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Effect of n-3 polyunsaturated fatty acid supplementation on muscle mass and function with aging: A meta-analysis of randomized controlled trials☆

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ABSTRACT

The results of randomized controlled trials (RCTs) investigating supplemental n-3 polyunsaturated fatty acids (PUFA) on muscle mass and function have been inconsistent. The present study aimed to quantitatively evaluate the effect of n-3 PUFA supplementation on indicators of muscle mass and function in healthy subjects. A systematic literature search was conducted up to July 2020 with databases of PubMed and Web of science. The random-effects model was implemented to calculate the weighted mean difference of net change of indicators regarding muscle mass and function. A total of nine studies (thirteen treatment groups) with 2067 participants were included for data analysis. The summary estimate showed that n-3 PUFA supplementation significantly increased the grip strength (1.17 kg; 95% CI: 0.27, 2.08 kg). Non-significant effect was observed with respect to muscle mass parameters, including fat mass (-0.67 kg; 95% CI: -2.20, 0.87 kg) and lean mass (0.33 kg; 95% CI: -0.35, 1.00 kg). Regarding muscle function indicators, there were non-significant effects on walking speed (-0.01 m•s^{-1}; 95% CI: -0.03, 0.01 m•s^{-1}), time up and go test (-0.25 s; 95% CI: -0.55, 0.04 s), respectively. The findings of this study indicated that supplementation with n-3 PUFA might have beneficial effects to improve muscle mass and function in healthy participants. However, there was no significant improvement in the subjects' muscle mass. Whether n-3 PUFA supplementation has favorable effects in participants with sarcopenia are warranted to be further investigated.

1. Introduction

The gradual loss of age-related muscle mass and muscle function are responsible for the impairment of quality of life and activity in the elderly [1]. With the improvement of the methodology and technology for measuring body composition and health status of the elderly, scientific communities give increasing attention to muscle mass and muscle function [2]. It has been reported that about 10% of muscles have disappeared at the age of 50, and muscle function will decline by 12% - 14% every ten years from the age of 50. At the age of 70 - 80, the lower limb muscle mass of males and females would be reduced by 0.7% - 0.8% every year [3-5]. Extensive evidence indicated that the loss of muscle mass and muscle function would affect neuromuscular connection, sensitivity of hormone receptor and bone density, leading to physical disability and function, depression, cardiac metabolism and death [6,7]. Therefore, it is a pivotal public health problem to maintain muscle mass and function with the increase of age [8].

Due to the adverse effects, there is no recommended drug to improve muscle mass and function [9]. A large amount of research has focused on increasing muscle mass and improving muscle function through strengthening exercise and resistance training [10]. However, it is unclear how to control the time, frequency and intensity of exercise so as to achieve the purpose of increasing health and strengthening muscle, especially for the aged. Meanwhile, for the elderly with weak sports ability and without the supervision of professionals, there are certain risks in sports reinforcement and resistance training. Therefore, exercise

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strengthening and resistance training are not suitable for all the elderly.

To date, nutrition intervention has received increasing attention to protect against the decline of muscle mass and muscle function. Of these, n-3 polyunsaturated fatty acid (PUFA) might be an alternative supplement for improving muscle mass and function. Animal experiments have shown that n-3 PUFA intervention has a protective effect on muscle mass and could improve fat metabolism and muscle metabolism [11-13]. Clinical trials have observed that n-3 PUFA could slow down the decline of muscle mass and muscle function, promote the muscle protein synthesis rate, improve muscle tissue loss and muscle steatosis [2,14,15]. In a randomized controlled trial (RCT), n-3 PUFA supplementation has beneficial effects on muscle mass and muscle function in the elderly [16]. However, there are still several inconsistent results regarding n-3 PUFA supplementation on muscle mass and function [17,18]. These results on the effects of n-3 PUFA supplementation on muscle mass and function need to be reviewed and summarized objectively. Therefore, we performed the present systematical review and meta-analysis to quantitatively evaluate n-3 PUFA supplementation on muscle mass and function with RCTs.

2. Materials and methods

The present study was on the basis of the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement [19].

2.1. Study selection

A systematic literature search was performed up to July 2020, and systematic literature retrieval was conducted in PubMed and Web of science databases. Fish oil, n-3 polyunsaturated fatty acid (PUFA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) were paired with sarcopenia, skeletal muscle, lean mass, fat mass, muscle mass and muscle function as the search terms. Meanwhile, manual search and scrutinize the reference lists of original articles, recent reviews and meta-analyses were conducted by using Baidu and Google Scholar.

2.2. Inclusive criteria

Trials included in the meta-analysis must meet the following criteria: (1) Randomized controlled trials designed in parallel or cross-over design; (2) Using n-3 PUFA as interventions; (3) The study provided available data to calculate average differences between baseline and end points, including fat mass, lean mass, walking speed, timed up and go test and grip strength.

2.3. Data extraction and quality assessment

The data extraction was independently performed by two investigators, and any controversy is settled by consensus through discussion. Basic information of each identified article was extracted, including the first author, year of publication, region/country, sample size, gender, average age, intervention duration, dose of n-3 PUFA intake, and intervention type. For inclusive trials, the mean and standard deviation (SDs) of the data at baseline and end point were extracted for the intervention group and the control group, respectively. If the participant has multiple time points of the study, the results of the last time point are extracted for data synthesis. For trials where SDs were not provided directly, they were calculated from standard errors of means (SEM) or 95% confidence intervals (CI) using the formulae listed in the Cochrane handbook [20].

