Review Article

# Differences in the Impact of Various Types of Exercise on Irisin Levels: A Systematic Review and Meta-Analysis

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## Abstract

**Background:** Irisin, a myokine that is responsive to exercise, induces significant changes in subcutaneous adipose tissue. By promoting the browning of white fat tissue, it enhances energy expenditure, thereby addressing overweight and obesity. This systematic review and meta-analysis aimed to compare the effects of different types of physical exercises on irisin levels in overweight and obese adults. **Methods:** Specifically, the review focused on studies involving obese or overweight individuals who participated in exercise training for a minimum of 8 weeks, with measured and reported changes in serum irisin levels compared to a control group. Data were collected from four databases (Google Scholar, ISI Web of Science Core Collection, PubMed, and Scopus). The risk of bias was assessed using the Begg and Egger tests, and the results were synthesized. **Results:** Initial searches identified 560 titles, out of which only seven met the criteria for inclusion in the systematic review. Statistical analysis demonstrated a significant increase in serum irisin concentration (SMD = 0.957, $P = 0.005$) among obese and overweight individuals who engaged in exercise, compared to the passive control group. High-intensity interval training (HIIT) (SMD = 1.229, $P < 0.001$) had a more pronounced effect on increasing serum irisin levels than other exercise protocols. Furthermore, the effectiveness of exercise varied based on the participants' weight status (significant changes for overweight individuals; $P < 0.001$ and insignificant changes for obese individuals; $P = 0.1$), age (significant changes for those under 40 years old; $P < 0.001$ and insignificant changes for those over 40 years old; $P = 0.322$), and gender (significant changes for men; $P < 0.001$ and insignificant changes for women; $P = 0.285$). **Conclusions:** Consequently, exercise can elevate serum irisin levels, leading to alterations in adipose tissue phenotype and thermogenesis, ultimately contributing to weight reduction in obese and overweight individuals.

**Keywords:** *Aerobic exercise, high-intensity interval training, myokine, obesity, overweight, resistance training*

## Introduction

Obesity and overweight are defined as the abnormal or excessive accumulation of fat in individuals, placing them in the overweight (OW) category (30 > BMI ≥25 kg/m$^2$) or obese category (BMI ≥30 kg/m$^2$) based on their body weight relative to their height.[1] To manage and prevent obesity, a healthy diet must be combined with balanced physical activity and energy intake.[1] Physical activity has therapeutic potential in reducing overweight and obesity.[2] One possible mechanism for this effect is the increased production of irisin and thermogenesis. Physical exercise stimulates the expression of peroxisome proliferator-activated receptor-gamma coactivator-1alpha (PGC1-α) in muscles and the FNDC5 gene, which codes for a membrane protein involved in the production of irisin. Irisin is released from skeletal muscle and promotes the browning of white fat tissue, resulting in heat production and increased energy utilization in fat tissue.[3] Irisin levels are elevated in individuals engaged in physical exercise, and there is a positive correlation between irisin levels and resting energy expenditure in obese individuals.[4] Irisin, in addition to being a myokine, is also known as an adipokine released from fat tissue, with muscle tissue accounting for 72% of total irisin and the remaining 28% distributed across fat tissue and other tissues.[5] Thus, different exercise protocols can influence the release of irisin by affecting these various tissues.[6]

Studies examining the effects of physical exercise on irisin levels have yielded varying results and have indicated that exercise type, intensity, and duration are



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important factors influencing irisin levels.[7-9] Aerobic exercise, for example, has been shown to improve mitochondrial biogenesis, likely due to the up-regulation of PGC-1α.[3] This pathway subsequently increases FNDC5 expression, leading to the release of irisin, which can affect obesity, adipose tissue metabolism, and insulin resistance through its role in thermogenesis and the browning process.[10] Studies have also demonstrated that long-term aerobic training at moderate intensity increases irisin levels[11] and contributes to optimal body composition. Resistance training and skeletal muscle contraction can activate PGC-1α and consequently increase irisin production.[10,12] Although there is limited research on the effects of high-intensity interval training (HIIT) on irisin, it is believed that HIIT, as a fast and intense training modality, can significantly elevate irisin levels in the bloodstream.[13] Combined training programs that target both strength and endurance in the muscles can also enhance irisin release.[14] While clinical data have demonstrated the positive impact of physical activity on various health conditions, including the potential role of irisin in improving these disorders,[3] there is still much to uncover regarding the effects of different exercise types and the underlying reasons for variations in outcomes across different exercise modalities and intensities.

Previous reviews have reported that both acute and long-term exercise training can effectively up-regulate PGC-1α expression.[10]

In skeletal muscle or cardiac muscle, exercise induces beneficial changes in adipose tissue, bone, and the release of irisin.[10] Both speed/power and endurance training protocols serve as strong stimuli for irisin release when performed with sufficient intensity and/or duration.[15] Acute exercise increases the concentration of irisin. Although no significant relationship has been established between irisin concentration and age, training intensity, exercise type (aerobic or resistance), factors such as fitness level and body mass index (BMI) have been identified as predictors of irisin concentration.[16] A meta-analysis examining 59 studies conducted on healthy individuals, as well as those with obesity, overweight, and various diseases such as diabetes, kidney diseases, and psychological problems demonstrated that exercise can elevate irisin levels.[8] It has also been reported that chronic and acute exercise training leads to increased circulating irisin levels (plasma/serum) in healthy individuals, with a greater increase observed in acute aerobic and chronic resistance protocols.[17] Another meta-analysis involving 16 studies comprising 412 participants, conducted on healthy individuals, revealed a significant increase in irisin levels following continuous endurance training, whereas intermittent training did not result in circulating irisin changes. The study reported that acute endurance training can elevate irisin in healthy individuals, while acute interval training does not have the same effect.[18]

To the best of our knowledge and based on the existing literature, no study has specifically examined the effects of exercise solely on obese or overweight populations without any other health issues. In this study, we focus exclusively on individuals who are obese or overweight, without any comorbid conditions that could impact irisin levels. The study duration was set at 8 weeks, and the sports protocols were classified into one of the following categories: aerobic, resistance, periodic, and combined, based on standard definitions. Entry criteria for participants included meeting specific criteria for obesity or overweight based on BMI, rather than percentage or mass of fat or other measurement methods for obesity and overweight. Therefore, individuals under 18 years of age were excluded from this study, as the focus was on BMI. Previous studies have included intervention populations consisting of various individuals (healthy, sick, obese, overweight, children, and teenagers), with or without control groups. These studies involved different types of exercises, without clearly defining the meaning of intensity or execution methods, and varying durations, ranging from acute to long-term chronic exercises.

