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Review

The Impact of n-3 Polyunsaturated Fatty Acids on Muscle Mass, Strength, and Physical Function in Older Adults: An Umbrella Review

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Abstract

Background: Population aging is accelerating worldwide, making sarcopenia an increasingly important public health concern. Currently, effective and widely accepted interventions remain limited. This umbrella review aimed to examine the effects of n-3 polyunsaturated fatty acid (n-3 PUFA) supplementation on sarcopenia-related outcomes and to inform clinical decision-making and future research. **Method:** A comprehensive literature search was performed in PubMed, Web of Science, EBSCO, and ScienceDirect to identify randomized controlled trials (RCTs) and meta-analyses of RCTs evaluating the effects of n-3 PUFA supplementation on muscle-related outcomes in adults aged ≥55 years. Primary outcomes included skeletal muscle mass, muscle strength, and physical function. The methodological quality of the included meta-analyses was assessed using A Measurement Tool to Assess Systematic Reviews 2 (AMSTAR 2), and the certainty of the evidence was evaluated using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach. In addition, the corrected covered area (CCA) was used to assess the degree of overlap among primary studies included in the systematic reviews. A random-effects model was applied to estimate the pooled effect sizes, standardized mean differences (SMDs), and 95% confidence intervals. **Results:** A total of seven RCTs and seven meta-analyses met the inclusion criteria. The interventions involved the administration of n-3 PUFAs through diet or supplementation, with most studies applying mixtures rich in eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), and a few using flaxseed oil rich in alpha-linolenic acid (ALA). The n-3 PUFA dosage ranged from 1.3 g/day to 14 g/day, and intervention duration ranged from 6 weeks to 6 months. Overall, n-3 PUFA supplementation was associated with a modest but measurable increase in muscle strength and showed potential benefits for lower-limb physical performance and muscle mass. However, a high degree of overlap among primary studies was observed (CCA = 14.02%), indicating substantial redundancy in the evidence base. Moreover, the certainty of the evidence ranged from moderate to very low. While moderate certainty was observed for some outcomes (e.g., lower body strength, lower-extremity physical function), most muscle strength and function outcomes, including grip strength, walking speed, and upper body strength, were rated as low or very low certainty, largely due to the limited number of trials and methodological constraints. **Conclusion:** In summary, n-3 PUFA supplementation, particularly marine-derived n-3 PUFAs, may offer preliminary benefits in attenuating age-related declines in muscle mass and function among healthy older adults. However, given the predominantly low-to-very-low certainty of the evidence and the high degree of overlap among primary studies, the overall reliability of the findings may be compromised. Therefore, large-scale, methodologically rigorous, and high-quality RCTs are urgently needed to validate these preliminary findings and establish evidence-based clinical guidelines for the use of n-3 PUFAs in the prevention and management of sarcopenia. The PROSPERO Registration: CRD420251165901 (https://www.crd.york.ac.uk/PROSPERO/view/CRD420251165901).

Keywords: fatty acids; n-3 polyunsaturated fatty acids; sarcopenia; muscle strength; umbrella review

1. Introduction

Sarcopenia is a progressive and systemic skeletal muscle disorder characterized by the accelerated loss of muscle mass and function. It is primarily age-related and has been associated with an increased risk of several adverse outcomes, including falls, mobility limitations, declines in muscle function, and higher mortality, imposing a substantial economic burden on healthcare systems [1,2,3]. With the rapid progression of global population aging, sarcopenia has emerged as a significant public health concern. Epidemiological evidence indicates that the prevalence among individuals aged 60 to 70 ranges from 5% to 13%, while the prevalence among those aged ≥80 years ranges from 11% to 50% [4]. Consequently, the prevention and management of sarcopenia have become critical public health priorities.

Currently, in the absence of approved pharmacological therapies, the management of sarcopenia primarily relies on non-pharmacological approaches, particularly nutritional and exercise interventions [5,6,7]. Adequate protein and energy intake have been demonstrated to be fundamen-

tal to nutritional strategies designed to counteract muscle loss [8,9,10]. Supplementing with branched-chain amino acids (BCAAs) has been shown to enhance muscle protein synthesis and improve muscle mass and grip strength in older adults [11,12]. Additionally, supplementation with β-hydroxy-β-methylbutyric acid (HMB) has been shown to improve muscle quality and reduce fat infiltration [13]. Accumulating evidence suggests that other nutrients, such as probiotics, n-3 polyunsaturated fatty acids (n-3 PUFAs), and vitamin D, may contribute to attenuating muscle loss and improving physical function [5].