The quality of randomized controlled trials was assessed using the Jadad scoring criteria, including the following items: (1) randomization, (2) random sequence generation, (3) allocation concealment, (4) blinding, and (5) reporting the reason of dropout. One aspect of the trial report will get one point. The trial with Jadad score ≥ 4 was regarded as a high-quality study, whereas the score < 4 was indicative of a low-quality study [21].

2.4. Data analysis

The random effects model described by DerSimonian and Laird was performed to calculate the 95% confidence interval of indicators regarding muscle mass and function [22]. Inter-study heterogeneity was assessed by I^2, and the I^2 values of 25%, 50% and 75% were defined as low, medium and high heterogeneity, respectively [20]. To identify the sources of heterogeneity, subgroup and meta-regression analyses were conducted to focus on the following information: study duration ($<$ 20 and $\geq$ 20 weeks), dosage of n-3 PUFA supplementation ($<$ 3 g and $\geq$ 3 g), region (America and Europe), Jadad score ($<$ 4 and $\geq$ 4) and mean age ($\leq$ 72.5 years old and $>$ 72.5 years old). In addition, meta regression was used to assess whether there was a significant linear relationship between effect size and confounding factors. To test whether the overall effect was stable, sensitivity analysis was performed by re-calculating the summary estimate with deleting one trial at a time. Begg's test was adopted to examine publication bias with a significant level at $P <$ 0.1 [23]. Statistical analysis was conducted with STATA 11.0 for windows (Stata CORP, College station, TX). Two-tailed P value $\leq$ 0.05 was deemed as statistically significant.

3. Results

3.1. The process of study selection

The literature retrieval process is shown in (Fig. 1). After 824 duplicates were deleted, 5571 articles were retrieved from PubMed and Web of Science databases. After excluding unrelated studies, cell models, animal studies, and epidemiological studies, nine articles were eligible for this study.

3.2. Study characteristics

The included articles contain basic information as shown in (Table 1). Two trials were conducted in American [15,24], three in Canada [25-27], and the other four in Scotland [17], Poland [18], Brazil [28], and France [29]. Four studies conducted exercise training plan during n-3 PUFA supplementation. Of the included trials, four trials were considered to be of high quality according to the Jadad scoring criteria.

3.3. Effects of n-3 PUFA supplementation on muscle mass indicators

A total of nine trials were included in this study, of which four trials (five treatment groups) reported the effect of n-3 PUFA supplementation on fat mass [15,18,25,26]. The pooled effect showed that supplementation with n-3 PUFA did not exert fat mass change (−0.67 kg; 95% CI: −2.20, 0.87 kg; P = 0.396), with a significant between-study heterogeneity ($I^2 = 87.4\%$, $P < 0.001$) (Fig. 2A). The mean change in lean mass was evaluated in four trials (five treatment groups) [18,25-27], and n-3 PUFA supplementation had no significant effect on lean mass gain (0.33 kg; 95% CI: −0.35, 1.00 kg; P = 0.343; I^2 = 0.0%; $P_{\text{for heterogeneity}}$ = 0.456) (Fig. 2B).

3.4. Effects of n-3 PUFA supplementation on muscle function indicators

Seven trials (eleven treatment groups) provided available data on the walking speed [17,18,24,26-29], and the summary estimate showed that n-3 PUFA supplementation did not exert significant effect on walking speed (−0.01 m•s^{-1}; 95% CI: −00.3, 0.01 m•s^{-1}; P = 0.172) with no heterogeneity between the studies (I^2 = 0.0%, P = 0.635) (Fig. 3A). The mean variation of time up and go test was reported in five