Considering the aforementioned benefits of exercise and its role in irisin release as an effective substance for improving conditions like obesity and overweight, the fundamental

**Table 1: Inclusion and exclusion criteria**

| | Inclusion | Exclusion |
|---|---|---|
| Population | Obese or overweight adults based on BMI:<br>OW=25 ≤BMI <30, Obese=30 ≤BMI, 18 ≤age. | Not being within the defined range (age<18 or BMI <25)<br>Having at least one disease or disorder other than obesity and overweight |
| Intervention | Supervised exercise training protocol: aerobic, resistance, HIIT, combined | Not being clear or based on the standard definition of the implementation protocol.<br>Implementation of any other intervention along with exercise (such as drug interventions, diet, and psychological interventions) |
| Comparator | After intervention results with before.<br>Case result group with control group. | Unavailability of exact before and after values for participants in each group. |
| Outcomes | Irisin serum or plasma concentration measured by ELISA method. | Serum or plasma concentration of irisin measured by a method other than ELISA |
| Study design | Randomized or non-randomized Controlled trails. | Non-controlled trails |

question here is which types of exercise training can have a more significant impact on irisin release in obese and overweight individuals without any other health disorders. Therefore, the objective of this study is to determine whether there are any differences in irisin levels among different types of exercise in healthy overweight and obese adults through a meta-analysis and systematic review.

## Methods

### Eligibility criteria

#### *Information sources and search strategy*

The inclusion and exclusion criteria in this research are shown in Table1. This systematic review followed the PRISMA 2020 guidelines.[19] English databases such as PubMed, Google Scholar, ISI Web of Science Core Collection, and Scopus were utilized in this research (2012–2023). A thorough search was conducted using search strategies that targeted specific keywords, titles, and abstracts. The phrases and words listed in Table 2 were employed during the exploration process. Furthermore, references cited in each article, available review articles, and meta-analyses were thoroughly examined until February 1, 2023.

In addition to the database searches, manual searches were performed on the reference lists of included studies to identify potentially relevant titles. The abstracts of these articles were checked for relevant inclusion criteria. If necessary, the full text was further investigated. Additionally, snowballing citation tracking was conducted, preferably using Web of Science.

### Selection process

Two of the authors (JR and AT) independently screened the retrieved records, including titles and abstracts. The same authors also independently screened the gathered full texts. Disagreements between the two authors were discussed in a joint reanalysis. In cases where no consensus was reached, a third author (MK) made the final decision. All potentially relevant articles were added to EndNote, and duplicates were removed. From the remaining cases, after reviewing the abstract, if they met the inclusion criteria, the full text was studied for further review. The process of selecting studies is shown in Figure 1.

This meta-analysis focused on researching the effects of aerobic, resistance, combined, and HIIT exercise training on plasma irisin in overweight and obese individuals under pre- and post-test conditions. According to references, the definition of aerobic training in this study considered the continuous and balanced use of large muscle groups, maintaining moderate to vigorous physical activity for an extended period.[20] Resistance training involves exercises targeting a specific muscle or muscle group against an

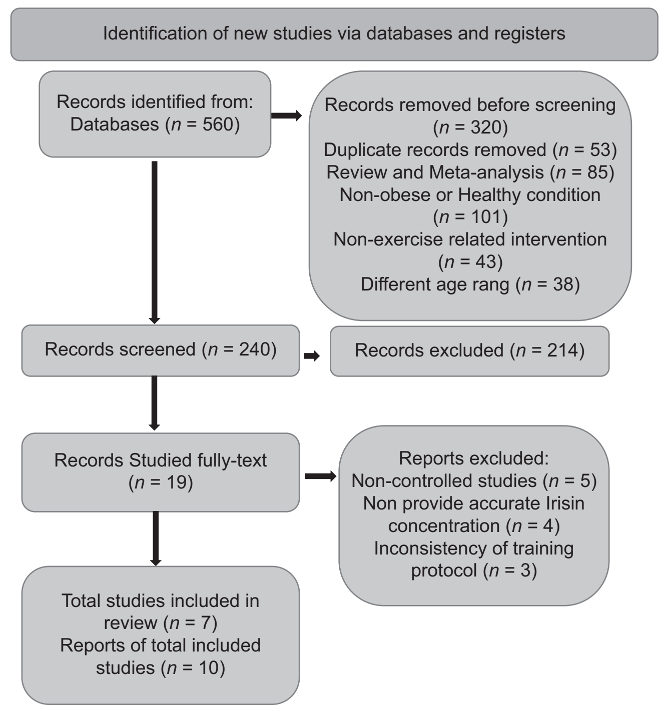


**Figure 1: Flowchart illustrating the different phases of the search and study selection**

**Table 2: Search strategies and results**

| Search databases | Search strategy | Identified Studies |
|---|---|---|
| ISI Web of Science | Irisin OR FNDC5 (Topic) AND exercise OR aerobic training OR resistance training OR combined training OR HIIT training OR physical (Topic) AND obesity OR overweight (Topic) NOT mice OR rat OR mouse (Topic) | 297 |
| PubMed | ((((((((irisin) OR FNDC5)) AND ((((((exercise) OR physical) OR aerobic training) OR resistance training) OR combined training) OR HIIT) AND (obesity) AND (overweight)) NOT (((mice) OR rats) OR mouse) | 131 |
| Google Scholar | (Irisin OR FNDC5) AND (exercise OR physical OR aerobic OR resistance OR combined OR HIIT OR training) AND (obesity OR overweight) -mice -rat -mouse | 66 |
| Scopus | (TITLE-ABS-KEY (irisin) OR TITLE-ABS-KEY (FNDC5))) AND ((TITLE-ABS-KEY (exercise) OR TITLE-ABS-KEY (aerobic training) OR TITLE-ABS-KEY (resistance training) OR TITLE-ABS-KEY (combined training) OR TITLE-ABS-KEY (HIIT) OR TITLE-ABS-KEY (physical))) AND (TITLE-ABS-KEY (obesity) OR TITLE-ABS-KEY (overweight))) AND NOT ((TITLE-ABS-KEY (mice) OR TITLE-ABS-KEY (rats) OR TITLE-ABS-KEY (mouse)) | 66 |

external resistance, such as free weights, weight machines, or body weight, with the goal of improving muscle fitness based on 1RM.[20] Combined training includes both aerobic and resistance training in a single session,[21] while HIIT involves performing repeated high-intensity exercise movements alternated with low-intensity exercises or rest periods of varying durations.[20,21]

