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# Effects of resistance training on insulin sensitivity in the elderly: A meta-analysis of randomized controlled trials

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A R T I C L E I N F O

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A B S T R A C T

*Objective:* We performed a systematic review and meta-analysis of randomized controlled trials (RCTs) assessing the effect of resistance training in older adults on insulin sensitivity. Methods: Cochrane, Embase, PubMed, Web of Science and EBSCO were searched from inception to April 2021. We integrated randomized controlled trials published in English, and participants were non-athletic and aged ≥60 years. The outcome of interest was the change in insulin sensitivity, derived from the homeostatic model of insulin resistance (HOMA-IR) and hemoglobin A1c (HbA1c). Results: 12 RCTs were included in this meta-analysis comparing resistance training (n = 232) with control (n = 209). Resistance exercise significantly reduced HOMA-IR level (d = −0.25, 95% CI, −0.43 to −0.06; P < 0.05) and HbA1c levels of (d = −0.51, 95% CI, −0.84 to −0.18; P < 0.05). Subgroup analysis of HOMA-IR revealed that the variables "population", "training intensity" and "period" had significant effects on HOMA-IR, with the largest effect sizes for high-intensity (d = −0.43, 95%CI, −0.85 to −0.22, P < 0.05) and long-term (more than 12 weeks) (d = −0.43, 95%CI, −0.85 to −0.22, P < 0.05) training programs in older adults without type 2 diabetes (T2D) (d = −0.23, 95%CI, −0.42 to −0.04, P < 0.05). Subgroup analysis of HbA1c suggested that resistance training programs with moderate intensity (d = −0.51, 95%CI, −0.90 to −0.12, P < 0.05) and short term (less than or equal to 12 weeks) (d = −0.49, 95%CI, −0.84 to −0.14, P < 0.05) have greater effects on HbA1c. Conclusion: The findings of this meta-analysis suggest that resistance training is effective for inducing improvement in insulin sensitivity for elderly. Subgroup analysis showed that high intensity and long period of resistance exercise improve HOMA-IR in healthy old adults, and that resistance training with moderate intensity and short period improve HbA1c in T2D old people. More studies with high methodological qualities and large sample sizes need to be done to further confirm our conclusion.



## Author contributions

L.J.J and L.J.H searched the literatures, analyzed data and wrote manuscript. L.Y.F supported writing manuscript. All authors have read and agreed to the published version of the manuscript.

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## 1. Introduction

Insulin resistance is defined as a weak biological response to normal or higher insulin levels.[1] The role of insulin is to facilitate the uptake and storage of nutrients in various tissues (especially skeletal muscle, liver and adipose tissue).[2] Skeletal muscle accounts for 40% of total body weight and almost 80% of glucose uptake in a healthy person, making it a major site for the development of peripheral insulin resistance.[3–6] Cardiovascular risk factors include diabetes, metabolic syndrome, atherosclerosis, obesity, and non-alcoholic fatty liver disease (NAFLD), in which insulin resistance plays a mechanism role. In addition, insulin resistance has been identified as an independent factor in the increased incidence of cardiovascular diseases (coronary artery disease, heart failure, stroke).[2,7]

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Aging is often accompanied by features such as reduced physical activity, sarcopenia, decreased muscle strength, obesity, and these factors often contribute to decreased insulin sensitivity in older adults.[8,9] It has been shown that aging itself has a negligible effect on the decline in insulin sensitivity after adjusting for age-related differences in physical activity and body composition.[8] Thus, increasing physical activity or engaging in regular exercise may avoid or improve insulin resistance in older adults,[10–12] and this protection may be independent of exercise-related body composition changes.[13]

The traditional form of exercise recommended for older patients with type 2 diabetes is endurance exercise, which has been associated with weight loss, improved glucose tolerance and cardiovascular disease.[10,14–18] Over time, researchers have found that resistance exercise can be used in the management of diabetes.[19,20] As a result, the American Diabetes Association's position statement[21] includes resistance training as part of a comprehensive exercise program for older adults, and the American College of Sports Medicine[22] recommends that people with T2D (type 2 diabetes) include progressive resistance training (PRT) as part of their exercise program. In addition, although meta-analyses have investigated the effect of resistance training on insulin sensitivity, most of them have focused only on T2D patients and did not discuss the effect in healthy older adults.[23–25] However, old non-T2D people are also at high risk of insulin resistance, which may worsen into T2D. Therefore, this meta-analysis also included old adults without T2D, including those with obesity and low physical activity level,[26–30] so as to provide guidance for the prevention of T2D in old people. Moreover, because most older adults with type 2 diabetes are overweight and sedentary, resistance training is a more attractive and easier form of exercise for them to maintain.[31] Thus, we presented the Meta-analysis with the aim to determining the effects of resistance training on insulin sensitivity for older adults, and to obtain the dose-response relationships of resistance training on insulin sensitivity in old adults with or without T2D through subgroup analysis of the population, intensity, period, volume and other variables.

The indexes related to insulin resistance selected for this Meta-analysis were the homeostatic model of insulin resistance (HOMA-IR)[32,33] and hemoglobin A1c (HbA1c). Although the hyperinsulinemic-euglycemic glucose clamp technique is considered the gold standard for in vivo measurement of insulin action, this technique is rarely applied in exercise-related experiments due to its invasive nature. Homeostatic model has been shown to correlate well with the clamp technique, and it is calculated from basal glucose and insulin concentrations [(glucose $\times$ 0.056) (insulin)]/22.5. HOMA-IR is an indicator of basal insulin resistance, with lower HOMA values indicating lower insulin resistance.[34] HbA1c was used as another indicator in this Me-ta-analysis. HbA1c can be used to estimate blood glucose concentrations over three months and is a robust indictor of glycaemic control.[35]

## 2. Materials and methods

This meta-analysis is reported in accordance with the PRISMA guidelines.[36] The protocol was registered with Prospero in May 2021 (CRD42021250166).

### 2.1. Eligibility criteria

#### 2.1.1. Types of participants

Studies were eligible if participants were older adults (aged ≥60 years), with a study mean age ≥65 years. Participants may of any gender or nationality and they must be nonathletic.

#### 2.1.2. Types of interventions

Studies were eligible if the interventions were resistance training (eg, elastic band, weight machines, etcs) which were not combined with other exercise modes and life-style components. The resistance training programs lasted ≥6 weeks and were conducted in any setting (eg, laboratory, home, gym, etcs).