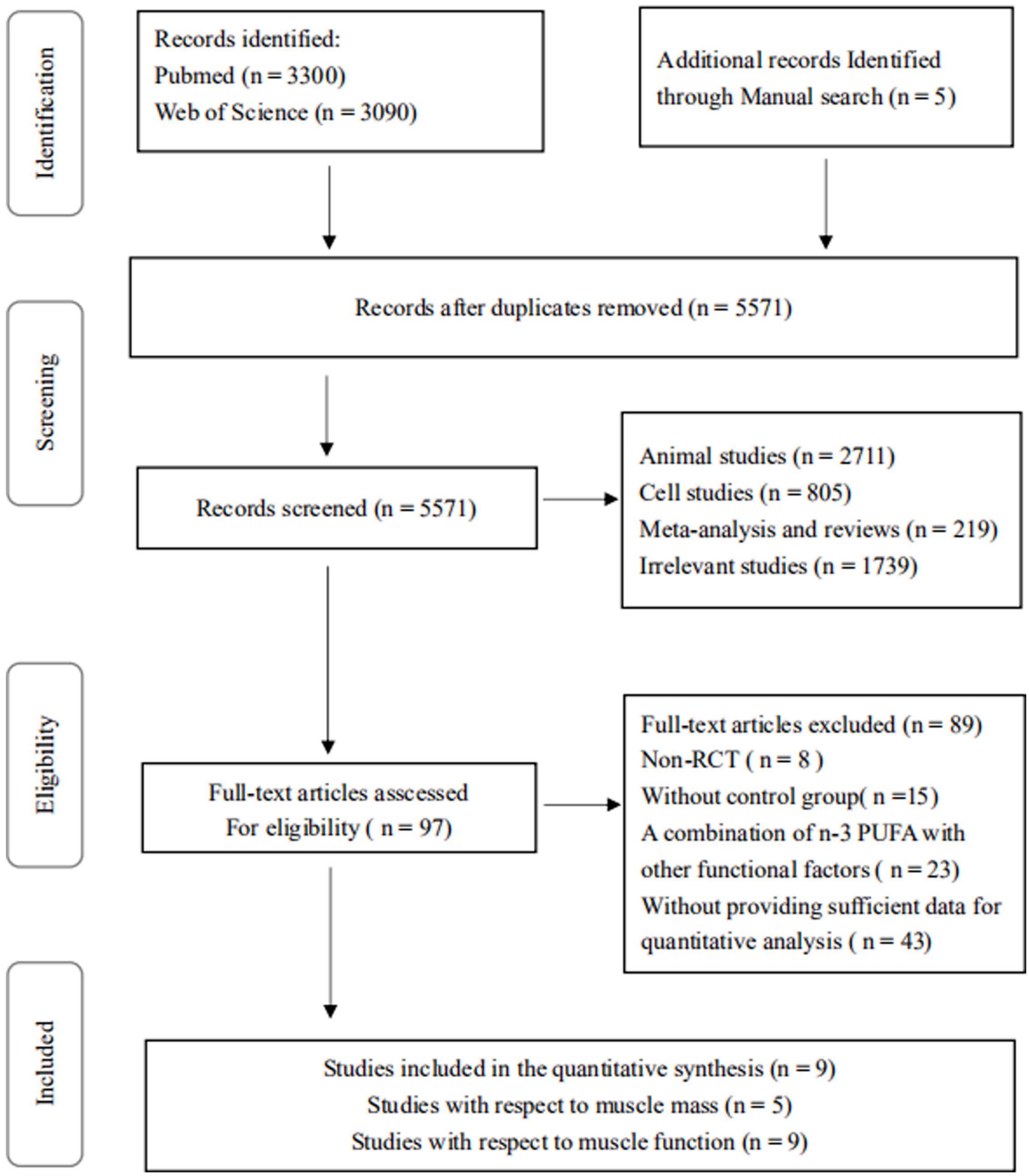

Fig. 1. Flowchart of the literature search.

trials (seven treatment groups) [18,25-28], and no significant effect was observed (−0.25 s; 95% CI: −0.55, 004 s; $P = 0.093$, $I^2 = 84.7\%$, $P_{\text{for heterogeneity}} < 0.001$) (Fig. 3B). For grip strength [15,25,29], n-3 PUFA supplementation significantly improved grip strength in healthy participants (1.17 kg; 95% CI: 0.27, 2.08 kg, $P = 0.011$, $I^2 = 52.8\%$, $P_{\text{for heterogeneity}} = 0.096$) (Fig. 4).

3.5. Subgroup analysis

The trials stratified by duration of n-3 PUFA supplementation indicated that the pooled effect with intervention < 20 weeks significantly reduced the time up and go test (−0.26 s; 95% CI: −0.44, −0.09 s). In addition, the pooled estimate of the trials with Jadad score < 4 indicated a significant reduction in time up and go test (−0.38 s; 95% CI: −0.68, −0.08 s), but not in trials with Jadad score ≥ 4. The summary effect showed that n-3 PUFA supplementation significantly reduced the time up and go test in subjects whose mean age was ≤ 72.5 years (−0.47 s; 95% CI: −0.78, −0.17 s), but not in subjects whose mean age was > 72.5 years. The source of partial heterogeneity might be attributed to mean age with meta-regression analysis ($P = 0.065$) (Table 2).

3.6. Sensitivity analysis and publication bias

Sensitivity analysis showed that except for fat mass and time up and go test, n-3 PUFA supplementation had no substantial effect on the combined estimates of lean mass, walking speed and grip strength, after deletion of each trial at a time. As for fat mass and time up and go test, Bell and his colleagues' experiment had a greater influence on overall study stability [26], which may be the reason for the high heterogeneity of the overall result. When the study was deleted, there was no influence on the overall results.

The Begg's rank correlation test showed no significant publication bias regarding fat mass ($P = 0.862$), lean mass ($P = 0.375$), walking speed ($P = 0.278$), time up and go test ($P = 0.625$) and grip strength (P

Table 1
Characteristics of the nine randomized controlled trials.