### Data extraction

Titles and abstracts were checked by AT. The authors (JR, MK, and AT) screened the studies and examined the variables, including participants' characteristics (age, BMI, sample size), protocol details (type, intensity, duration, and frequency), and outcome (irisin concentration). Following data extraction, statistical steps, and meta-analysis were performed by MM. The risk of bias was assessed using the Egger and Begg bias tool.

### Data synthesis

The effect size in this research was reported using standard mean difference (SMD), based on a review of the research background and current studies. The same methods (data assimilation) were used to calculate the average difference in pre- and post-irisin levels.

### Study quality

The TESTEX quality checklist[22] was employed to assess the quality of the studies, and reviewers assigned scores based on the established criteria.

### Data items

The review included studies that investigated and reported the concentration of irisin after a specified period of time (8 weeks). Studies using a concentration-checking method other than the ELISA method were excluded from the final review.

Based on the reported M ± SD (Mean ± Standard deviation) before and after the intervention in the available literature, the effect size was calculated and reported using the mean changes before and after the intervention.

### Effect measures

Data analysis was performed using comprehensive meta alaysis (CMA) V.2. Based on the results report in the available literature, the effect size was calculated and reported based on the mean changes before and after the intervention. Heterogeneity was expected in the size and characteristics of the study populations and in the characteristics of the interventions, such as the protocol training, participant's BMI, and their demographic varaibles. To determine the heterogeneity across the studies, the $Chi^2$ and $I^2$ tests were used.[23] Heterogeneity was interpreted as not important when $I^2$ was less than 50%. For the $Chi^2$ test, a p□value less 0.05 was used to determine statistical significance in heterogeneity.[23]

### Synthesis methods

Information regarding the examination of concentration in the exercise and control groups was collected from the tables or text of the included studies and organized in an Excel spreadsheet. The table contained details such as author names, year of publication, country, and information related to subgroups, including BMI, subjects' gender, age, and type of exercise protocol performed. To standardize the unit of measurement, micrograms per milliliter (μg/ml) were used as the final unit of data in the synthesis stage. For studies that reported concentrations in nanograms per milliliter (ng/ml), unit conversion was performed. Table 5 presents the numbers related to the effect size and overall heterogeneity, effect size and heterogeneity for each subgroup, and the results of the adjustment.

## Results

In total, 560 articles were identified during the search process, out of which 240 articles were screened. Among the 19 articles that were studied in full text, seven articles were selected for analysis. These seven articles consisted of 10 training groups, including four HIIT, two aerobic, two resistance, and two combined groups. A total of 217 participants (mean age 35.83 ± 4.48) were included in this systematic review and meta-analysis.

Intervention Details

The information extracted from the studies has been summarized and is presented in Table 3.

### Measuring the quality of studies

The quality assessment of the studies was conducted using the TESTEX method. The results of this assessment can be seen in Table 4. The TESTEX method examines 12 fields, which have a total score of 15. The average score of the seven included studies was 10.57, with the lowest score being 10 and the highest score being 11. The publication bias was measured as 0.02 using Bagg's test (Begg ranked correlation method) and 0.006 using Egger's test (Egger regression method).

### Systematic review

In the current review, seven articles with ten controlled exercise training groups were included, evaluating the effect of exercise training (aerobic, resistance, combined, and HIIT) on serum irisin changes. All ten training groups exhibited an increase in serum irisin concentration. Out of these, seven groups showed a significant intragroup increase, while three groups showed an insignificant intragroup increase. Moreover, eight training groups demonstrated significant differences between the training and control groups after exercise training, whereas two groups reported insignificant differences between the training and control groups afterward.

