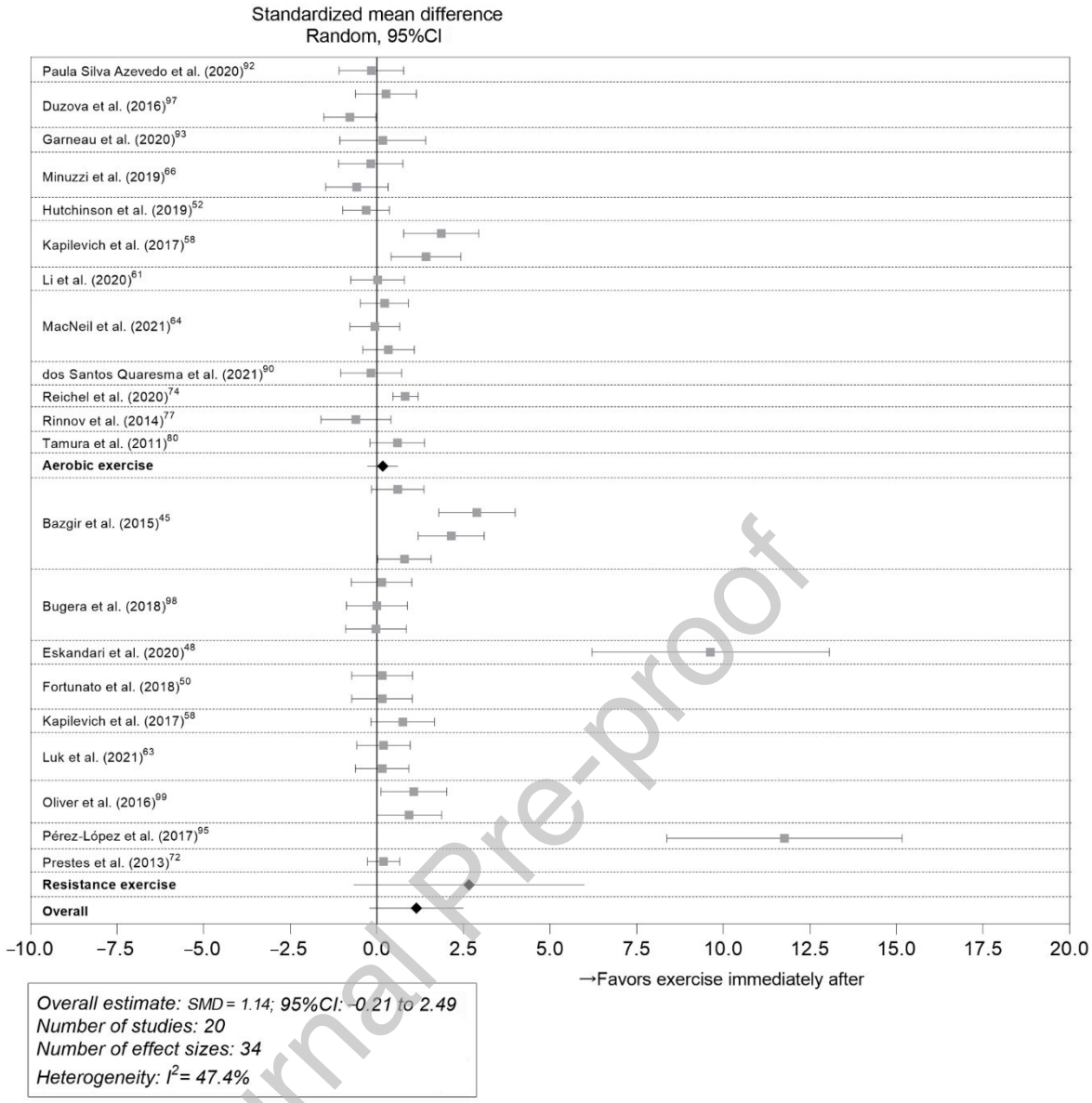

Fig. 2. Forest plot of overall and specific effects on IL-15 expression immediately following a single bout of exercise. 95%CI = 95% confidence interval; I^2 = heterogeneity test; SMD = standardized mean difference.