Author, Year	Country	No. (Intervention / Control)	Gender (F/M);	Mean Age, year	Training	Duration	Study Design	Dose of n-3 PUFA Intake per day	Control	Health status	Jadad Score
Rodacki, 2012	Brazil	30 (15/15)	30/0	64 ± 1.4	Yes	150 days	Cross-over	2 g (0.40 g EPA and 0.30 g DHA)	None	Healthy females	2
Hutchins-Wiese, 2013	American	118 (79/39)	118/0	64 - 95	No	6 months	Parallel	2 g (0.72 g EPA and 0.48 g DHA)	Olive oil	Healthy females	3
Smith, 2015	American	44 (29/15)	29/15	60 - 85	No	6 months	Parallel	4 g (1.86 g EPA and 1.50 g DHA)	Corn oil	Healthy subjects	3
Logan, 2015	Canada	24 (12/12)	24/0	66 ± 1	No	12 weeks	Parallel	3 g (2.0 g EPA and 1.0 g DHA)	Olive oil	Healthy females	3
Krzyminska-Siemaszko, 2015	Poland	50 (30/20)	33/17	74.6 ± 8.0	No	12 weeks	Parallel	1.3 g (0.66 g EPA and 0.44 g DHA)	Vitamin E	Low muscle mass subjects	2
Bell, 2017	Canada	49 (25/24)	0/49	73 ± 1	Yes	20 weeks	Parallel	3 g (0.70 g EPA and 0.445 g DHA)	Safflower oil	Healthy males	5
Da Boit, 2017	Scotland	50 (23/27)	23/27	70.65 ± 3.95;	Yes	18 weeks	Cross-over	3 g (2.10 g EPA and 0.60 g DHA)	Safflower oil	Healthy subjects	4
Cornish, 2018	Canada	23 (11/12)	0/23	≥ 65	Yes	12 weeks	Parallel	3 g (1.98 g EPA and 0.99 g DHA)	Mixed oil	Healthy males	4
Rolland, 2019	France	1679 (839/840)	1087/592	75.34 ± 4.42	No	36 months	Cross-over	2 g (0.225 g EPA and 0.8z DHA)	Paraffin oil	Healthy subjects	4

Abbreviations: F, female; M, male; No., number of included subjects; PUFA, polyunsaturated fatty acids.

= 0.178) (Table 3).

4. Discussion

This systematic review and meta-analysis examined the effects of n-3 PUFA supplementation on muscle mass and function in the elderly. The findings indicated that supplement with n-3 PUFA significantly increased their grip strength. However, no other benefits were observed regarding other indicators. Due to limited trials reported the dose of n-3 PUFA intervention on muscle mass and function, dose-response analysis was not conduced in this study. Therefore, the recommend dose and duration could not obtain in this study. However, 3 gram per day of n-3 PUFA supplementation might have a protective effect on muscle mass and function with a duration of 12 weeks.

The muscle mass and function of the elderly gradually decrease with the increase of age, and can develop into sarcopenia in severe cases [8]. It is a kind of senile syndrome which is increasingly serious with the aging of the population. At present, there is no unified drug treatment for this situation [30]. Increasing evidence shows that nutrition is an effective way to improve and delay the decline of muscle mass and muscle function in the elderly [31]. It is well known that n-3 PUFA, such as marine-derived fish oil has strong anti-inflammatory effect, and has good effect on improving cardiovascular disease, diabetes, depression, cognitive status and lowering blood pressure [32,33]. Meanwhile, regarding n-3 PUFA supplementation on muscle mass and muscle function, studies have shown that supplementing more than 3 g of n-3 PUFA every day can improve and delay the decline of muscle mass and function [10]. At present, the mechanism of n-3 PUFA on muscle protection is considered to be able to inhibit protein degradation [12], reduce proinflammatory cytokines in *vivo* [16], stimulate muscle protein synthesis through mTOR-p70s6k signal pathway [34], activate human skeletal muscle satellite cells [35], and reduce the production of mitochondrial reactive oxygen species [36]. Thus, supplemental n-3 PUFA has achieved the purpose of delaying muscle aging.

The research thinks that the loss of muscle mass is considered to be a major determinant of power loss in the process of aging [37]. By analyzing the effects of n-3 PUFA supplementation on indicators of muscle mass, it was found that n-3 PUFA supplementing can prevent muscle mass degradation due to aging. Recently, a study found that providing 3 g/d n-3 PUFA to elderly people ($n = 29$) for six months could increase the thigh muscle area of subjects [15]. Besides, there is evidence that older females may be better than males in increasing muscle mass with n-3 PUFA supplementation. Da Boit and his colleagues found that after 18 weeks of n-3 PUFA supplementation and resistance training, the muscle mass of females increased significantly compared with the control group, and there was no change in males, showing a significant gender difference [17]. In a 12week RCT for people with low muscle mass and low muscle mass risk, n-3 PUFA supplementation was not found to improve muscle mass in low muscle mass and low muscle mass risk groups [18]. This result may be related to short supplement time and insufficient supplement dose. To sum up, supplemental n-3 PUFA has suggested a beneficial effect on improving human muscle mass. After data synthesis with meta-analysis, it was found that n-3 PUFA supplementation had no significant effect on fat mass and lean mass. Moreover, there are differences in the intervention period and dose of each study, so the current meta-analysis could not draw a reliable conclusion on the optimal supplementary dose and duration. Therefore, the dose and duration of n-3 PUFA supplementation to improve muscle mass need to be further explored.