**Table 3: Intervention details of the studies**

| Study (country) | Total Sample Size | Training Protocol | BMI | Gender | Age | Training Protocol Description | Length of the Intervention (by week) | Sessions Per week | Statistical Measures In Training Group (Originally) | Statistical Measures In control Group (Originally) | Intragroup Results | Intergroup Results |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bonfante *et al*. 2017 (Brazil)[24] | 22 | CT | 30≤ BMI | Male | Up 40 | AT: 55-85%vo2peak<br>RT: 6-10 RM | 8 | 3 | Pre: 4.15±0.32<br>Post: 4.21±0.32 | pre: 4.36±0.23<br>post: 3.57±0.94 | ↑ | ↑* |
| Tofighi *et al*. 2017 (Iran)[25] | 20 | HIIT | 30≤ BMI | Female | Less 40 | 90% RHR | 8 | 3 | Pre: 162.73±4.45<br>Post: 175.55±7.22 | Pre: 162.03±2.45<br>Post: 162.29±4.36 | ↑* | ↑* |
| Rezaeimanesh. 2020 (Iran)[26] | 24 | AT | 25≤ BMI <30 | Male | Less 40 | 60-80% MHR | 8 | 3 | Pre: 4.14±0.79<br>Post: 5.1±1.43 | Pre: 4.17±0.76<br>Post: 4.1±0.94 | ↑* | ↑* |
| Rezaeimanesh. 2020 (Iran)[26] | 24 | HIIT | 25≤ BMI <30 | Male | Less 40 | 90% MHR | 8 | 3 | Pre: 4.05±0.82<br>Post :5.78±1.75 | Pre: 4.17±0.76<br>Post: 4.1±0.94 | ↑* | ↑* |
| Jafari M *et al*. 2020 (Iran)[27] | 20 | HIIT | 25≤ BMI <30 | Male | Less 40 | 90% MHR | 8 | 3 | Pre: 6.3±2.7<br>Post: 7.2±2.5 | Pre: 5.9±2.6<br>Post: 5.02±1.66 | ↑* | ↑* |
| Poutafkand *et al*. 2020 (Iran)[28] | 24 | AT | 30≤ BMI | Female | Up 40 | 50-80% RHR | 8 | 3 | Pre: 14.8±49.83<br>Post: 15.9±13.11 | Pre: 14.12±93.38<br>Post: 15.11±18.51 | ↑ | ↑ |
| Poutafkand *et al*. 2020 (Iran)[28] | 23 | RT | 30≤ BMI | Female | Up 40 | 50-65% 1RM | 8 | 3 | Pre: 8.3±79.88<br>Post: 9.5±67.24 | Pre: 14.12±93.38<br>Post: 15.11±18.51 | ↑ | ↑ |
| Haghighi *et al*. 2022 (Iran)[29] | 20 | RT | 25≤ BMI <30 | Male | Less 40 | 85-90% 1RM | 8 | 3 | Pre: 3.46±0.84<br>Post: 4.74±1.04 | Pre: 3.26±0.80<br>Post: 3.44±0.72 | ↑* | ↑* |
| Haghighi *et al*. 2022 (Iran)[29] | 20 | HIIT | 25≤ BMI <30 | Male | Less 40 | 85-95% MHR | 8 | 3 | Pre: 3.87±0.82<br>Post: 4.73±0.89 | Pre: 3.26±0.80<br>Post: 3.44±0.72 | ↑* | ↑* |
| Nazari *et al*. 2017 (Iran)[30] | 20 | CT | 25≤ BMI <30 | Male | Less 40 | AT: 50-85% MHR<br>RT: 50-80% 1RM | 8 | 3 | Pre: 34.8±14.28<br>Post53.6±23.92 | Pre: 33.1±13.03<br>Post: 33.6±12.36 | ↑* | ↑* |

**Table 4: Results of measuring the quality of studies**

| Study | Eligibility criteria included | Randomization method stated | Allocation concealment | Groups similar at baseline | Assessor blinded | Outcome measures assessed | Intention-to-treat analysis | Between-group statistical comparisons | Point measures for all outcomes | Activity monitoring controls | Relative exercise intensity adjusted | Exercise energy expenditure information | Overall TESTEX |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bonfante *et al.* 2017[24] | 1 | 0 | 1 | 1 | 1 | 2 | 0 | 2 | 1 | 0 | 0 | 1 | 10 |
| Tofighi *et al.* 2017[25] | 1 | 0 | 1 | 1 | 1 | 2 | 0 | 2 | 1 | 0 | 0 | 1 | 10 |
| Rezaeimanesh. 2020[26] | 1 | 0 | 1 | 1 | 1 | 2 | 0 | 2 | 1 | 0 | 1 | 1 | 11 |
| Jafari M *et al.* 2020[27] | 1 | 0 | 1 | 1 | 1 | 2 | 0 | 2 | 1 | 0 | 1 | 1 | 11 |
| Poutafkand *et al.* 2020[28] | 1 | 0 | 1 | 1 | 1 | 1 | 0 | 2 | 1 | 0 | 1 | 1 | 10 |
| Haghighi *et al.* 2022[29] | 1 | 0 | 1 | 1 | 1 | 2 | 0 | 2 | 1 | 0 | 1 | 1 | 11 |
| Nazari *et al.* 2017[30] | 1 | 0 | 1 | 1 | 1 | 2 | 0 | 2 | 1 | 0 | 1 | 1 | 11 |

Based on the type of training protocol:
Among the four HIIT groups, all showed a significant intragroup increase. Additionally, one aerobic group, one resistance group, and one combined group exhibited a significant intragroup increase, whereas another aerobic group, another resistance group, and another combined group showed an insignificant intragroup increase.

Based on the BMI of participants:
In the four groups that performed exercises in obese individuals (30 ≤ BMI), three groups showed an insignificant increase, and only one group showed a significant increase. In all six groups that performed exercises in overweight individuals (25 ≤ BMI <30), there were significant increases in irisin levels.

Based on the gender of participants:
Among the seven groups performed by male participants, six showed a significant increase, while one showed an insignificant increase. In the three groups performed by female participants, two showed an insignificant increase, and only one showed a significant increase.

### Meta-analysis

The data used for the present meta-analysis consisted of 111 exercise training groups and 106 participants in the control groups. The overall changes were calculated as SMD = 0.957 (CI: 0.535-1.379), with a $P$ value of less than 0.005. The analysis showed a heterogeneity of I2 = 53% with a $P$ value of less than 0.05. The Begg test indicated publication bias with a $P$ value of 0.02, and the Egger test showed a $P$ value of 0.006. Changes in each subgroup based on exercise protocol, age, gender, and BMI in the intervention groups were calculated and presented in Table 5 and Figure 2.

## Discussion

Based on our findings, this meta-analysis is the first study to investigate the effect of four different exercise protocols on changes in plasma irisin in obese and overweight individuals (without any other health disorders). The results of the present study demonstrate the following:

The effect of different exercise protocols on irisin levels is increased in obese and overweight individuals.

This effect varies among participants based on factors such as age, sex, BMI, and the type of exercise protocol implemented.

Among the aerobic, resistance, combined, and HIIT exercise protocols, HIIT resulted in the most significant changes (SMD = 1.229 (0.609, 1.989), $P < 0.001$). The overall heterogeneity in the studies was significant (I2 = 53%, $P < 0.05$), which may be attributed to factors such as age, gender, and BMI. These factors were also examined separately in this study.