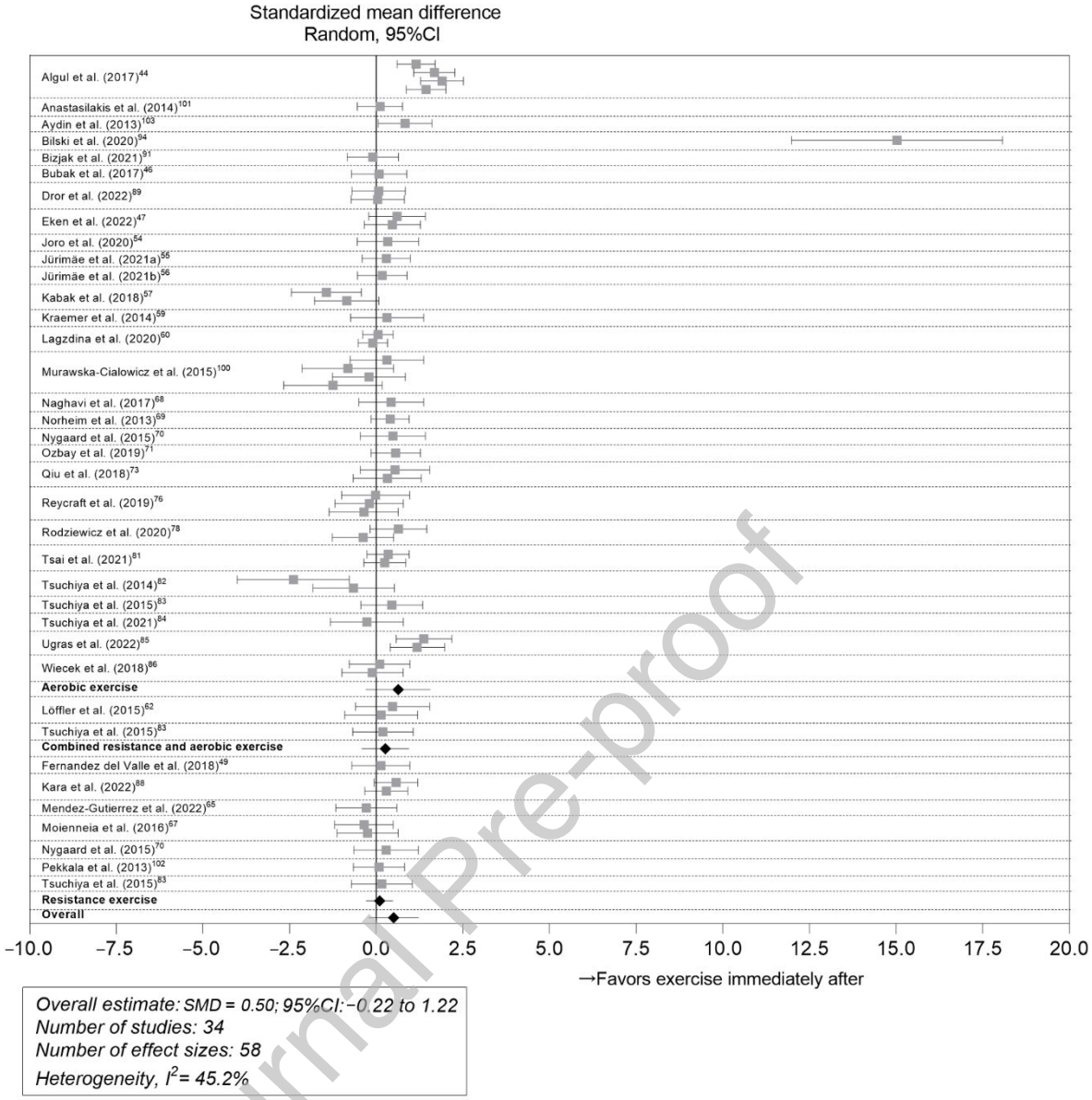

Fig. 3. Forest plot of overall and specific effects on irisin expression immediately following a single bout of exercise. 95%CI = 95% confidence interval; I^2 = heterogeneity test; SMD = standardized mean difference.