#### 2.1.3. Types of comparisons

Studies were eligible if the control groups were non-exercising, stretching, sham or usual care.

#### 2.1.4. Types of outcomes

Studies were eligible if they included at least one outcome of interest (HOMA-IR or HbA1c).

#### 2.1.5. Types of studies

Studies were eligible if they were randomized controlled trials (RCTs) published in English.

Studies were excluded if they were (1) duplicate publications; (2) literature review papers; (2) letters to the editor; (3) abstracts published in conference proceedings; (4) animal model studies. Articles for which full text or raw data were not available were also excluded. Table 1 shows the inclusion and exclusion criteria under the PICOS criteria.

### 2.2. Search strategy and study selection

PubMed, Cochrane, Embase, Web of Science, and EBSCO databases were searched from inception to April 2021. The search keywords included population (eg, aged), intervention (eg, resistance training), and outcomes (eg, insulin resistance, insulin sensitivity, HOMA-IR, Glycosylated Hemoglobin). For the PubMed search, we used the Mesh Database and combined Mesh terms with entry terms, and we made adjustments to other databases. Moreover, we used the filters as follows: randomized controlled trial (publication types) or randomized (title/abstract) or placebo (title/abstract). The complete search strategy used in PubMed is showed in Table A1. Search results were collated using Endnote software and duplicates were removed. Two authors (LJJ, LJH) independently read the titles and abstracts retrieved to get the articles that meet the requirements, and then read the full texts for final eligibility. Disagreements were re-solved through the third reviewer (LYF) or a consensus meeting.

### 2.3. Data extraction

Two researchers independently extracted all data and compiled the results. In case of disagreement, a third researcher intervened. If relevant data were not available in the article, we contacted the authors to obtain the original data. We extracted the following information: lead author, year of publication; participant demographics; health condition, age, sample size of people in the experimental and control groups; exercise characteristics: type, frequency, duration, and intensity; and reported outcomes.

**Table 1**
PICOS criteria for inclusion and exclusion of studies.

| Parameter | Defined criteria for the current study |
|---|---|
| P (population) | Older adults (aged ≥60 years), non-athletic |
| I (intervention) | Resistance training |
| C (comparison) | Usual care or sham training |
| O (outcomes) | HOMA-IR; HbA1c |
| S (study design) | Randomized controlled trials |

### 2.4. Quality and risk of bias assessment

We assessed the risk of bias of the included studies according to the Cochrane Risk of Bias tool, which includes seven different domains, as follows. (1) generation of allocation, (2) concealment of allocation, (3) blinding of participants and personnel, (4) blinding of outcome assessment, (5) incomplete outcome data processed, (6) free-form selective reporting bias, (7) other forms of bias. Publication bias was assessed by examining funnel plots. Sensitivity analyses tested the robustness of the pooled results by removing trials with an assessed risk of bias.

### 2.5. Data synthesis and analysis

Each result is expressed as mean difference (MD) with standard deviation (SD) and reported with 95% confidence intervals (CIs). Appropriate formulas were used to transit interquartile ranges, and 95% CIs and Standard Errors to Means and Standard Errors (SDs).[37] A fixed effects model was used for pooled effects estimation, taking into ac-count the differences between studies and weighting each study accordingly. Heterogeneity between studies was measured by the $I^2$ statistic and Cochran's Q test. An $I^2$ greater than 50% or a p-value of 0.10 or less for the Q test indicated the presence of heterogeneity.[38] We used Review Manager software version 5.3 or Stata software version 15.0 to perform quantitative pooled analyses of the data. Subgroup analyses were conducted to explore possible associations between the dose of resistance training and the effectiveness of the intervention. The dose of resistance training includes intensity (low, moderate or vigorous), frequency, volume (number of sets, repetitions), and duration (more or less than 12 weeks). Moreover, taking into account the effect of baseline glucose concentration, we divided the population into T2D group and non-T2D group.

## 3. Results

### 3.1. Literature search and trial selection

The flow diagram reporting trial selection is shown in Fig. 1. A total of 1445 potentially eligible articles were identified. After removing duplicates reviews and animal experiments, 947 articles remained for screening. By screening the titles and abstracts, 906 articles were excluded, and 29 articles were deleted after reading the full text, leaving 12 articles for quantitative synthesis and finally 12 articles were included in the meta-analysis.

### 3.2. Description of the included trials

Included trial characteristics are summarized in Table 2. In this meta-analysis, a total of 232 old people were included in the experimental group and 209 in the control group. The participants in all studies were older people over 60 years old and physically inactive.

A brief description of the exercise programs is given in Table 3. The interventions were all resistance exercise. The duration of the intervention ranged from 6 weeks to 52 weeks. The frequency varied from 2 to 4 times per week, in which 3 times per week is the most common. The number of sets ranged from 1 to 6, and Dipietro[27] didn't report it clearly. The units of intensity were all converted to 1RM (one repetition maximum).[39] We took the maximum intensity as the final intensity if the intervention was progressive in intensity.[29–31,40–43] In the study by Dipietro,[27] exercise intensity was in the form of the percentage of peak oxygen uptake ($VO_2$peak), and in the study by Kim,[30] the Borg RPE Scale was used to obtain exercise intensity. Intensities were divided according to the American College of Sports Medicine (ACSM). Weighting lower or equal to 50% 1RM were classified as ‘light’, 51%~69% were ‘moderate’, 70% or higher were ‘vigorous’. In the study by Andersen,[41] a total of 2 groups of RCT data were included, in which the intervention intensity was 8–20RM and 8RM. In the study by Dipietro,[27] a total of 3 groups of RCT data were included, in which the intervention period were 12 weeks, 24 weeks and 36 weeks. In the study by Fatouros,[26] a total of 3 groups of RCT data were included, in which the intervention intensity was 45%~50% 1RM, 60%~65% 1RM and 80%~85% 1RM. In the study by Shabkhiz,[44] a total of 2 groups of RCT data were included, in which the intervention subjects were healthy elderly and T2DM elderly. Therefore, the data included in the analysis consist of 18 experiments.

The indexes collected in this study are shown in Table 2. We selected HOMA-IR and HbA1c to investigate the effect of different exercise intensities, training periods, frequencies and different number of sets on insulin sensitivity in older people with and without T2D.