Exercise training, regardless of the type of protocol, led to significant incremental changes in men, overweight

**Table 5: Results in each subgroup**

| Subgroups | Division | Sample size | Number of studies | MD (95% CI), Random or fix, *P* | $I^2$ ($P_{heterogeneity}$) |
|---|---|---|---|---|---|
| Total | - | 217 | 10 | 0.957 (0.535,1.379), Random <0.005 | 53 (<0.05) |
| Protocol training | Aerobic | 48 | 2 | 0.473 (-0.469, 1.415), Random 0.325 | 61.74 (0.106) |
| | Resistance | 43 | 2 | 0.611 (-0.632, 1.854), Random 0.335 | 74.25 (0.049) |
| | Combined | 42 | 2 | 1.220 (0.559, 1.880), Fix 0.001 | 0 (0.637) |
| | HIIT | 84 | 4 | 1.229 (0.609, 1.989), Fix <0.001 | 51.53 (0.103) |
| Participant's BMI | Obese | 89 | 4 | 0.89 (-0.169, 1.954), Random 0.1 | 81.50 (0.001) |
| | Overweight | 128 | 6 | 1.048 (0.677, 1.419), Fix <0.001 | 0 (0.885) |
| Gender | Male | 150 | 7 | 1.093 (0.749, 1.438), Fix <0.001 | 0 (0.906) |
| | Female | 67 | 3 | 0.745 (-0.621, 2.111), Random 0.285 | 85.17 (0.001) |
| Age of participants | >40 years | 69 | 3 | 0.432 (-0.422, 1.286), Random 0.322 | 67.04 (0.048) |
| | <40 years | 148 | 7 | 1.176 (0.823, 1.529), Fix <0.001 | 9.41 (0.357) |
| Adjust | - | 217 | 10 | 0.641 (0.386,0.897), <0.05 | - |

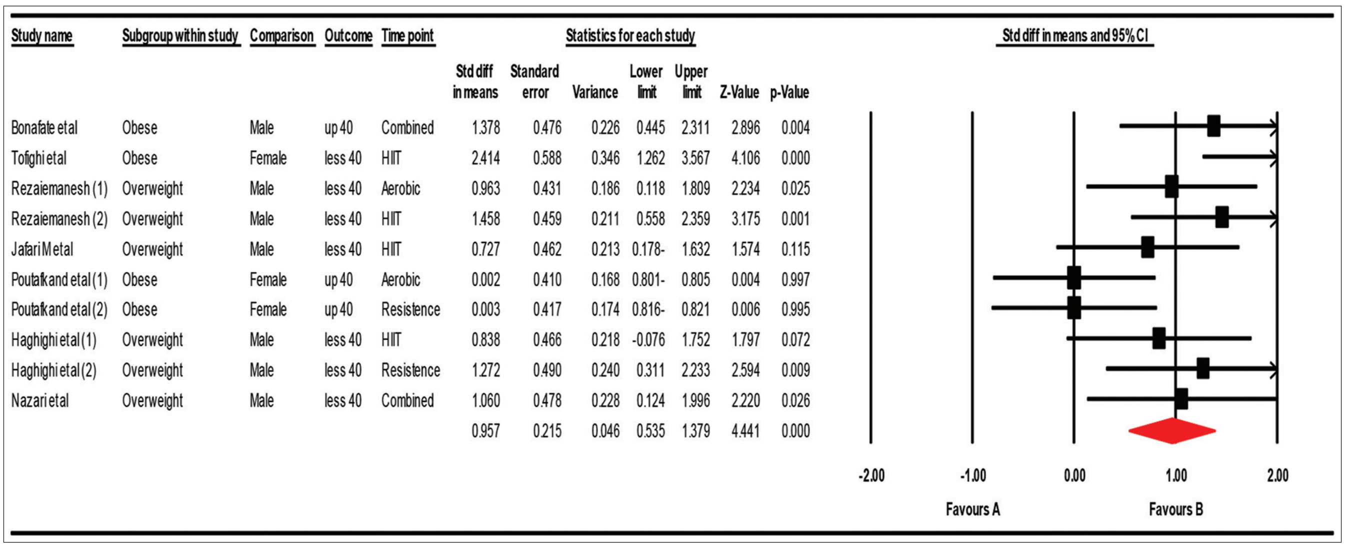


**Figure 2: The forest plot**

individuals, and individuals under 40 years old. However, it showed insignificant changes in women, obese individuals, and individuals over 40 years old.

As previously mentioned, exercise is a practical solution for preventing and treating excess weight and the problems associated with it.[2] Among the effects of exercise, one of the causes is the release of the myokine irisin and its thermogenic effect. This myokine increases the expression of UCP1,[3] enabling white adipose tissue to acquire the characteristics of brown adipose tissue.[31] Brown adipose tissue is metabolically more active than white fat tissue.[32] Therefore, it can be said that exercise-induced irisin may have a therapeutic effect on overweight individuals.[33]

Previous research has been conducted to diagnose the effects of exercise, and several studies have shown that long-term exercise has a positive impact. Specifically, in obese individuals, various types of exercises have been studied. Endurance and combined exercises in obese older women, combined and resistance training in obese middle-aged men, endurance and resistance training in young obese men,[8] and 6-month daily aerobic training in obese men[34] have all been found to increase the amount of irisin in the blood. Regardless of the intervention duration, high-intensity exercises with supplement consumption,[35] aerobic exercises in obese individuals,[36-39] resistance exercises in overweight and obese people,[40] and HIIT training in these populations[39] have all shown a significant increase in irisin levels. However, taekwondo training in obese teenagers[41] and aerobic training in overweight girls[42] have shown a decrease in irisin levels. Additionally, aerobic exercises did not produce significant changes in obese individuals,[43] resistance exercises in obese and overweight individuals,[44,45] combined exercises in obese men.[24] In any case, the overall effect of the present meta-analysis was statistically significant, indicating that exercise increases serum irisin levels, with SMD = 0.957 (CI: 0.535-1.379), $P < 0.005$.

There is consistent evidence supporting the positive effect of HIIT and combined exercises. Qiu *et al*.[46] (2015)

reported that resistance training and HIIT have a greater effect on increasing irisin in obese and overweight individuals compared to other types of exercises. Li *et al*.[9] (2018) found that combined exercises have a greater impact on increasing irisin in obese and overweight subjects compared to other types of exercises. Batumi (2020),[47] Rezaeimanesh (2020),[26] Jafari *et al*. (2019),[27] Tofighi *et al*. (2017),[25] and Winn *et al*. (2017)[39] all reported a significant increase in irisin levels due to HIIT exercises. However, inconsistent evidence exists regarding the significant effect of HIIT and combined exercises. Archundia-Herrera *et al*.[42] (2017) reported that HIIT exercises did not have a significant effect. Bonfante *et al*. (2017)[24] and Brinkmann *et al*. (2020)[48] found the effect of combined exercises to be insignificant. Norheim *et al*.[49] (2017) reported a decrease in irisin levels due to combined exercises.