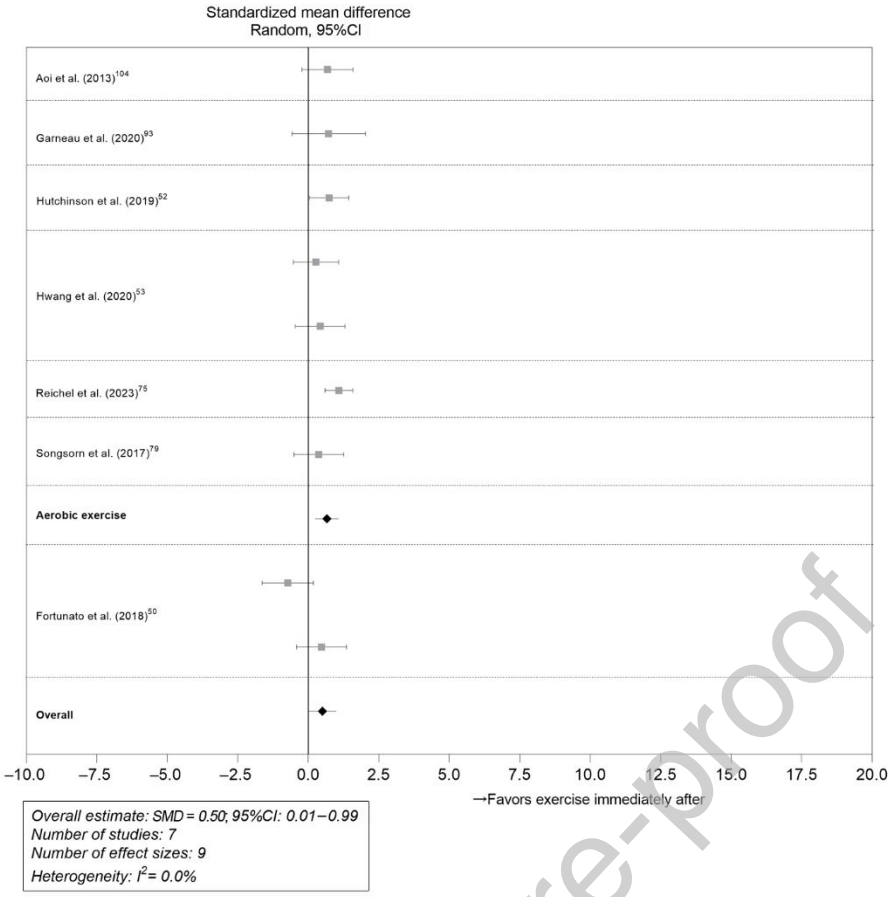

Fig. 4. Forest plot of overall and specific effects on SPARC expression immediately following a single bout of exercise. 95%CI = 95% confidence interval; I^2 = heterogeneity test; SMD = standardized mean difference.

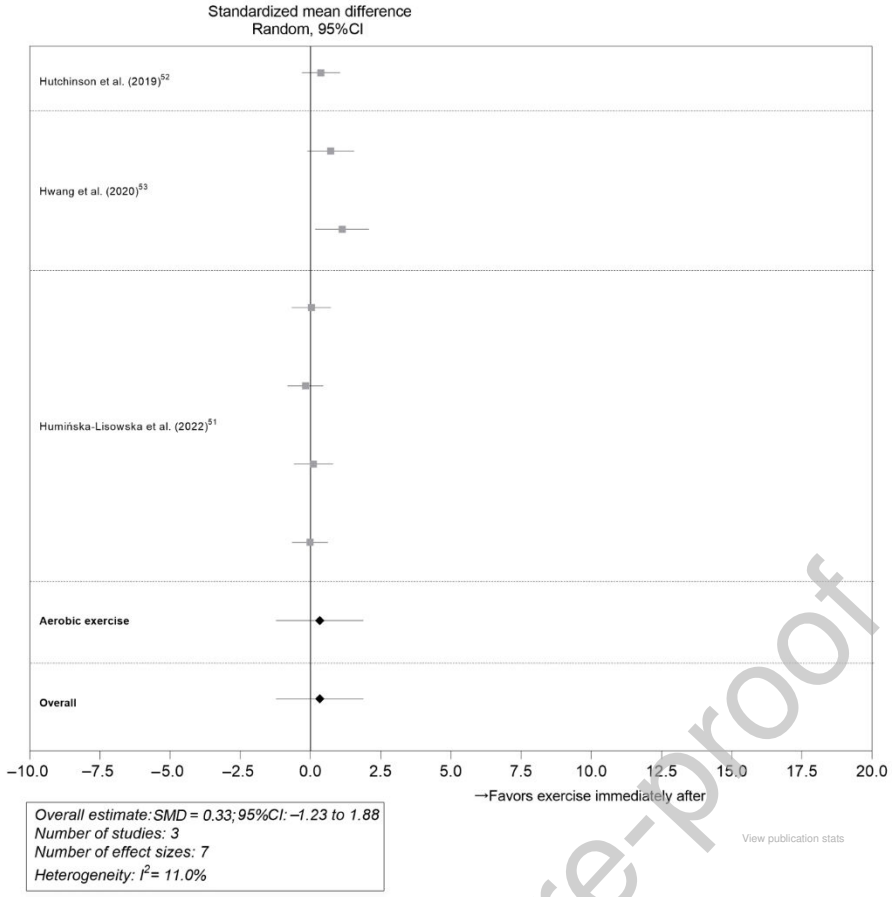

Fig. 5. Forest plot of overall and specific effects on OSM expression immediately following a single bout of exercise. 95%CI = 95% confidence interval; I^2 = heterogeneity test; SMD = standardized mean difference.

Graphical abstract