### 3.3. Methodological quality assessment

The results of the Cochrane scale evaluation are shown in Fig. 2. 7 of the included articles clearly stated the method of group allocation.[27–30,42,43,45] Since the included experiments were all human studies, subjects were required to sign an informed consent form, and the exercise intervention process required supervision by relevant research staff, blinding of participants and personnel was difficult to ensure. Therefore, all articles in this study were evaluated as high risk in terms of blinding. 3 articles were evaluated as high risk due to high staff turnover during the intervention.[29,30,43] The included studies were free from selective reporting and other biases.

### 3.4. Synthesis of the results

#### 3.4.1. Analysis of HOMA-IR

Fig. 3 summarizes the effect of resistance exercise on HOMA-IR in older adults. After heterogeneity test, $I^2 = 0\% < 50\%$, and $P > 0.1$ for Q test, suggesting that there was no heterogeneity among the selected literatures in this study, and fixed effect could be selected for Meta analysis. 14 experiments with a total of 374 participants provided data on HOMA-IR. Overall, resistance exercise significantly reduced HOMA-IR level ($d = -0.25$, 95% CI, −0.43 to −0.06; $P < 0.05$).

The results of subgroup analysis are shown in Table 4. In the subgroup analysis of participants, we observed a significant reduction of HOMA-IR in older adults without T2D ($d = -0.23$, 95% CI, −0.42 to −0.04, $P < 0.05$), while found no significant change in older people with T2D. In the subgroup analysis of exercise period, we observed a significant change in HOMA-IR levels for more than 12 weeks resistance exercise ($d = -0.43$, 95%CI, −0.85 to −0.22, $P < 0.05$), but no significant change was found in HOMA-IR for resistance training of 12 weeks or fewer ($P > 0.05$). In the subgroup analysis of exercise intensity, we observed a significant change in HOMA-IR levels for high-intensity resistance exercise ($d = -0.43$, 95%CI, −0.85 to −0.22, $P < 0.05$), but found no significant change in HOMA-IR for low-intensity($P > 0.05$) and moderate-intensity resistance exercise($P > 0.05$). In the subgroup analysis of exercise frequency, we observed a no significant change in HOMA-IR for 2 d per week($P > 0.05$), 3 d per week and 4 d peer week resistance exercise($P > 0.05$). In the subgroup analysis of progression in intensity, we observed a significant change in HOMA-IR levels for resistance exercise without progression ($d = -0.21$, 95%CI, −0.42 to −0.01, $P < 0.05$), but found no significant change in HOMA-IR for resistance training with progressive intensity($P > 0.05$). In the

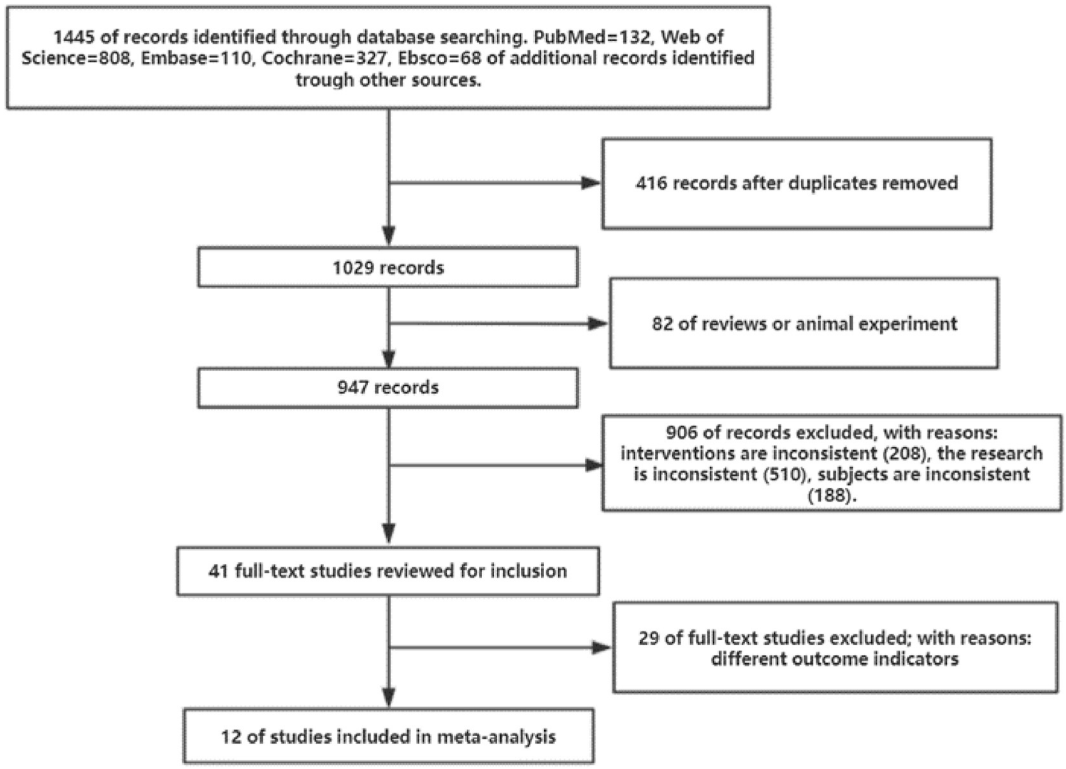


**Fig. 1.** Flow diagram of literature selection.

subgroup analysis of the number of sets, we observed no significant change in HOMA-IR for 3 times per session ($P > 0.05$) and 4 times per session ($P > 0.05$).

### *3.4.2. Analysis of HbA1c*

Fig. 4 summarizes the effect of resistance exercise on HbA1c in older adults. After heterogeneity test, $I^2 = 0\% < 50\%$, and $P > 0.1$ for Q test, suggesting that there was no heterogeneity among the selected literatures in this study, and fixed effect could be selected for Meta analysis. 5 studies with a total of 219 participants provided data on HbA1c. Overall, resistance exercise significantly reduced HbA1c levels (−0.51, 95% CI, −0.84 to −0.18; $P < 0.05$).

The results of subgroup analysis are shown in Table 4. In the subgroup analysis of exercise period, we observed a significant change in HbA1c levels for short-term resistance training which lasted 12 weeks or fewer ($d = -0.49$, 95%CI, −0.84 to −0.14, $P < 0.05$), but no significant change was found in HbA1c for long-term resistance training that lasted more than 12 weeks ($P > 0.05$). In the subgroup analysis of exercise intensity, we observed a significant change in HbA1c levels for moderate-intensity resistance exercise ($d = -0.51$, 95%CI, −0.90 to −0.12, $P < 0.05$), but found no significant change in HbA1c for high-intensity($P > 0.05$).