In order to evaluate muscle function, the included studies evaluated the subjects' walking speed, time up and go test, grip strength, and one-repetition maximum (1-RM) muscle strength. It has found that n-3 PUFA supplementation could increase walking speed and 6-minutes walking distance [24,26,28]. In a study of all female subjects, n-3 PUFA supplementation significantly reduced the duration of the drag experiment, and significant change in this parameter was also observed in Bell's study [25,26]. Smith and his colleagues found that six months of n-3 PUFA treatment increased grip strength and 1-RM muscle strength compared with the control group [15]. Accordingly, the mass of muscle protein synthesis has been increased in older subjects with n-3 PUFA supplement [14]. Similarly, Lalia and his colleagues also found that fish oil supplementation for 12 weeks improved muscle protein synthesis

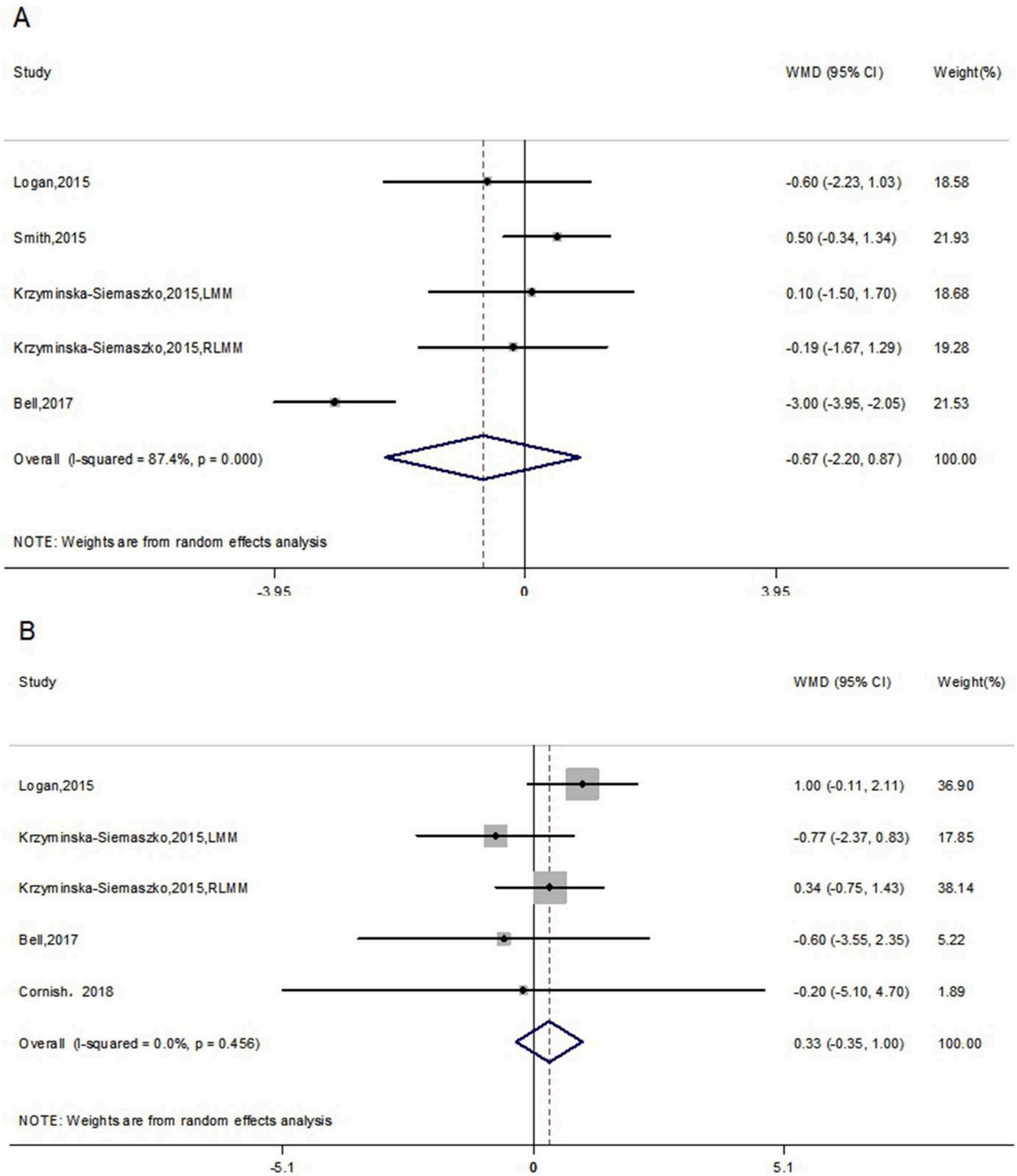

Fig. 2. Effect of n-3 PUFA supplementation on fat mass (A), lean mass (B) of study subjects. The pooled effect was calculated by using a random-effects model. The diamonds denote the summary risk estimate, and the horizontal lines represent the 95% CI. Abbreviations: LMM, subjects with low muscle mass; RLMM, subjects with risk of low muscle mass; WMD, weighted mean difference; CI, confidential interval.

and increased fractional synthesis rates in mitochondria and sarcoplasma after exercise [38]. In addition, another study has found that small doses of n-3 PUFA supplementation for more than 3 years, either alone or in combination with multi domain lifestyle interventions, including physical activity counseling, have no significant effect on muscle mass and function for the elderly [29]. To obtain the summary estimates, the pooled effects of the present meta-analysis suggested that n-3 PUFA supplementation significantly increased the grip strength, but has no significant effect on walking speed and time up and go test.