n-3 PUFAs, primarily comprising eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are widely found in marine-derived foods and certain plant oils [14]. As a dietary supplement, n-3 PUFAs are generally well tolerated in humans and have been associated with minimal long-term adverse effects. Their safety has been recognized by regulatory authorities, including the Food and Drug Administration (FDA) and the European Food Safety Authority (EFSA). The EFSA recommends a daily intake of 250 mg of EPA and DHA for adults [15]. Similarly, the World Health Organization (WHO) suggests an intake of 200–500 mg/day of EPA and DHA [16]. For individuals following vegetarian or vegan diets, adequate intake of plant-derived n-3 fatty acids should be ensured. A number of studies suggest that supplementation with n-3 PUFAs may also mitigate age-related declines in muscle mass and function [17,18,19,20,21,22]. From a mechanistic perspective, sarcopenia is influenced by multiple biological processes, including imbalances in muscle protein synthesis and degradation, impaired neuromuscular signaling, and dysregulated metabolic pathways [1]. Therefore, several underlying biological mechanisms have been proposed to support the hypothesis that supplementing with n-3 PUFAs improves muscle health. First, n-3 PUFAs exhibit significant anti-inflammatory properties, which have been shown to reduce levels of circulating pro-inflammatory cytokines (e.g., interleukin-6 and tumor necrosis factor-α), thereby slowing muscle catabolism [23]. Second, n-3 PUFAs may enhance insulin sensitivity and activate the mechanistic target of rapamycin (mTOR) signaling pathway, promoting muscle protein synthesis [24]. Additionally, n-3 PUFAs have been observed to improve mitochondrial function by enhancing glycolytic capacity, basal oxidative metabolism, total mitochondrial activity, and mitochondrial content in muscle cells [25,26].

Although numerous systematic reviews and meta-analyses have attempted to synthesize evidence from clinical trials to evaluate the effects of n-3 PUFAs supplementation on muscle health in older adults, the evidence remains inconsistent [24,27,28]. Many reviews have concentrated on the combined effects of nutritional supplementation and exercise interventions, with limited evaluation of n-3 PUFAs supplementation alone. This lack of clarity underscores the need for a comprehensive synthesis of the available evidence. Therefore, this umbrella review aims to integrate existing systematic reviews and meta-analyses, and to evaluate the effects of n-3 PUFAs supplementation on muscle-related outcomes in older adults. By synthesizing and grading the available evidence, this study aims to elucidate the potential role of n-3 PUFAs in the prevention and management of sarcopenia and to provide a foundation for clinical decision-making and future research.

2. Method

The present work adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and related standards [29]. An umbrella review methodology was employed. Methodological challenges were identified, including overlap among eligible reviews and variability in reported effect size metrics. In response, an integrated synthesis strategy was applied. For outcomes considered critical, quantitative analyses were conducted through the re-extraction and reanalysis of data from original randomized controlled trials (RCTs), identified through a new systematic search and screening process based on predefined eligibility criteria. For the remaining outcomes, a structured qualitative synthesis was undertaken to systematically summarize the available evidence. This umbrella review was registered in PROSPERO (registration number: CRD420251165901).

2.1 Information Sources and Search Strategy

A structured search strategy was formulated using the Population, Intervention, Comparison, Outcome, and Study design (PICOS) framework as a guiding reference (**Supplementary Table 1**). Comprehensive searches were carried out in PubMed, Web of Science, EBSCO, and ScienceDirect. All available records from database inception to August 30, 2025 were retrieved, without imposing language limitations.

Search keywords encompassed terms related to sarcopenia, omega-3 fatty acids, and aging. These included: “Sarcopenia”, “muscular atrophy”, “Fatty Acids, Omega-3”, “omega-3 fatty acid”, “docosahexaenoic”, “eicosapentaenoic”, as well as age-related descriptors such as “Aged”, “elderly”, and “aging”. Boolean operators (AND and OR) were applied to combine the search terms as appropriate. Detailed search strategies for each database were presented in **Supplementary Table 2A**.

To maximize retrieval of relevant trials, reference lists of original RCTs cited in eligible meta-analyses were reviewed. Supplementary searches were also performed within the same databases. The complete search process was presented in **Supplementary Table 2B**.

2.2 Inclusion and Exclusion Criteria

Eligibility criteria were established in line with the PICOS framework. For meta-analyses, eligible studies were those based on RCTs, with primary outcomes encompass-

ing at least one of the following: body composition, muscle function tests, or muscle strength. Studies were excluded if: (1) studies that did not include RCTs; (2) studies with participants younger than 60 years or those with conditions such as cancer, renal failure, hepatitis, or diabetes; (3) interventions involving n-3 PUFAs combined with other components (e.g., protein or vitamins); and (4) studies that did not report any muscle-related outcome data.

For RCTs, trials investigating the effects of n-3 PUFAs supplementation on skeletal muscle mass in older adults were included. The exclusion criteria were as follows: (1) non-RCT studies; (2) studies involving participants aged <55 years or those with conditions such as cancer, renal failure, hepatitis, or diabetes; (3) interventions involving n-3 PUFA combined with other components (e.g., protein or vitamins); (4) interventions combining n-3 PUFAs supplementation with exercise; and (5) studies that did not report any muscle-related outcomes.

2.3 Study Selection

All records identified through the database searches were imported into EndNote 20 (version 20.0, Clarivate, Philadelphia, PA, USA) for reference management. Duplicate citations were removed prior to screening. Titles and abstracts were independently reviewed by two investigators (YS and TW) to identify potentially relevant studies. Full-text articles were subsequently evaluated for eligibility. Any disagreements during the selection process were resolved through discussion with a third reviewer (SY).

2.4 Data Extraction

Data were independently extracted from the eligible full-text articles by two researchers using a predefined data extraction form. The extracted information included first author, publication year, number of included studies, and sample size. Participant characteristics, intervention details, and outcome measures were also recorded. Additionally, pooled effect sizes (with 95% confidence intervals), heterogeneity (I^2), publication bias reported in the meta-analyses, as well as means, standard deviations, and risk of bias assessments for outcome measures in RCTs were also extracted.