The effect size of the four different exercise protocols on serum irisin concentration, as indicated in Table 5, exhibited significant variations. Notably, the effect size was higher in men (1.09) compared to women (0.74) based on the specific exercise protocol used in men. Among women, only the HIIT protocol resulted in significant changes in irisin serum concentration. These differences may be attributed to variations in body composition between men and women, particularly in terms of fat and lean mass. Men tend to have higher lean mass while women tend to have more fat mass.[50] Furthermore, gender can influence the composition of fat tissue and muscle tissue, as well as impact behavior, lifestyle, and life choices. These factors can potentially alter biological processes and the effects of exercise on various biological pathways.[51] Our findings are consistent with the results obtained by Rezaei Menesh in 2020,[26] Jafari *et al*. in 2020,[27] and Otero *et al*.[38] in 2018.

### The effect of four different exercise protocols on serum irisin concentration according to body mass index (BMI)

The results obtained from studying the effect of different exercise protocols on increasing irisin serum concentration in obese and overweight individuals [based on Table 5] showed significant values for the effect size of the four types of protocols in both the overweight group (BMI below 30) and the obese group (BMI above 30). These values indicate the impact of exercise on both groups. The effect size was larger (1.04) in the group of obese individuals compared to the group of overweight individuals (0.89). Considering that plasma irisin levels are significantly higher in obese patients compared to individuals with normal weight and the positive correlation between plasma irisin levels and body weight, BMI, and fat mass,[52] the reason for this difference could be the presence of more adipose tissue in obese individuals. It has been shown that irisin can also be secreted from the adipose tissue of rodents.[5]

Analyzing the individual effects of each type of exercise protocol in each group, it was found that in the overweight group, resistance training, HIIT, and aerobics had a significant effect size, while combined exercises showed a non-significant effect size. In the obese group, none of the exercise protocols individually produced a significant effect size. These findings align with the research conducted by Otero *et al*.[38] in 2018 and Jafari *et al*.[27] in 2020.

Furthermore, it has been reported that irisin is secreted not only by muscles but also by adipose tissue. It appears that reducing adipose tissue through HIT can affect irisin concentration.[53,54] In other words, reducing fat tissue, which is the target tissue of irisin and the source of its secretion, can modulate its concentration.[53] Irisin induces fat browning by up-regulating the expression of uncoupling protein 1 (UCP1).[54] It can stimulate mitochondrial biogenesis by improving the expression of peroxisome proliferator-activated receptor-alpha (PPARA) and mitochondrial transcription factor A (TFAM).[54] Irisin has been reported to modulate the function of various organs, including the heart, skeletal muscles, liver, bones, brain, adipose tissue, pancreas, ovaries, and kidneys, at different levels. Irisin not only increases oxidative capacity but also stimulates muscle hypertrophy by affecting the Akt/mTOR/p70S6 pathway.[44] Although it is released from various tissues, skeletal muscle accounts for more than 70% of irisin secretion in humans.[53]

### The effect of four different exercise protocols on serum irisin concentration according to age

The results obtained from the effects of different exercise protocols on increasing irisin serum concentration in obese and overweight individuals showed significant findings. The total effect size of the four types of protocols in both age groups, individuals aged 40 and under 40 years and those aged 40 years and above, demonstrated significant values, indicating the effectiveness of exercise training in both age groups. The effect size was found to be higher (1.17) in the under 40 age group compared to the over 40 age group (0.43). This difference can be attributed to the decline in muscle mass associated with aging. In individuals under 40 years of age, higher levels of this muscle-originated myokine were released, as it is known that regardless of gender, ethnicity, or other factors, individuals experience a muscle mass loss of approximately 1 to 2% per year starting from their fourth decade onwards.[55]

Regarding the individual effect size of each protocol in the under 40 age group, resistance training, HIIT, and aerobic training protocols, respectively, exhibited significant effect sizes, while combined exercises did not show a significant effect size. In the over 40 age group, only combined and aerobic exercises resulted in a significant effect size, whereas the effect size associated with resistance training protocols and HIIT was not statistically significant.

## Conclusions

In fact, the findings of the present study have implications for various training protocols, different genders, varying levels of overweight, and different age groups. Among the four different types of training protocols that can be selected to design a training program aimed at increasing the concentration of serum irisin, the HIIT training protocol demonstrates the most significant impact in inducing these changes. If individuals fall within the overweight range as determined by their BMI, HIIT training can have the most profound effect on increasing serum irisin levels. However, in obese individuals, no specific type of training proves superior to other methods. When considering the gender of the participants engaged in the exercise program, HIIT appears to have the greatest influence on increasing serum irisin levels in males, while no particular exercise type demonstrates superiority over other methods in females.

### Limitations of the study

This study is subject to several limitations that arise from the stages of data collection through to the presentation of findings. Firstly, the search was confined to only four databases (Web of Science, Google Scholar, PubMed, and Scopus) to manage duplicate data. Secondly, only articles written in English were considered for evaluation within these databases. However, no automation tools, such as Robot Reviewer, were employed for systematic search, thereby introducing a potential risk of bias.

Another limitation of this systematic review and meta-analysis pertains to the selected studies. The present systematic review and meta-analysis have identified certain constraints associated with the included studies. The TESTEX scale, which is recommended for evaluating methodological quality and risk of bias in sports science research, was employed. However, it was determined that the included studies were of moderate or good quality. It is worth noting that the overall quality may have been diminished due to the inclusion of controlled experimental studies in this analysis. Therefore, conducting systematic reviews and meta-analyses with higher quality studies necessitates the inclusion of randomized controlled experimental studies.

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### Conflicts of interest

There are no conflicts of interest.

### Author Contribution

JR and MK conceived and designed research. AT collected articles. JR and ATcontributed analytical tools.MM analyzed data. JR and AT wrote the manuscript. All authors read and approved the manuscript.