Supplemental n-3 PUFA on muscle mass and function were carried in middle-aged subjects. Compared with the control group, n-3 PUFA supplementation could improve muscle strength, restrict human activity

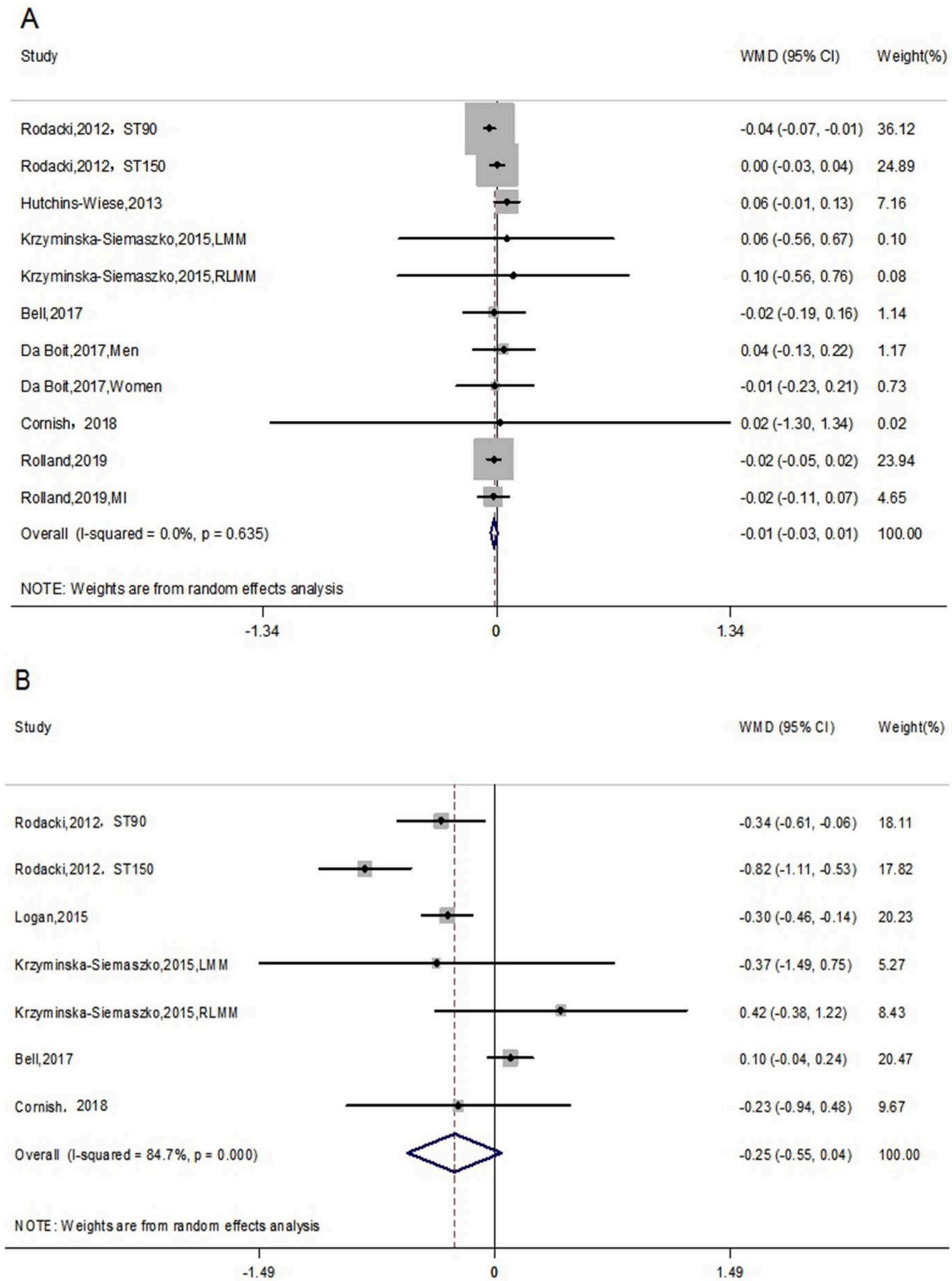

Fig. 3. Effect of n-3 PUFA supplementation on walking speed (A), time up and go test (B) of study subjects.
The pooled effect was calculated by using a random-effects model. The diamonds denote the summary risk estimate, and the horizontal lines represent the 95% CI. Abbreviations: ST90, strength-training group supplemented with fish oil during 90 d; ST150, strength-training group supplemented with fish oil during 150 d; LMM, subjects with low muscle mass; RLMM, subjects with risk of low muscle mass; WMD, weighted mean difference; CI, confidential interval.