2.5 Methodological Quality Assessment

The methodological quality was independently assessed by two researchers using the A Measurement Tool to Assess Systematic Reviews 2 (AMSTAR 2) tool. This instrument includes 16 methodological criteria, of which seven items (Items 2, 4, 7, 9, 11, 13, and 15) are designated as critical domains with substantial influence on the final quality judgment [30]. Ratings within these key domains were used to derive the overall methodological classification. Based on this assessment, studies were categorized as high, moderate, low, or critically low in methodological quality.

2.6 Evidence Quality Assessment

The quality of evidence was assessed using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach. The certainty of evidence for each outcome was rated as high, moderate, low, or very low. The evaluation considered multiple methodological domains, including study design, result consistency, between-study heterogeneity, indirectness of evidence, and the potential for publication bias [31].

2.7 Assessment of Overlap Among Primary Studies

To quantify the degree of overlap among primary studies across the included meta-analyses, the corrected covered area (CCA) was calculated [32]. The CCA was calculated using the following formula: $\mathrm{CCA} = (N - r) / (rc - r)$, where N represents the total number of occurrences of primary studies across all included meta-analyses (including repeated counts), r represents the number of unique primary studies, and c represents the total number of included meta-analyses. The degree of overlap was interpreted as follows: a CCA value <5% indicates slight overlap, 5%–10% indicates moderate overlap, and >10% indicates high overlap.

2.8 Evidence Map

An evidence map was constructed in the form of a bubble chart. The magnitude of each bubble reflected the corresponding study sample size, while color coding was used to distinguish outcome categories. Study conclusions reported by the original authors were plotted along the horizontal axis and classified as beneficial, probably beneficial, harmful, no differential effect, or inconclusive. Methodological quality, as assessed by AMSTAR 2, was displayed on the vertical axis.

2.9 Statistical Analysis

Statistical analyses were performed using Comprehensive Meta-Analysis software (CMA, version 4.0.0; Biostat, Inc., Englewood, NJ, USA). Characteristics of the included meta-analyses were summarized qualitatively. Summary effect estimates with corresponding 95% confidence intervals were reported, together with measures of between-study heterogeneity and assessments of publication bias. For RCTs, given the variability in n-3 PUFA dosage, sources, and intervention duration across studies, potential clinical heterogeneity was anticipated. Therefore, a random-effects model was applied to perform the meta-analysis, and standardized mean differences (SMDs) with 95% confidence intervals were calculated. Heterogeneity was assessed using the Cochran's Q test and the I^2 statistic, with a p-value < 0.05 from the Cochran's Q test or I^2 >75% indicating substantial heterogeneity [33].

3. Results

3.1 Literature Search

Fig. 1 Illustrates the study identification and selection workflow for both the meta-analyses (Fig. 1A) and the RCTs (Fig. 1B).

As shown in Fig. 1A, a total of 643 records were retrieved from databases. Duplicate removal led to the exclusion of 182 records, leaving 461 publications for initial screening. Based on title and abstract evaluation, 443 records were removed according to the predefined eligibility criteria. The remaining 18 articles were sought for full-text retrieval and assessed for eligibility. Of these, 11 reports were excluded due to out-of-scope patient populations (n = 5), interventions not meeting inclusion criteria (n = 3), or lack of meta-analyzable outcome data (n = 3). Ultimately, seven meta-analyses were included in the umbrella review. Details of excluded studies are summarized in **Supplementary Table 3**.

In addition to the umbrella review, an updated meta-analysis of eligible RCTs was conducted. Fig. 1B depicts the selection process for original studies included in the updated meta-analysis. The initial search identified 1130 records. After removing 110 duplicates, 1020 records were screened based on titles and abstracts, of which 1003 were excluded. The full texts of the remaining 17 articles were assessed for eligibility. In addition, individual studies included in the aforementioned meta-analyses were screened for eligibility. After removing overlapping studies and applying the same inclusion criteria, a total of seven unique RCTs were ultimately included in the updated meta-analysis.

3.2 Characteristics of Reviews and Meta-Analyses

The included reviews were published between 2020 and 2023, with sample sizes ranging from 488 to 2438 participants. All reviews examined the intake of n-3 PUFAs through diet or supplementation. Reported outcomes primarily included measures of body composition, muscle performance, and muscle strength. An overview of the main characteristics of these reviews is provided in Table 1 (Ref. [34,35,36,37,38,39,40]).

In addition, seven RCTs published between 2009 and 2022 were included. All studies enrolled participants aged 60 years or older and assessed n-3 PUFAs exposure via diet or supplements. Intervention durations varied from 6 weeks to 6 months. Baseline characteristics of the included trials are summarized in Table 2 (Ref. [19,20,41,42,43,44,45]).