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## References

1. World Health Organization. Draft Recommendations for the Prevention and Management of Obesity Over the Life Course, Including Potential Targets. Geneva: World Health Organization; 2021.
2. Donnelly JE, Blair SN, Jakicic JM, Manore MM, Rankin JW, Smith BK, *et al*. Appropriate physical activity intervention strategies for weight loss and prevention of weight regain for adults. Med Sci Sports Exerc 2009;41:459-71.
3. Boström P, Wu J, Jedrychowski MP, Korde A, Ye L, Lo JC, *et al*. A PGC1-α-dependent myokine that drives brown-fat-like development of white fat and thermogenesis. Nature 2012;481:463-8.
4. Arhire LI, Mihalache L, Covasa M. Irisin: A hope in understanding and managing obesity and metabolic syndrome. Front Endocrinol 2019;10:524. doi: 10.3389/fendo. 2019.00524.
5. Roca-Rivada A, Castelao C, Senin LL, Landrove MO, Baltar J, Crujeiras AB, *et al*. FNDC5/irisin is not only a myokine but also an adipokine. PloS One 2013;8:e60563.
6. Kurdiova T, Balaz M, Vician M, Maderova D, Vlcek M, Valkovic L, *et al*. Effects of obesity, diabetes and exercise on Fndc5 gene expression and irisin release in human skeletal muscle and adipose tissue: *in vivo* and *in vitro* studies. J Physiol 2014;592:1091-7.
7. Andrade PA, Silveira BS, Rodrigues AC, da Silva FO, Rosa CB, Alfenas RG. Effect of exercise on concentrations of irisin in overweight individuals: A systematic review. Sci Sports 2018;33:80-9.
8. Jandova T, Buendía-Romero A, Polanska H, Hola V, Rihova M, Vetrovsky T, *et al*. Long-term effect of exercise on Irisin Blood levels—systematic review and meta-analysis. Healthcare 2021;9:1438. doi: 10.3390/healthcare 9111438.
9. Li H, Tian Y, Liu J, Cao Z. PO-256 influences of exercise on circulating irisin in overweight or obese individuals: A system review. Exersise Biochemistry Reviwe 2018;1. doi: 10.14428/ebr. v1i5.11043.
10. Chen N, Li Q, Liu J, Jia S. Irisin, an exercise-induced myokine as a metabolic regulator: An updated narrative review. Diabetes Metab Res Rev 2016;32:51-9.
11. Kraemer R, Shockett P, Webb N, Shah U, Castracane V. 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.
12. Motahari Rad M, Bijeh N, Attarzadeh Hosseini SR, Raouf Saeb A. The impact of different modes of exercise training on irisin: a systematic review and meta-analysis research. Journal of Advances in Medical and Biomedical Research 2021;29:125-38.
13. Eaton M, Granata C, Barry J, Safdar A, Bishop D, Little JP. Impact of a single bout of high-intensity interval exercise and short-term interval training on interleukin-6, FNDC5, and METRNL mRNA expression in human skeletal muscle. J Sport Health Sci 2018;7:191-6.
14. Amanat S, Sinaei E, Panji M, Mohammadpor Hodki R,

Bagheri-Hosseinabadi Z, Asadimehr H, *et al*. A randomized controlled trial on the effects of 12 weeks of aerobic, resistance, and combined exercises training on the serum levels of nesfatin-1, irisin-1 and HOMA-IR. Front Physiol 2020;11:562895. doi: 10.3389/fphys. 2020.562895.