## *3.5. Publication bias and sensitivity analysis*

The scatter plot of the funnel plot of outcome indicators for the included studies was largely symmetrically distributed from left to right, indicating that there was no publication bias (Fig. 5). Sensitivity analyses of the included studies and exclusion-by-exclusion of the literature did not significantly change the outcomes of the outcome indicators, indicating that the results of the Meta-analysis of this study were stable and reliable.

## 4. Discussion

This is a systematic review and meta-analysis focused on the effect of resistance training on insulin sensitivity and its possible moderator variables in older adults. The quantitative analysis showed significant positive effects of HOMA-IR and HbA1c after resistance training. Moreover, subgroup analysis suggested that (a) a significant improvement of HOMA-IR in non-T2D older adults (b) a significant decrease of HOMA-IR in high-intensity subgroup and a significant decrease of HbA1c in moderate-intensity subgroup; (c) a significant reduction of HOMA-IR when the duration of the resistance training program lasted more than 12 weeks and a significant reduction of HbA1c when the intervention was less than or equal to 12 weeks.

## *4.1. Population*

In our Meta-analysis, it was found that healthy older adults experienced significant improvements in HOMA-IR after a period of resistance exercise, compared to older adults with T2D who did not. In terms of HbA1c, we only included participants with T2D, and the result showed a significant improvement. The result that HOMA-IR is improved after resistance training in healthy old people is consistent with previous studies. Previous studies have shown that resistance training reduces plasma insulin response to glucose without decreasing glucose tolerance in non-T2D subjects, suggesting an increase in insulin sensitivity.[46–50] However, as for the effect of resistance training on HOMA-IR in T2D old adults, the present finding is contrary to most published studies. There are several studies showed that people who suffer from insulin resistance were more sensitive to resistance training. Miller et al.[50] showed that glucose tolerance responded better to resistance training in those with higher initial blood glucose levels. Holton

**Table 2**
Details of included studies.

| First author, year | Study Area | Subject | Control | | Exercise | | Endpoints | Results |
|---|---|---|---|---|---|---|---|---|
| | | | Sample Size | Age | Sample Size | Age | | |
| Andersen 2016(1/2)[33] | Denmark | healthy older men | 8 | 67.4 ± 2.7 | 9 | 69.1 ± 3.1 | HOMA-IR | There were no significant differences between 16 weeks group and 56 weeks group. |
| Botton 2018[34] | Brazil | overweight, T2DM elderly | 13 | 68.6 ± 7.06 | 13 | 70.6 ± 6.7 | HbA1c | The training program did not induce significant reduction in glycated hemoglobin values of patients who already had suitable glycemic control. |
| Brooks 2006[22] | Spain | T2DM elderly | 31 | 66 ± 1 | 31 | 66 ± 2 | HOMA-IR HbA1c | This was accompanied by reduced insulin resistance [ST: median (interquartile range) −0.7(3.6) vs CON: 0.8(3.8), p = 0.05]; |
| Castaneda 2002[32] | Latin America | T2DM elderly | 31 | 66 ± 1 | 29 | 66 ± 2 | HbA1c | Sixteen weeks of RT (three times per week) resulted in reduced plasma glycosylated hemoglobin levels (from 8.7 ± 0.3 to 7.6 ± 0.2%) |
| de Carvalho Bastone 2020[41] | Brazil | Elderly | 18 | 72.50 ± 7.88 | 17 | 77.55 ± 4.40 | HOMA-IR HbA1c' | There were no significant differences between groups |
| Dipietro 2008(1/2/3)[30] | the United States | inactive older women | 8 | 74 ± 5 | 8 | 74 ± 5 | HOMA-IR | We observed significant improvements in 2-h glucose concentrations at 3, 6, and 9 months among women in the $RT_L$ |
| Fatouros 2005(1/2/3)[38] | Greece | overweight and inactive elderly | 10 | 69.8 ± 5.1 | 14<br>12<br>14 | 71.1 ± 3.6<br>69.7 ± 3.8<br>70.8 ± 2.8 | HOMA-IR | HOMA-IR increased in all exercise groups (15−39%; P < 0.05). However, no significant differences were observed between groups in the percent HOMA-IR increase |
| Hsieh 2018[35] | Taiwan, China | T2DM elderly | 15 | 71.8 ± 4.5 | 15 | 70.6 ± 4.2 | HbA1c | There were no significant differences between groups |
| Kim 2018[36] | Korea | Inactive elderly | 10 | >65 | 12 | >65 | HOMA-IR | After six weeks of exercise training, participants in the combined exercise group exhibited significant reduction in insulin, HOMA-IR and chemerin levels, while significant reduction was observed in HOMA-IR only in the resistance exercise group compared with the control group. |
| Rech 2019[37] | Brazil | T2DM elderly | 20 | 68 ± 6.5 | 14 | 70.5 ± 7.4 | HbA1c | No significant differences were found for blood lipid profile and glycated hemoglobin for both groups after the intervention period |
| Shabkhiz 2020(1/2)[39] | Iran | non-T2DM men | 12 | 72.08 ± 5.33 | 12 | 72.08 ± 5.33 | HOMA-IR | RT significantly decreased glucose and insulin concentration and HOMAIR compared with the C group (main effect for training; p = 0.001, p = 0.01, p = 0.001; respectively) |
| | | T2DM men | 10 | 72.45 ± 6.00 | 10 | 72.45 ± 6.00 | | RT showed also a decreasing in the values of HOMA-IR, CRP and TNF-α |
| Tomeleri 2018[40] | Brazil | inactive older women | 23 | 68.8 ± 4.9 | 22 | 72.1 ± 6.3 | HOMA-IR | |

The values are shown as the means ± SD.
ST = strength training plus standard care. CON = standard care alone. RT = resistance training. $RT_L$ = lower-intensity resistance training.
T2DM = Type 2 Diabetes Mellitus; RM = repetition maximum; rep = repetitions; HOMA-IR = Homeostatic Model of Insulin Resistance; HbA1c = Hemoglobin A.