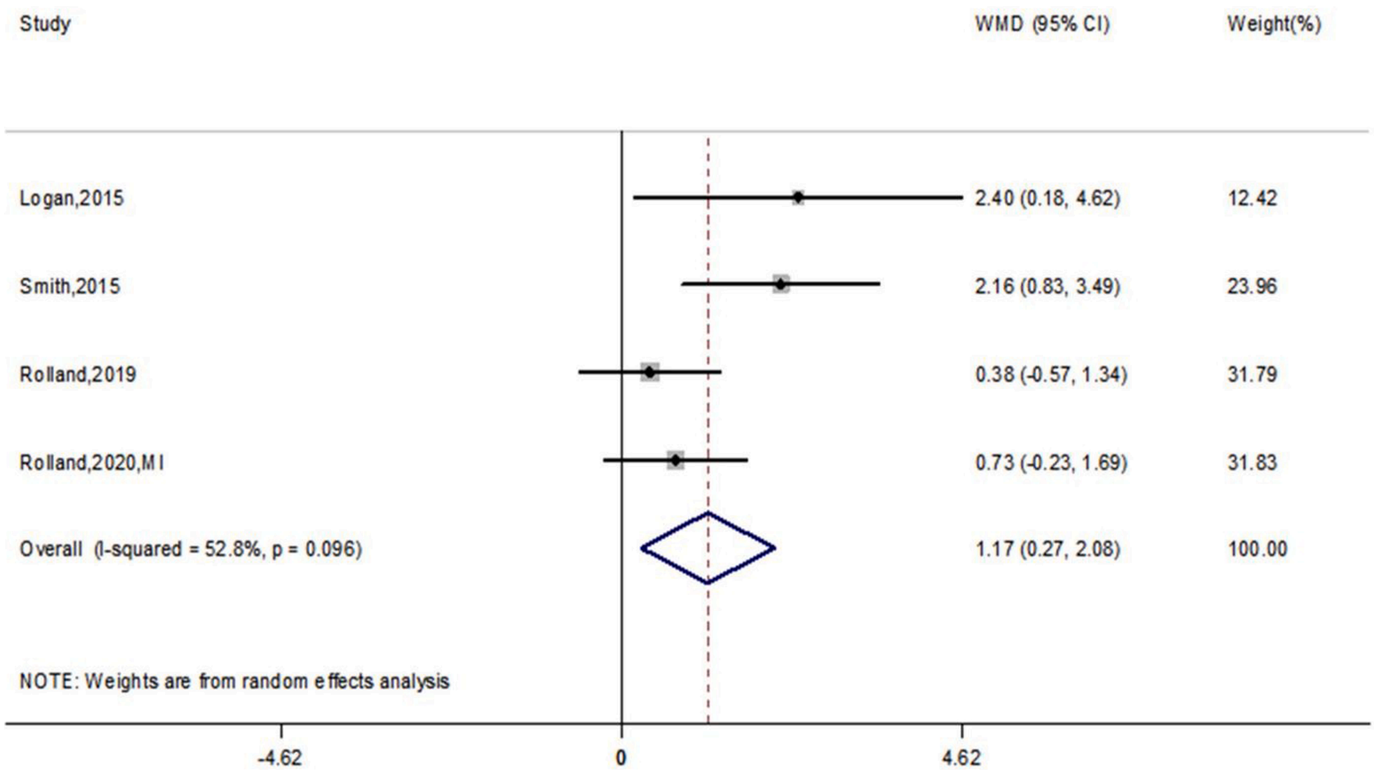

Fig. 4. Effect of n-3 PUFA supplementation on grip strength of study subjects.
The pooled effect was calculated by using a random-effects model. The diamonds denote the summary risk estimate, and the horizontal lines represent the 95% CI. Abbreviations: MI, group supplemented with n-3 PUFA and multidomain intervention; WMD, weighted mean difference; CI, confidential interval.

and prevent muscle injury [39]. McGlory et al. found that in 20 trained young men who received 3.5 g EPA and 0.5 g DHA daily for 8 weeks, myofibrillar protein synthesis did not change and protein synthesis did not decrease after high-intensity exercise [40]. Another study reported that the subjects aged 25–45 years improved muscle protein fraction synthesis after 8 weeks of n-3 PUFA supplementation by activation of mTOR signal pathway [14]. Based on the above study, n-3 PUFA supplementation might have a positive effect on the muscle mass and function in middle-aged subjects.

Substantial evidence shows that age-related neuromuscular dysfunction occurs due to the decline of information processing, power generation, movement speed, motor control, gait, balance, coordination and reaction speed, which can lead to the loss of muscle mass and strength [41-42]. Recent studies have shown that age-related neuromuscular dysfunction precedes the loss of muscle mass and function, and might be a necessary condition for muscle mass and function loss [43]. One clinical trial reported that n-3 PUFA supplementation could improve peripheral neuromuscular function and relieve fatigue, but the effect on central neuromuscular function remained unclear [44]. Additionally, n-3 PUFA intervention could increase the nerve conduction velocity by 13% in diabetic rats, which supported that n-3 PUFA could improve muscle function by improving nerve function [45]. Further trials should focus on n-3 PUFA supplementation on neuromuscular function during aging.

Several advantages of this study should be considered. First, to the best of our knowledge, this is the first meta-analysis to evaluate the effects of n-3 PUFA supplementation on muscle mass and muscle function in older adults, and this study has important implications for future efforts to improve muscle mass and function decline with population aging. Second, the sensitivity analysis showed that the pooled effect was not significantly exerted after the deletion of each trial, indicating the stability of the analysis results. In addition, the Begg's test found no indication of publication bias, suggesting that missing data or unpublished studies did not affect the overall analysis. Simultaneously, the limitations of study should need to be acknowledged. First, the participants of these trials were elderly people over 60 years old, and most of the elderly were healthy people. Only one study had the characteristics of low muscle mass and risk of low muscle mass, and the coverage of age and health status was limited. Second, considering limited participants included the trials, insufficient sample-size and statistical power would influence the summary estimate, and the effects of n-3 PUFA supplements on each analysis index should be carefully explained with caution. Third, only four studies were rated as high quality studies according to the Jadad scoring criteria, and most trials did not report random sequence generation or allocation concealment. Therefore, low quality randomized controlled trials may partially affect the aggregate estimates. Fourth, the doses of n-3 PUFA were ranged from 1.3 to 4 gs per day for each trial, and the duration of the trial was ranged from 12 weeks to 6 months. Due to inconsistencies in the dose and duration of n-3 PUFA interventions, this meta-analysis was unable to draw reliable conclusions regarding the optimal dose and duration for improving muscle mass and function. Finally, the control group received different types of placebos, including olive oil, corn oil, vitamin E, safflower oil, Omega 3–6–9 blend and flavored paraffin oil. As a result, placebo differences may bias the final results.