3.3 Methodological Quality

Based on the AMSTAR 2 evaluation, four of the included systematic reviews were classified as low methodological quality [34,35,36,37], while three were rated as critically low quality [38,39,40]. The methodological quality of the included studies is summarized in Table 3 (Ref. [34,35,36,37,38,39,40]). The most common critical deficiencies included the lack of a preregistered protocol (item 2), incomplete or insufficiently described search strategies (item 4), failure to provide a list of excluded studies with corresponding justifications (item 7), and inadequate consideration of risk of bias in primary studies when interpreting findings (item 13). Additionally, none of the reviews provided a clear rationale for the selection of study design (item 3), nor did they report funding sources for the included primary studies (item 10). Several non-critical limitations were also observed, including insufficient reporting of study selection and data extraction procedures, as well as incomplete evaluation and reporting of between-study heterogeneity.

3.4 GRADE

The GRADE evaluation indicated that the overall certainty of evidence across all assessed outcomes ranged from moderate to very low. Evidence ratings were determined based on multiple methodological domains, including risk of bias, publication bias, imprecision, inconsistency, and indirectness. During the grading process, substantial heterogeneity was identified in several analyses, which reduced estimate precision and resulted in downgrading of evidence quality. In addition, wide confidence intervals and pooled estimates that did not reach statistical significance were common reasons for further downgrades. Evidence quality was further downgraded due to the inclusion of participants with chronic conditions and studies in which n-3 PUFAs supplementation was combined with exercise-based interventions. Among the included reviews, only one review (Maha Timraz et al. [37]) was assessed as having a serious risk of bias as well as concerns regarding publication bias. A summary of the GRADE ratings for the associations between n-3 PUFAs supplementation and related outcomes is provided in **Supplementary Table 4**.

3.5 Overlap Among Primary Studies

Across the seven included meta-analyses, a total of 44 unique primary studies were identified, with 81 total occurrences of primary studies. Based on the formula, the CCA was calculated to be 14.02%, indicating a high degree of overlap among the included meta-analyses and suggesting substantial redundancy in the evidence base.

3.6 Main Findings of the Umbrella Review

This umbrella review integrated evidence from previously published systematic reviews and meta-analyses, suggesting a potential beneficial association between n-3 PUFAs intake and indicators of muscle health, although the overall strength of the supporting evidence was limited.

All included meta-analyses evaluated n-3 PUFAs supplementation as a major intervention. Primary outcomes across studies focused on muscle strength, such as handgrip strength, and muscle function, including walking speed and the timed up-and-go test.