**Table 3**
Details of resistance exercise protocols (according to FITT criteria).

| First author, year | Intervention Details | Frequency | Intensity | Duration | Sets*Reps |
|---|---|---|---|---|---|
| Andersen 2016(1/2)[41] | Leg press, seated leg extension, hamstring curl, lateral pull-down and lateral dumbbell raises. At the end of each training session 5 min of core training (crunches, hip extension, side bends, diagonal lifts, and trunk rotation) was performed. | 2 d per week | (week 0–4): 16–20 RM<br>(week 5–8): 12 RM<br>(week 9–12): 10 RM<br>(week 13–52): 8 RM | 16 weeks<br>52weeks | (week 0–12): 3 sets<br>(week 13–52): 4 sets |
| Botton 2018[29] | Functional exercises (squat and steps up and down); Traditional exercises (leg press, leg extension, leg curl, hip abduction, inclined bench press, low row, biceps curl, triceps, crunch) | 3 d per week | Functional exercises: additional load or step if < 6 on OMNI scale;<br>Traditional exercises: (week 1–8): 15RM, (week 9–12): 12RM | 12 weeks | Functional exercises: (week 1–4): 2 sets*10reps, (week 5–8): 3 sets*10 reps; (week9–12): 3 sets*15reps<br>Traditional exercises: (week 1–4): 2 sets*12 reps, (week 5–8): 3 sets*12 reps; (week9–12): 3 sets*10 reps |
| Brooks 2006[31] | strength training using five pneumatic machines: upper back, chest press, leg press, knee extension and flexion | 3 d per week | (week 1–8): 60–80% 1RM<br>(week 10–14): 70–80% 1RM | 16 weeks | 3 sets*8reps |
| Castaneda 2002[40] | PRT using five pneumatic resistance training machines (chest and leg press, upper back, knee extension, and flexion; Keiser Sports Health Equipment, Fresno, CA) | 3 d per week | (week 1–8): 60–80% 1RM<br>(week 10–14): 70–80% 1RM | 16 weeks | 3 sets*8reps |
| de Carvalho Bastone 2020[45] | resistance training included the following muscle groups: shoulder abductors, flexors and extensors; scapular adductors; elbow flexors and extensors; hip adductors, abductors, flexors, and extensors; knee flexors and extensors. Elastic bands, dumbbells, and ankle weights were used as resistance. Ankle plantar- and dorsiflexion from a stand position and sit-to-stand from a chair | 3 d per week | 80% 10RM | 12 weeks | 3 sets*8reps |
| Dipietro 2008 (1/2/3)[27] | using Thera-Bands, Thera-Balls, and hand weights | 4 d per week | 45%–50% VO2peak<br>90 (85–97) beats $\cdot$ $min^{-1}$ | 12 weeks<br>24 weeks<br>36 weeks | |
| Fatouros 2005 (1/2/3)[26] | eight resistance exercises: chest press, leg extension, shoulder press, leg curls, latissimus pull down, leg press, arm curls, and triceps extension; abdominal crunches and lower back exercises | 3 d per week | 45–50% 1RM<br>60–65% 1RM<br>80–85% 1RM | 24 weeks | (week 1–4): 1 sets*6reps<br>(week 5–12): 2 sets*8reps<br>(week 13–20): 3 sets*10reps<br>(week 21–24): 4 sets*10-12reps |
| Hsieh 2018[42] | eight RT exercises: the chest press, shoulder press, biceps curl, hip abduction, standing hip flexion, leg press, standing calf raise, and abdominal crunch | 3 d per week | Beginning: 40–50% 1RM (for the chest press and leg press); 12 to 13 on the Borg scale (for the shoulder press, biceps curl, hip abduction, standing hip fl exion, standing calf raise, and abdominal crunch). Ending: 75% 1RM; 14 to 16 on the Borg scale | 12 weeks | 3 sets*8-12reps |
| Kim 2018[30] | six pieces of outdoor exercise equipment, including pull weight, chair pull, leg extension, sky-walk and cross-country. | 3 d per week | (week 1–2): Borg scale (RPE) '6'<br>(week 3–4): Borg scale (RPE) '7'<br>(week 5–6): Borg scale (RPE) '8' | 6 weeks | 1-3 sets*12-15reps |
| Rech 2019[43] | functional exercises: partial squat and bench stepping;<br>traditional resistance exercises: unilateral leg press, unilateral knee extension, knee flexion, plantar flexion, bench press, low row, biceps curl, elbow extension, hip abduction and abdominal crunches | 3 d per week | Beginning: 15RM<br>Ending: 12RM | 12 weeks | functional exercises: (week 1–4): 2 sets*10reps<br>(week 5–8): 3 sets*10reps<br>(week 9–12): 3 sets*15reps traditional resistance exercises: (week 1–4): 2 sets*12reps<br>(week 5–8): 3 sets*12reps<br>(week 9–12): 3 sets*10reps |
| Shabkhiz 2020(1/2)[44] | the machines used were leg press, leg extension, seated leg curl, seated calf, bench press, compound row, triceps press, and bicep curl | 3 d per week | 70% 1RM | 12 weeks | 3 sets*10reps |
| Tomeleri 2018[28] | Participants performed the following exercises: chest press, seated row, triceps pushdown, preacher curl, horizontal leg press, knee extension, knee curl and seated calf raise | 3 d per week | 10-15RM | 12 weeks | 3 sets*10-15reps |

Borg's RPE scale: Borg's Rating of Perceived Exertion (RPE) Scale; OMNI RPE scale: OMNI Rating of Perceived Exertion (RPE) Scale.