15. Fatouros IG. Is irisin the new player in exercise-induced adaptations or not? A 2017 update. Clin Chem Lab Med 2018;56:525-48.
16. Fox J, Rioux B, Goulet E, Johanssen N, Swift D, Bouchard D, *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.
17. 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.
18. 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.
19. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, *et al*. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. Int J Surg 2021;88:105906. doi: 10.1016/j.ijsu. 2021.105906.
20. American College of Sports Medicine. ACSM's Guidelines for Exercise Testing and Prescription. Lippincott Williams and Wilkins Philadelphia; 2013.
21. Campbell MD, Rutherford ZH. The role of physical activity and exercise in managing obesity and achieving weight loss. Practical Guide to Obesity Medicine. Edited by Jolanta Urszula Weaver. St. Louis, MO, United States: Elsevier; 2018. p. 215-30.
22. Smart NA, Waldron M, Ismail H, Giallauria F, Vigorito C, Cornelissen V, *et al*. Validation of a new tool for the assessment of study quality and reporting in exercise training studies: TESTEX. JBI Evid Implement 2015;13:9-18.
23. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ 2003;327:557-60.
24. Bonfante ILP, Chacon-Mikahil MPT, Brunelli DT, Gaspari AF, Duft RG, Lopes WA, *et al*. Combined training, FNDC5/irisin levels and metabolic markers in obese men: A randomised controlled trial. Eur J Sport Sci 2017;17:629-37.
25. Tofighi A, Alizadeh R, Tolouei Azar J. The effect of eight weeks high intensity interval training (hiit) on serum amounts of fgf21 and irisin in sedentary obese women. Studies in Medical Sciences 2017;28:453-66.
26. Rezaeimanesh D. Effects of interval training on irisin and insulin resistance in overweight men. Arch Pharm Pract 2020;11:78-83.
27. Jafari M, Abbasi I, Aralloo SF. The effect of eight weeks high-intensity interval training (HIT) on of irisin levels in obese young men. Thrita 2019;8. doi: 10.5812/thrita. 99505.
28. Poutafkand F, Marefati H, Taherichadorneshin H. A comparison of the effects of resistance and endurance training protocols on serum irisin level and alkaline phosphatase activity in sedentary obese women. Polish Journal of Sport and Tourism 2020;27:23-8.
29. Haghighi AH, Hajinia M, Askari R, Abbasian S, Goldfied G. Effect of high-intensity interval training and high-intensity resistance training on Irisin and fibroblast growth factor 21 in men with overweight and obesity. Can J Physiol Pharmacol 2022;100:937-44.
30. Nazari Y, Nikbakht M, Habibi A. An investigation into irisin levels: Acute and chronic effects of combined training and its association with anthropometric variables in overweight men. J Chem Health Risks 2017;7:171-9.
31. Wu J, Boström P, Sparks LM, Ye L, Choi JH, Giang A-H, *et al*. Beige adipocytes are a distinct type of thermogenic fat cell in mouse and human. Cell 2012;150:366-76.
32. Enerbäck S. Human brown adipose tissue. Cell Metab 2010;11:248-52.
33. Højlund K, Boström P. Irisin in obesity and type 2 diabetes. J Diabetes Complications. 2013;27:303-4.
34. Rashid FA, Abbas HJ, Naser NA, Ali A. Effect of long-term moderate physical exercise on irisin between normal weight and obese men. ScientificWorldJournal 2020;2020:1897027. doi: 10.1155/2020/1897027.
35. Batitucci G, Brandao CFC, De Carvalho FG, Marchini JS, Pfrimer K, Ferrioli E, *et al*. Taurine supplementation increases irisin levels after high intensity physical training in obese women. Cytokine 2019;123:154741. doi: 10.1016/j.cyto. 2019.154741.
36. Inoue K, Fujie S, Hasegawa N, Horii N, Uchida M, Iemitsu K, *et al*. Aerobic exercise training-induced irisin secretion is associated with the reduction of arterial stiffness via nitric oxide production in adults with obesity. Appl Physiol Nutr Metab 2020;45:715-22.
37. Korkmaz A, Venojärvi M, Wasenius N, Manderoos S, Deruisseau KC, Gidlund E-K, *et al*. Plasma irisin is increased following 12 weeks of Nordic walking and associates with glucose homoeostasis in overweight/obese men with impaired glucose regulation. Eur J Sport Sci 2019;19:258-66.
38. Otero-Díaz B, Rodríguez-Flores M, Sánchez-Muñoz V, Monraz-Preciado F, Ordoñez-Ortega S, Becerril-Elias V, *et al*. Exercise induces white adipose tissue browning across the weight spectrum in humans. Front Physiol 2018;9:1781. doi: 10.3389/fphys. 2018.01781.
39. Winn NC, Grunewald ZI, Liu Y, Heden TD, Nyhoff LM, Kanaley JA. Plasma irisin modestly increases during moderate and high-intensity afternoon exercise in obese females. PloS One 2017;12:e0170690. doi: 10.1371/journal.pone. 0170690.
40. Kim H-J, Lee H-J, So B, Son JS, Yoon D, Song W. Effect of aerobic training and resistance training on circulating irisin level and their association with change of body composition in overweight/obese adults: A pilot study. Physiol Res 2016;65:271-9.
41. Roh H-T, Cho S-Y, So W-Y. Effects of regular taekwondo intervention on oxidative stress biomarkers and myokines in overweight and obese adolescents. Int J Environ Res Public Health 2020;17:2505. doi: 10.3390/ijerph 17072505.
42. Archundia-Herrera C, Macias-Cervantes M, Ruiz-Muñoz B, Vargas-Ortiz K, Kornhauser C, Perez-Vazquez V. Muscle irisin response to aerobic vs HIIT in overweight female adolescents. Diabetol Metab Syndr 2017;9:1-7. doi: 10.1186/s13098-017-0302-5.
43. Aydin S, Aydin S, Kuloglu T, Yilmaz M, Kalayci M, Sahin İ, *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.
44. Rioux BV, Brunt KR, Eadie AL, Bouchard DR, Fox J, Sénéchal M. Impact of acute circuit training on irisin in younger and older overweight adults. Appl Physiol Nutr Metab 2021;46:1248-56.
45. Tibana R, da Cunha Nascimento D, Frade de Souza N, De Souza V, de Sousa Neto I, Voltarelli F, *et al*. Irisin levels are not associated to resistance training-induced alterations in body mass composition in older untrained women with and without obesity. J Nutr Health Aging 2017;21:241-6.
46. Qiu S, Cai X, Sun Z, Schumann U, Zuegel M, Steinacker JM. Chronic exercise training and circulating irisin in adults: A meta-analysis. Sports Med 2015;45:1577-88.
47. Batumi A. The changes of irisin levels in athletes after eight

weeks intensity internal training. Journal of Humanities Insights 2020;4:41-4.

48. Brinkmann C, Weh-Gray O, Bloch W, Brixius K, Predel H-G, Kreutz T. Effects of a combined endurance/strength training program on circulating irisin levels in overweight/obese men and women with type 2 diabetes mellitus. Exp Clin Endocrinol Diabetes 2022;130:37-42.
49. Norheim F, Langleite TM, Hjorth M, Holen T, Kielland A, Stadheim HK, *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.
50. Bredella MA. Sex Differences in Body Composition. In: Mauvais-Jarvis, F. (eds) Sex and Gender Factors Affecting Metabolic Homeostasis, Diabetes and Obesity. Advances in Experimental Medicine and Biology. Springer, Cham 2017;1043. doi.org/10.1007/978-3-319-70178-3_2.
51. Moreira-Pais A, Ferreira R, Neves JS, Vitorino R, Moreira-Gonçalves D, Nogueira-Ferreira R. Sex differences on adipose tissue remodeling: From molecular mechanisms to therapeutic interventions. J Mol Med 2020;98:483-93.
52. Pardo M, Crujeiras AB, Amil M, Aguera Z, Jiménez-Murcia S, Baños R, *et al*. Association of irisin with fat mass, resting energy expenditure, and daily activity in conditions of extreme body mass index. Int J Endocrinol. 2014;2014:857270. doi: 10.1155/2014/857270.
53. Motahari Rad M, Bijeh N, Attarzadeh Hosseini SR, Raouf Saeb A. The impact of different modes of exercise training on irisin: A systematic review and meta-analysis research. J Adv Med Biomed Res 2021;29:125-38.
54. Piccirillo R. Exercise-induced myokines with therapeutic potential for muscle wasting. Front Physiol 2019;10:287. doi: 10.3389/fphys. 2019.00287.
55. Arnold A-S, Egger A, Handschin C. PGC-1α and myokines in the aging muscle – A mini-review. Gerontology 2011;57:37-43.