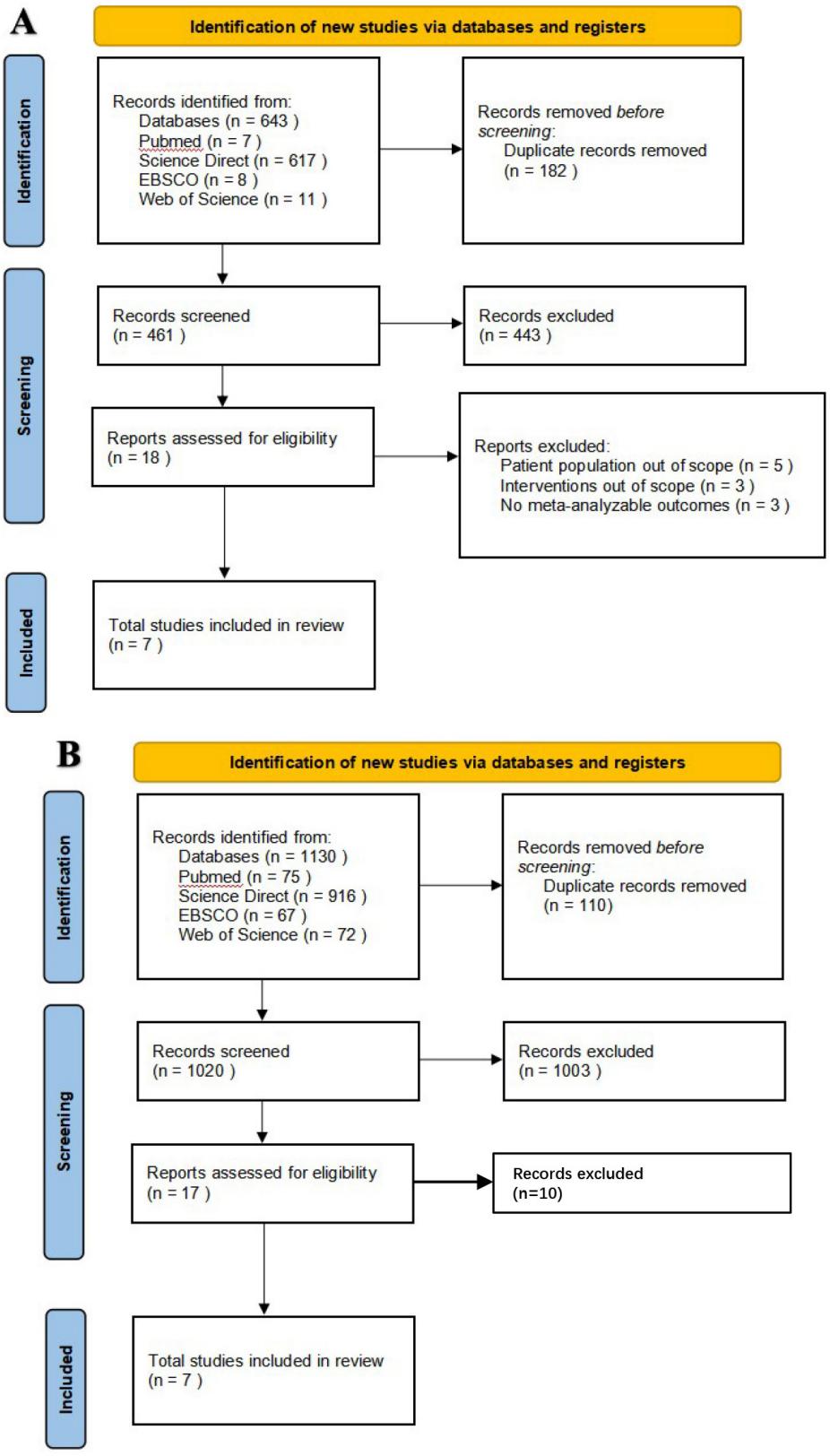

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart illustrating the screening process applied during the systematic literature search. (A) Study selection for umbrella review. (B) Study selection for the updated meta-analyses.

Table 1. Characteristics of the included reviews with meta-analyses.

First author, year	Number of studies included	Sample size	Participants	Intervention	Outcome measures
Stephen M Cornish, 2022 [40]	16	2438	Adults ≥55 years old, without major disease conditions	Supplemental fish oil or n-3 (ALA, DHA, EPA) supplementation	Lower body strength, upper body strength and walking speed
Felipe Mendes Delpino, 2021 [34]	11	534	Healthy adults	Supplementing with n-3 polyunsaturated fatty acids	Lean body mass
Wen-jun Ma, 2021 [39]	9	2067	Healthy older adults aged 60 and above	Supplementing with n-3 polyunsaturated fatty acids	Fat mass, lean mass, walking speed, tTimed Up and Go test and grip strength
Ya-Hui Huang, 2020 [38]	10	552	Adults aged 60 years or older.	Increase n-3 PUFAs intake through diet/supplements	Muscle mass, grip strength, one-repetition maximum leg strength, walk speed and Timed Up and Go test
Maha Timraz, 2023 [37]	5	488	Healthy adults with a mean sample age of 65 years or older	Long-chain n-3 polyunsaturated fatty acids (EPA/DHA) supplementation, such as fish oil or krill.	Hand grip strength
Heloisa C Santo André, 2023 [36]	14	1443	Healthy adults of any age, sex or training status, without chronic diseases.	Supplementation of n-3PUFA	Muscle mass, strength and function
Ping-tao Tseng, 2023 [35]	16	1868	Patients with a diagnosis of sarcopenia or high risk of sarcopenia.	N-3 polyunsaturated fatty acids (n-3 PUFAs) supplement	Upper-extremity muscle strength and lower-extremity physical function

ALA, alpha-linolenic acid; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; n-3 PUFAs, n-3 polyunsaturated fatty acids.

Table 2. Characteristics of included RCTs.

First author, year	Sample size	Participants	Intervention	Dose	Duration
Samantha L Logan, 2015 [20]	IG: 12 CG: 12	Healthy women between the ages of 60 and 76	Fish oil	3 g/d	12 weeks
Roma Krzymińska-Siemaszko, 2015 [41]	IG: 15 CG: 10	Older adults aged 60 or older with risk of low muscle mass	n-3 PUFAs	1.3 g/d	12 weeks
Saleh Aa Alkhedhairi, 2022 [19]	IG: 49 CG: 45	Healthy older adults with a body mass index (BMI) below 35 kg/m^2 and aged over 65 years	Krill oil	4 g/d	6 months
Stephen M Cornish, 2018 [45]	IG: 11 CG: 12	Healthy males aged 65 years or older	EPA and DHA	3 g/d	12 weeks
M S Brook, 2021 [44]	IG: 8 CG: 8	Healthy women aged 65 to 75	EPA and DHA	3.68 g/d	6 weeks
Stephen M Cornish, 2009 [43]	IG: 25 CG: 26	Healthy older adults	Flax oil	14 g/d	12 weeks
Mariasole Da Boit, 2017 [42]	IG: 27 CG: 23	Healthy older adults	Fish oil	3 g/d	18 weeks

RCTs, randomized controlled trials; IG, intervention group; CG, control group.

Table 3. Assessment results of AMSTAR 2.

First author, year	AMSTAR 2 items																
	1	2*	3	4*	5	6	7*	8	9*	10	11*	12	13*	14	15*	16	Confidence
Stephen M Cornish, 2022 [40]	Y	N	N	PY	Y	Y	N	Y	Y	N	Y	Y	Y	Y	Y	Y	Critically low
Felipe Mendes Delpino, 2021 [34]	Y	Y	N	Y	Y	Y	N	Y	Y	N	Y	Y	Y	Y	Y	Y	Low
Wen-jun Ma, 2021 [39]	Y	N	N	PY	N	Y	N	Y	Y	N	Y	Y	Y	Y	Y	Y	Critically low
Ya-Hui Huang, 2020 [38]	Y	N	N	PY	N	N	N	N	Y	N	Y	N	N	N	Y	Y	Critically low
Maha Timraz, 2023 [37]	Y	Y	N	PY	Y	Y	N	Y	Y	N	Y	Y	Y	Y	Y	Y	Low
Heloisa C Santo André, 2023 [36]	Y	Y	N	PY	Y	Y	N	Y	Y	N	Y	Y	Y	Y	Y	Y	Low
Ping-tao Tseng, 2023 [35]	Y	Y	N	PY	Y	Y	Y	PY	Y	N	Y	N	N	Y	Y	Y	Low

AMSTAR 2, A Measurement Tool to Assess Systematic Reviews 2; Y, Yes; PY, Partial yes; N, No; *, Critical item.