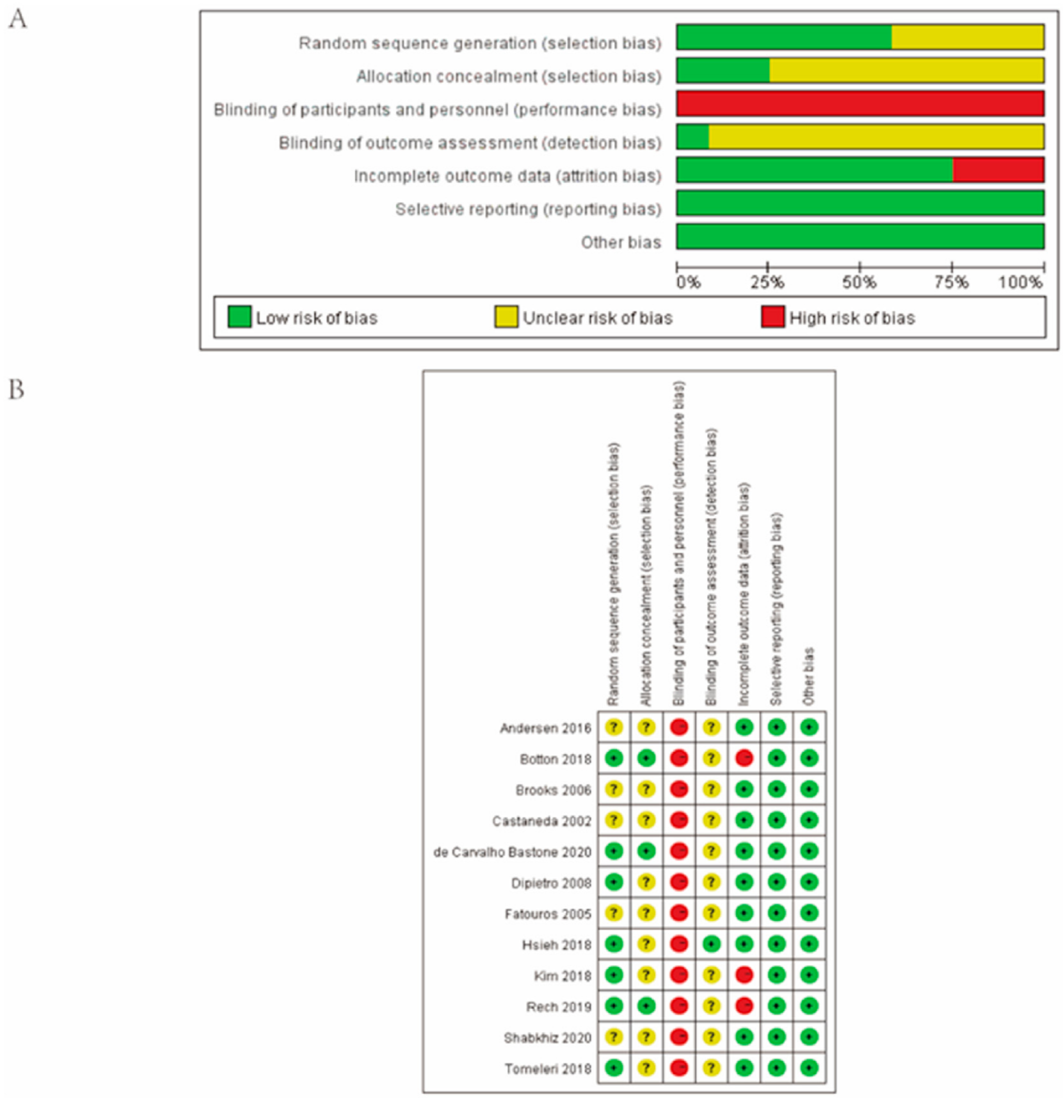


**Fig. 2.** The risk assessment of bias by cochrane.

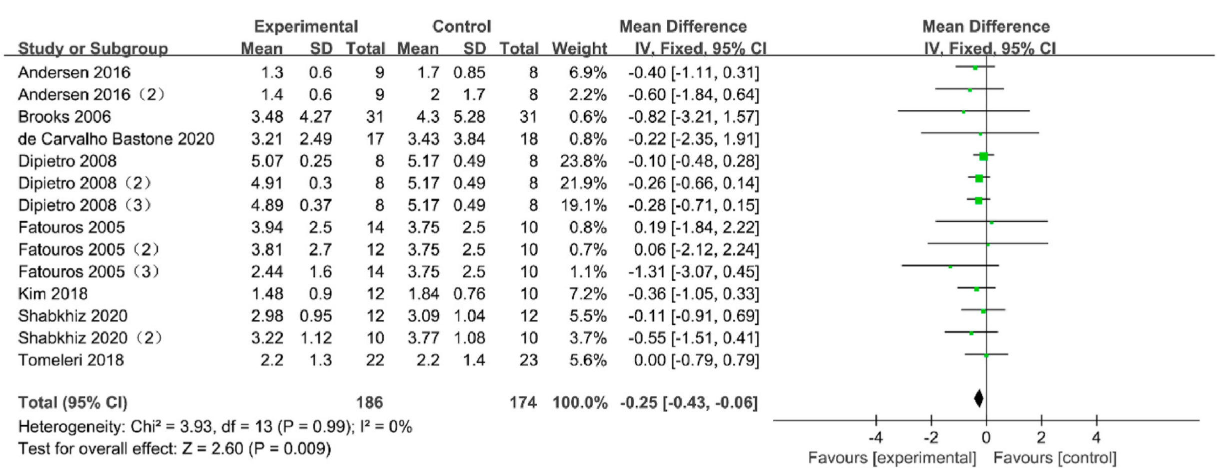


**Fig. 3.** Forest plot of the meta-analysis on HOMA-IR

**Table 4**
Results of subgroup analysis.

| Characteristic | HOMA-IR | | | HbA1c | | |
|---|---|---|---|---|---|---|
| | Studies | Effect size (90% CI) | P Value | Studies | Effect size (90% CI) | P Value |
| | n | | | | % | |
| Participants | | | >0.2 | | | >0.2 |
| Non-T2D | 13 | −0.23 (−0.42, −0.04) | | / | / | |
| T2D | 3 | −0.59 (−1.48, 0.31) | | 5 | −0.51 (−0.84, −0.18) | |
| Period | | | >0.2 | | | >0.2 |
| <-12 weeks | 6 | −0.17 (−0.44, 0.11) | | 3 | −0.49 (−0.84, −0.14) | |
| >12 weeks | 8 | −0.32 (−0.57, −0.06) | | 2 | 0.26 (−0.56, 1.07) | |
| Intensity | | | >0.2 | | | >0.2 |
| Low | 2 | −0.30 (−0.96, 0.35) | | / | / | |
| Moderate | 5 | −0.20 (−0.43, 0.02) | | 2 | −0.51 (−0.90, −0.12) | |
| High | 6 | −0.43 (−0.85, −0.22) | | 3 | −0.09 (−0.65, 0.47) | |
| Frequency | | | >0.2 | | | >0.2 |
| 2 d per week | 2 | −0.45 (−1.06, 0.17) | | / | / | |
| 3 d per week | 9 | −0.28 (−0.64,0.09) | | 5 | −0.37 (−0.69, −0.05) | |
| 4 d per week | 3 | −0.21 (−0.44, 0.02) | | / | / | |
| Progression | | | >0.2 | | | >0.2 |
| Yes | 4 | −0.42 (−0.88, 0.03) | | 5 | −0.37 (−0.69, −0.05) | |
| No | 10 | −0.21 (−0.42, −0.01) | | / | / | |
| Sets | | | >0.2 | | | >0.2 |
| 3 times | 6 | −0.25 (−0.64, 0.13) | | 5 | −0.37 (−0.69, −0.05) | |
| 4 times | 5 | −0.45 (−0.99,0.99) | | / | / | |