5. Conclusions

In conclusion, this systematic review and the meta-analysis provides evidence that n-3 PUFA supplementation has several benefits to improve muscle mass and function in healthy subjects. Additional long-term RCTs are warranted to verify whether supplementation n-3 PUFA has favorable effects on muscle mass and function in patients with sarcopenia with large sample-size.

Table 2
Subgroup and meta-regression analyses for fat mass, time up and go test and grip strength concentrations.

Factors stratified	Fat mass (kg) No.	Pooled effect (95%)	Heterogeneity I^2 (%)	P^a	P^b	Time up and go test (s) No.	Pooled effect (95%)	Heterogeneity I^2 (%)	P^a	P^b	Grip strength (kg) No.	Pooled effect (95%)	Heterogeneity I^2 (%)	P^a	P^b
Overall analysis	5	−0.67 (−2.20, 0.87)	87.4	< 0.001		7	−0.25 (−0.55, 0.04)	84.7	<0.001		4	1.17 (0.27, 2.08)	52.8	0.096	
Duration, weeks					0.539					0.593					0.439
<20	3	−0.22 (−1.13, 0.68)	0.00	0.834		4	−0.26 (−0.44, −0.09)	2.1	0.382		1	2.40 (0.18, 4.62)			
≥20	2	−1.24 (−4.67, 2.19)	96.6	0.00		3	−0.34 (−0.90, 0.21)	94.1	0.00		3	0.99 (0.05, 1.94)	57.4	0.095	
Dose of n-3 PUFA intake per day					0.548					0.394					0.133
<3 g	2	−0.06 (−1.14, 1.03)	0.00	0.794		4	−0.37 (−0.83, 0.09)	73.2	0.011		2	0.56 (−0.12, 1.23)	0.00	0.615	
≥3 g	3	−1.04 (−3.43, 1.35)	93.3	0.00		3	−0.12 (−0.46, 0.22)	85.2	0.001		2	2.22 (1.08, 3.36)	0.00	0.856	
Region					0.548					0.372					0.133
America	3	−1.04 (−3.43, 1.35)	93.3	0.00		5	−0.31 (−0.64, 0.01)	89.1	0.00		2	2.22 (1.08, 3.36)	0.00	0.856	
Europe	2	−0.06 (−1.14, 1.03)	0.00	0.794		2	0.13 (−0.62, 0.88)	21.1	0.260		2	0.56 (−0.12, 1.23)	0.00	0.615	
Jadad score					0.012					0.242					0.133
< 4	4	0.17 (−0.45, 0.78)	0.00	0.638		5	−0.38 (−0.68, −0.08)	71.0	0.008		2	2.22 (1.08, 3.36)	0.00	0.856	
≥ 4	1	−3.0 (−3.95, −2.05)				2	0.09 (−0.05, 0.23)	0.00	0.370		2	0.56 (−0.12, 1.23)	0.00	0.615	
Mean age, years					0.466					0.065					0.133
≤72.5	2	0.18 (−0.80, 1.16)	28.2	0.238		3	−0.47 (−0.78, −0.17)	79.6	0.008		2	2.22 (1.08, 3.36)	0.00	0.856	
>72.5	3	−1.1 (−3.21, 1.07)	87.5	0.00		4	0.09 (−0.05, 0.23)	0.00	0.550		2	0.56 (−0.12, 1.23)	0.00	0.615	

Abbreviations: CI, confidential interval; No., number of included studies; PUFA, polyunsaturated fatty acids.
P^a for heterogeneity; P^b for meta-regression analysis.

Table 3
Results of publication bias.

Parameters	No. of treatment groups	Pooled Effect (95% CI)	I^2 (%)	*P* for heterogeneity	*P* for Begg's test
Fat mass (kg)	5	−0.67 (−2.20, 0.87)	87.4	0.00	0.862
Lean mass (kg)	5	0.33 (−0.35, 1.00)	0.00	0.456	0.375
Walking speed ($m{\bullet}s^{-1}$)	11	−0.01 (−0.03, 0.01)	0.00	0.635	0.278
Time up and go test (s)	7	−0.25 (−0.55, 0.04)	84.7	0.000	0.625
Grip strength (kg)	4	1.17 (0.27, 2.08)	52.8	0.096	0.178

Abbreviations: CI, confidential interval; No., number of included studies.

Author statement

Wen-jun Ma: Writing - Original Draft; Xiao-fei Guo and Duo Li: Conceptualization Ideas, Supervision; Wen-jun Ma and Hui Li: Investigation, Data Curation, Formal analysis; Xiao-fei Guo, Hui Li, Wei Zhang, Jun Li., He Liu and Duo Li: Writing - Review & Editing, Validation; All of the authors read and approved the final manuscript for submission.

Declaration of Competing Interest

None.

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