Six reviews assessed the effects of n-3 PUFAs intake on muscle strength. Four of these reviews suggested a beneficial effect of n-3 PUFAs supplementation on improving muscle strength; two were rated as moderate-quality evidence, and two as low-quality. Stephen M. Cornish et al. [40] reported that supplementation with n-3 PUFAs alone was associated with improvements in lower-limb strength and modest improvements in upper-limb strength. Similarly, Ping-tao Tseng et al. [35] reported an association between high-dose n-3 PUFAs supplementation and enhanced upper-limb muscle strength. Wen-jun Ma et al. [39] demonstrated an improvement in handgrip strength among healthy participants receiving n-3 PUFAs supplementation. In addition, Heloisa C. Santo André et al. [36] found that n-3 PUFAs supplementation produced a marginally significant positive effect on individual muscle strength. However, a quantitative synthesis was not performed for muscle strength outcomes due to substantial heterogeneity in outcome assessment methods across studies (e.g., handgrip strength, upper- and lower-limb strength measures), which precluded meaningful data pooling and necessitated a qualitative synthesis. Across these studies, the reported effect sizes generally indicated small to moderate improvements, although the confidence intervals varied considerably [35,36,39,40].

Five reviews examined the relationship between n-3 PUFAs supplementation and lower-limb muscle function, with two indicating that n-3 PUFAs significantly improved functional mobility. The evidence quality of these two findings was rated as very low and moderate, respectively. Ya-Hui Huang et al. [38] found that participants receiving n-3 PUFAs supplementation exhibited a 0.3-second reduction in the timed up-and-go test compared with control groups, along with shorter completion times in other mobility assessments, indicating improved functional performance. Consistent with these findings, Ping-tao Tseng et al. [35] demonstrated that high-dose n-3 PUFAs supplementation was associated with improved lower-limb physical function. Detailed extraction of outcome data is presented in Table 4 (Ref. [35,36,37,38,39,40]).

To summarize, findings from the majority of included reviews were directionally consistent, indicating that n-3 PUFAs supplementation may confer potential benefits for muscle strength and functional performance among older adults. The evidence map summarizing these associations is shown in Fig. 2. In this figure, bubble size represents the sample size of each study, bubble color denotes different outcome categories, the horizontal axis reflects the direction of reported effects (e.g., beneficial, probably beneficial, no effect), and the vertical axis represents the methodological quality of the included reviews as assessed by AMSTAR 2. As shown in the figure, most studies were clustered in the “beneficial” or “probably beneficial” categories; however, the majority of these were rated as low or critically low methodological quality. This pattern suggests that, although the direction of evidence appears favorable, the overall strength and reliability of the supporting evidence remain limited.

The effect of n-3 PUFAs supplementation on muscle mass was evaluated using data from seven RCTs, comprising a total of 283 participants [19,20,41,42,43,44,45]. The random-effects model meta-analysis results, as shown in Fig. 3, indicated that, compared with the control group, n-3 PUFA supplementation significantly improved skeletal muscle mass in older adults (SMD: 0.263; 95% CI: 0.028 to 0.498; $p = 0.028$).

4. Discussion

This study integrated evidence from seven published meta-analyses and an updated quantitative synthesis of seven RCTs to provide a comprehensive evaluation of the effects of n-3 PUFAs supplementation on muscle-related outcomes in older adults. The major findings suggest that n-3 PUFAs, when administered as a major intervention, are associated with favorable effects on muscle strength and selected domains of muscle function, particularly lower-limb functional mobility. Based on the most recent meta-analysis, a significant improvement in muscle mass was also observed. Although the methodological quality of the included reviews was generally low to critically low and the certainty of evidence ranged from moderate to very low, the direction of effects was largely consistent. By integrating evidence across multiple levels and supplementing existing meta-analytic findings with reanalysis of primary RCTs, the

Table 4. Extracted data from reviews examining interventions involving supplementation with n-3 PUFAs alone.