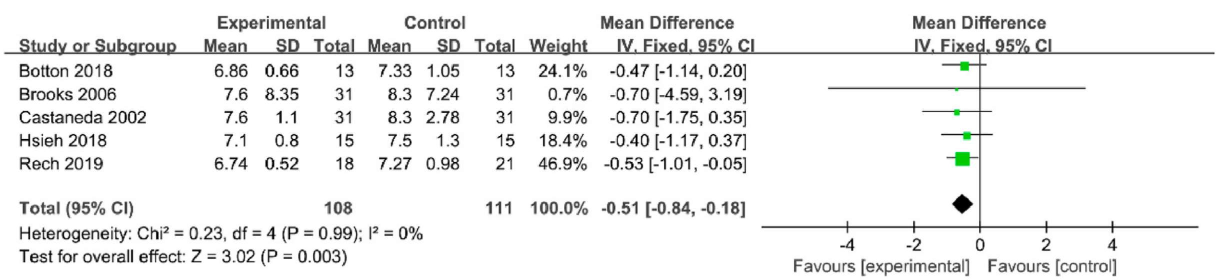


**Fig. 4.** Forest plot of the meta-analysis on HbA1c.

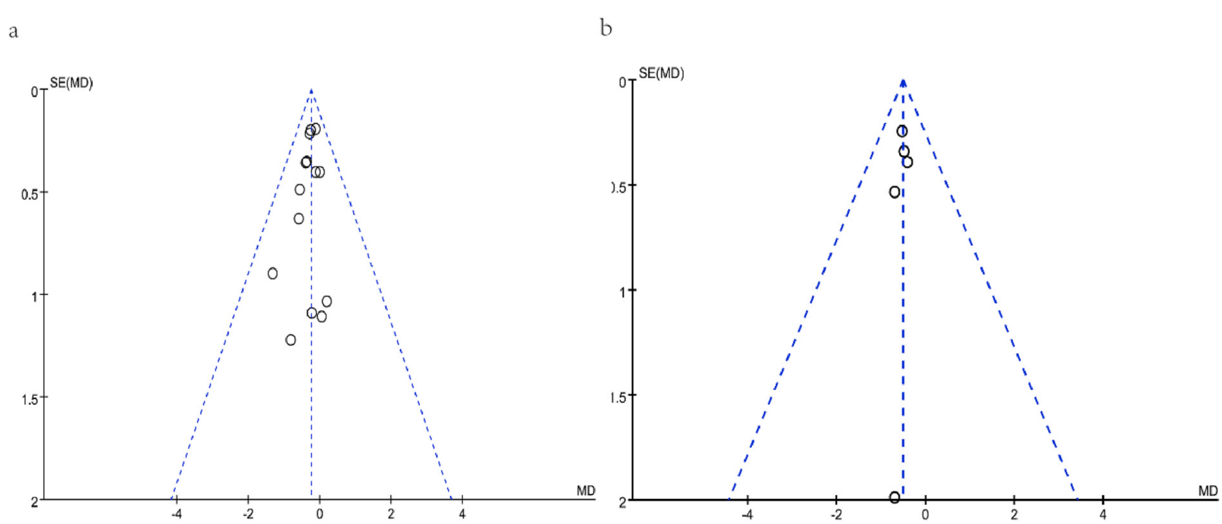


**Fig. 5.** Funnel plots of publication bias: (a). HOMA-IR; (b). HbA1C.

et al.[51] conducted a single leg resistance training in healthy and type 2 diabetic older adults and found that insulin sensitivity was improved in both groups after 6 weeks of resistance intervention, and that insulin receptor protein expression was upregulated in skeletal muscle in both groups. Hordern et al.[52] conducted a four-week progressive resistance training intervention in type 2 diabetic population, and they found that those with higher baseline glucose levels and lower insulin sensitivity gained greater benefit from resistance training. Thus, resistance training seems to work in old people with and without T2D, and future studies need to include old T2D people as subjects to further prove it.

### 4.2. Intensity

Since research on the effects of resistance training on insulin resistance in older adults has only recently emerged, it is generally recommended that older patients with T2D perform resistance training at moderate intensity with multiple repetitions,[22] given their low bone density and high blood pressure, but the moderate-intensity, high-volume model is considered to have a greater aerobic metabolism, which is not well adhered to in older adults.[40] However, our meta-analysis shows that only high-intensity resistance training has a significant effect on HOMA-IR. Fatouros et al.[26] found that moderate-intensity and high-intensity resistance training increased levels of adiponectin in the circulatory system, while low-intensity resistance exercise did not. Adiponectin is known to increase insulin sensitivity and affect carbohydrate and lipid metabolism, and it reduces circulating fatty acid levels and triglyceride levels in liver and muscle cells to improve insulin sensitivity.[23,53] Fatorous et al.[26] conducted resistance training intervention for the T2D elderly for 6 months, followed by detraining for 6 months, and found that only the high-intensity group had significantly higher adiponectin levels after detraining, indicating that high-intensity resistance training could provide enough stimulation to keep adiponectin levels higher than the pre-training value. Dipietro et al.[27] administered a low-intensity resistance training intervention to healthy older women and found a decrease in 2-h glucose concentrations in the subjects after nine months, suggesting that low-intensity resistance training increases peripheral insulin sensitivity, but basal insulin and glucose concentrations were not improved, which may be due to β-cell damage and may require higher intensity or longer interventions. Surprisingly, subgroup analysis indicates that moderate-intensity resistance training has a significant effect on HbA1c while high-intensity not, and this divergence may be caused by the small number of included studies. The study by Castaneda et al.[40] did not directly measure insulin resistance, compared to previous studies of moderate resistance interventions,[54–56] they observed more significant changes in HbA1c with high-intensity resistance training and HbA1c levels reflecting glucose control over the past 2–3 months. This suggests that high-intensity resistance training can better stimulate muscle uptake of glucose.