First author	Outcomes	Included studies	Sample size	95% CI	*p*-value	Heterogeneity	GRADE confidence in evidence
Wen-jun Ma [39]	Fat mass (kg)	4	IG: 109 CG: 77	[−2.20, 0.87]	$p = 0.396$	$I^2 = 87\%$	Moderate
Ya-Hui Huang [38]	Grip strength (kg)	3	IG: 59 CG: 45	[−0.64, 1.69]	$p = 0.370$	$I^2 = 85\%$	Very low
Wen-jun Ma [39]	Grip strength (kg)	3	IG: 332 CG: 307	[0.27, 2.08]	$p = 0.011$	$I^2 = 53\%$	Moderate
Maha Timraz [37]	Grip strength (kg)	5	IG: 280 CG: 208	[−0.05, 1.27]	$p = 0.070$	$I^2 = 90\%$	Low
Heloisa C Santo André [36]	Strength (kg)	11	IG: 644 CG: 627	[0.004, 0.240]	$p = 0.040$	$I^2 \approx 0\%$	Low
Stephen M Cornish [40]	Lower body strength (kg)	3	IG: 104 CG: 85	[0.39, 1.02]	$p < 0.001$	$I^2 = 0\%$	Moderate
Stephen M Cornish [40]	Upper body strength (kg)	4	IG: 1013 CG: 946	[0, 0.23]	$p = 0.050$	$I^2 = 77\%$	Low
Ping-Tao Tseng [35]	Upper body strength (kg)	16	1868	[0.03, 3.33]	-	-	Low
Heloisa C Santo André [36]	Function	7	IG: 614 CG: 568	[−0.09, 0.15]	$p = 0.580$	$I^2 \approx 0\%$	Low
Ping-Tao Tseng [35]	Lower-extremity physical function	16	1868	[0.16, 1.30]	-	-	Moderate
Stephen M Cornish [40]	Walking speed (m/s)	4	IG: 1005 CG: 947	[−0.11, 0.13]	$p = 0.840$	$I^2 = 60\%$	Low
Wen-jun Ma [39]	Walking speed (m/s)	7	IG: 486 CG: 415	[−0.03, 0.01]	$p = 0.172$	$I^2 = 0\%$	Low
Ya-Hui Huang [38]	Walking speed (m/s)	5	IG: 136 CG: 171	[−0.05, 1.67]	$p = 0.060$	$I^2 = 88\%$	Very low
Wen-jun Ma [39]	Timed Up and Go test (s)	5	IG: 110 CG: 84	[−0.55, 0.004]	$p = 0.093$	$I^2 = 85\%$	Moderate
Ya-Hui Huang [38]	Timed Up and Go test(s)	4	IG: 104 CG: 71	[−0.43, −0.17]	$p < 0.001$	$I^2 = 37\%$	Very low
Ya-Hui Huang [38]	One-repetition maximum leg strength (kg)	3	IG: 82 CG: 64	[−0.93, 0.62]	$p = 0.700$	$I^2 = 69\%$	Very low

IG, intervention group; CG, control group.

present review provides quantitative insight into the potential role of n-3 PUFAs in promoting muscle health in aging populations.

Previous studies have suggested that daily intake of at least 2 grams of fish oil–derived n-3 PUFAs could enhance muscle protein synthesis and contribute to increases in muscle mass in both physically untrained and trained older adults [46]. Consistently, a meta-analysis has indicated that doses exceeding 2 g/day are associated with favorable changes in muscle mass [38]. Several biological mechanisms have been proposed to explain how n-3 PUFAs promote muscle synthesis. One proposed mechanism involves the enhancement of amino acid and insulin-stimulated muscle protein synthesis following n-3 PUFAs supplementation [47,48]. In addition, n-3 PUFAs supplementation may attenuate muscle protein breakdown through activation of the mTORC1–p70S6K1 signaling cascade, thereby promoting an anabolic environment within skeletal muscle tissue [49]. Given that muscle mass is regulated by the dynamic balance between protein synthesis and breakdown, enhancement of anabolic signaling and suppression of catabolic processes may together contribute to muscle mass accretion. Consistent with these mechanistic insights, the findings of the present umbrella review and updated meta-analysis demon-

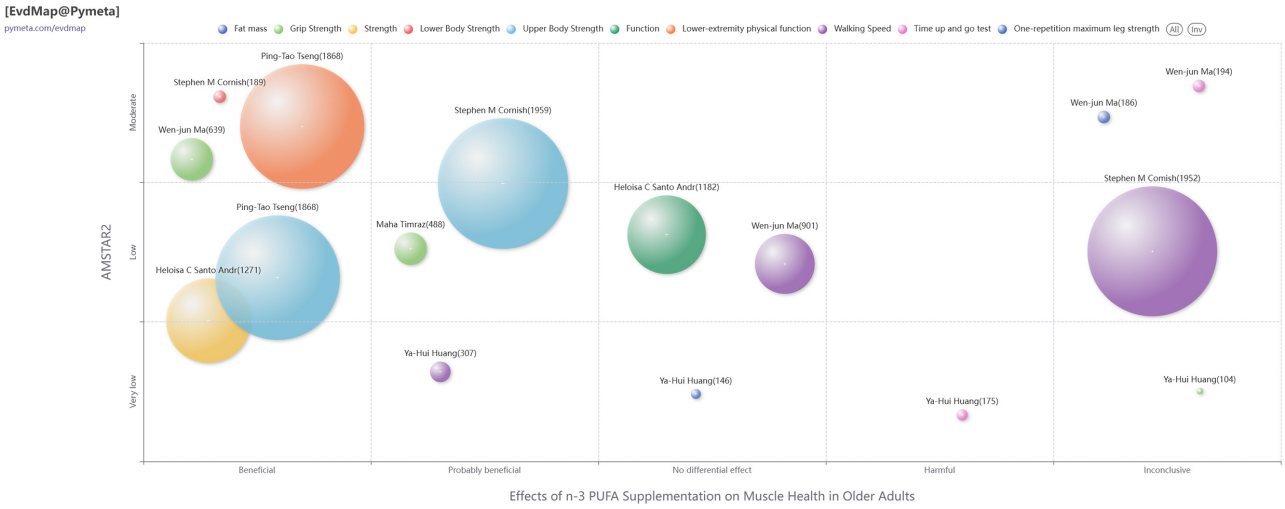

Fig. 2. Evidence map of reviews with meta-analyses. Figure created with Pymeta.