### 4.3. Period

Meta-analysis showed that resistance training for more than 12 weeks had a significant effect on HOMA-IR, while HbA1c level reduced when the intervention duration lasted less than or equal to 12 weeks. The result of subgroup analysis of the exercise period showed that the effect of long-term resistance training on HbA1c is not significant, which may be due to the small number of included studies. Only two articles were included into the long-term group, and the large standard deviation range of Brooks's study also led to this contrary result.[31] Frank et al.[53] found that 8 weeks of high-intensity resistance training improved glucose tolerance but not insulin sensitivity in healthy older adults. Shabkhiz et al.[44] found that older T2D patients who received 12 weeks of resistance training had poor improvement in insulin resistance. Geirsdottir et al.[23] showed no improvement in insulin resistance in three groups of healthy, pre-glycemic, and T2D elderly with 12 weeks of high-intensity resistance training intervention. In the study by Kim et al.,[30] elderly subjects exercising using outdoor gym equipment showed no increase in insulin sensitivity after 6 weeks. de Carvalho Bastone et al.[45] found no improvement in insulin sensitivity in older subjects who underwent a 12-week supervised home-based progressive resistance training program. Rech et al.[43] found that 12 weeks of resistance training was not sufficient to improve endothelial function and inflammatory marker levels in older adults with type 2 diabetes, nor did it reduce blood HbA1c levels, which was in contrast to our result. Older patients with type 2 diabetes may require longer interventions because changes in markers such as lipid profiles and glycated hemoglobin were not usually observed even though they had similar increases in strength and muscle mass compared to healthy subjects.[11,57] The absence of significant changes in these variables may be closely related to the lack of improvement in endothelial function, as glycemic control and blood cholesterol are important factors in vascular health and endothelial function. Yuan et al.[58] had prediabetic older adults perform elastic band training and found that 6 months of moderate-intensity elastic band resistance could improve insulin resistance and moreover protect the function of pancreatic islet β-cells. In addition, we recommend that subjects adhere to a long duration of exercise because the effect on insulin resistance obtained from exercise is diminishing after a period of detraining,[26] more so in the elderly.

### 4.4. Other moderators

Moderators such as weekly frequency, number of sets, progression in intensity must also be considered. However, the current subgroup analysis indicates that resistance training frequency and sets did not affect HOMA-IR in older adults over 60 years of age. A possible explanation is the variables of training volume. Training frequency, number of sets and repetitions, all reflecting training volume, cannot be separated. In general, increased training volume is responsible for higher physiological adaptions.[59] Additionally, the progressive number of sets can also explain the result. Training frequency also determines the recovery time between workouts and, therefore, largely depends on the total work (intensity, sets, repetitions) completed per session. Once the threshold is reached, additional resistance training days is likely to provide no further benefits and may affect recovery between training sessions and increase the risk of overtraining in older adults.[60] 2–3 sessions per week is recommended when high-intensity resistance training was performed.[59] In terms of progression in intensity, we found improvements of HOMA-IR with resistance training program using non-progressive intensity. One possible explanation for why progressive protocols not having significant effect on insulin sensitivity is that the training intensity increased gradually in progressive group,[30,31,41] while intensity was constantly high in non-progressive group.[26–28,44,45]

There are several possible mechanisms as to why resistance training improves insulin resistance in old adults. Firstly, a body composition with high skeletal muscle mass and low body fat would benefit insulin sensitivity. Poehlman et al.[61] subjected young women to a period of resistance training intervention and found that the increase in fat free mass (FFM) during resistance training contributed to increased glucose uptake but did not improve insulin sensitivity per kilogram of FFM, suggesting that the increase in insulin sensitivity was due to mass effect rather than to intrinsic muscle responsiveness to insulin. The inability of resistance training to improve insulin sensitivity per kilogram of FFM may be due to the inability of resistance training to increase muscle capillary density or change muscle fiber type (turning to a more insulin-sensitive muscle fiber type.) Brooks et al.[31] found that improvements in insulin resistance after resistance training correlated with the cross-sectional area of type I muscle fibers, and they chose to analyze type I muscle fibers because type I muscle fibers are more sensitive to insulin. Obesity is a major risk factor for developing insulin resistance. A study by Rice et al.[62] confirmed that visceral fat and abdominal subcutaneous fat are independently associated with blood glucose and insulin levels. However, it is doubtful that the improvement of insulin sensitivity after resistance training is simply due to changes of body composition. Another explanation may be the alterations in the muscle. Sparks et al.[63] found that nine months of resistance training increased the number of mitochondria in skeletal muscle and that lower mitochondrial content led to lower fasting fat oxidation and metabolic rates, suggesting that it may be intrinsically linked to obesity-related insulin resistance and abnormal fuel utilization patterns in T2D. Holten et al.[51] found by biopsy of muscle tissue that increased muscle GLUT4 content and expression and/or activity of various insulin signaling proteins were part of the mechanism behind the improved insulin action, however, they could not draw conclusions about the decisive functional relevance of changes in protein expression components, so further studies are needed to elucidate the effects of resistance exercise on changes in the insulin cascade. There are other possible mechanisms by which resistance training induces increased insulin sensitivity, such as changes in cytokines, adipokines, or other immune system biomarkers, but to date there is not enough research to support this hypothesis.

The limitations of this study are as follows. First, the total sample size is relatively small, with individual studies having a maximum of 31 participants, mostly <10, and the studies include both people with and without diabetes. Second, because it is difficult to blind exercise training in randomized controlled trials, the lack of blinding is a major factor affecting the risk of bias. Finally, due to the small number of included studies, subgroup analysis could not be performed for all variables in present study. Therefore, this meta-analysis could not obtain the most optimal weekly exercise volume of resistance training.

## 5. Conclusions

In conclusion, resistance training is a safe exercise modality and it is more endurable compared with endurance training in older adults. Resistance training is effective for inducing improvement in insulin sensitivity for the aged. The effects on HOMA-IR are more pronounced when older people underwent high-intensity resistance training for over 12 weeks. However, because of the insufficiency of included literatures, it is not yet clear in this meta-analysis whether resistance training also benefits HOMA-IR in T2D older adults. The effects on HbA1c are significant when moderate-intensity and short-term resistance training program were conducted, which was in contrary to most published studies. Thus, the results of this meta-analysis need to be further confirmed by more studies with high methodological quality and large sample sizes.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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