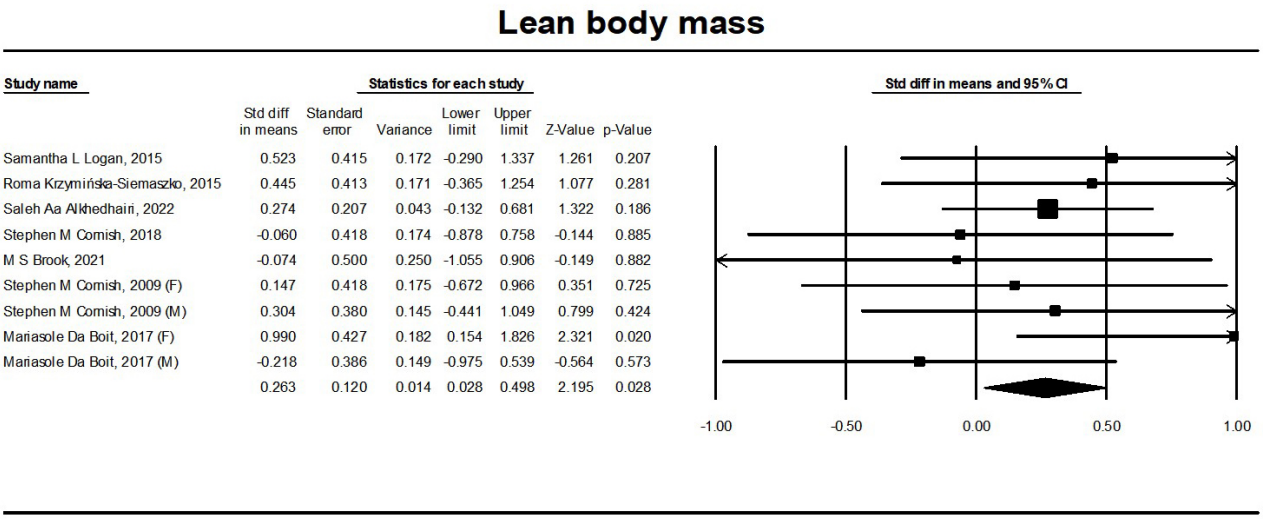

Fig. 3. Pooled analysis of the effects of n-3 PUFAs Supplementation on lean body mass in healthy older adults. Figure created with Comprehensive Meta-Analysis (CMA) software.

strated a positive effect of n-3 PUFAs supplementation on skeletal muscle mass in older adults. However, the magnitude of this effect should be interpreted cautiously, given the limited number of available RCTs and variability in intervention duration, dosage, and formulation across studies. Furthermore, differences in baseline n-3 PUFAs status among participants may have influenced the responsiveness to supplementation, potentially reflecting a ceiling effect in individuals with higher baseline n-3 levels derive less additional benefit than those with lower levels. Such variability may partly explain the heterogeneity and modest magnitude of effects observed across studies. Future research should therefore prioritize large-scale, long-term, and methodologically rigorous RCTs to further clarify dose-response relationships and to identify population most likely to benefit from n-3 PUFAs supplementation.

With respect to muscle strength, the present findings indicate that n-3 PUFAs supplementation is associated with improvements in muscle strength compared with placebo, which is largely consistent with previous studies [17,50]. The anabolic effects of n-3 PUFAs, characterized by simultaneous enhancement of muscle protein synthesis and suppression of protein breakdown, have been proposed as key biological mechanisms underlying these strength gains. In addition, n-3 PUFAs may improve neuromuscular function and muscle membrane fluidity, thereby enhancing contractile efficiency, which could further contribute to improvements in muscle strength [49,50,51]. Nevertheless, conflicting evidence has also been reported. For example, Yves Rolland et al. [52] demonstrated that daily low-dose n-3 PUFAs supplementation had no significant effect on muscle strength in older adults over three years. Such discrepancies may be explained by differences in supplementation

dose, intervention duration, and baseline participant characteristics, including age, physical condition, and nutritional status. Overall, current evidence suggests that beneficial effects on muscle strength may depend on adequate dosing and sufficient intervention duration.

Notably, the effects of n-3 PUFAs on lower-extremity physical function warrant particular attention in this context. Given that age-related decline disproportionately affects lower-limb muscle strength and function [53], improvements in lower-extremity performance are of substantial clinical relevance, as they are closely associated with mobility, independence, fall prevention, and overall quality of life in aging populations. Improvements in functional outcomes may therefore represent more meaningful clinical benefits than changes in muscle mass alone. Therefore, the observed benefits in lower-extremity function suggest that n-3 PUFAs supplementation may exert more robust and clinically perceptible effects on functional outcomes, supporting its potential role as a nutritional strategy for preventing or delaying functional decline in older adults.

Overall, this study systematically evaluated and synthesized the currently available evidence, reanalyzed the effects of n-3 PUFAs supplementation on muscle mass, and highlighted the role of n-3 PUFAs in muscle health, offering valuable insights for clinical practice and future research. Although some of the observed effects reached statistical significance, their magnitude was generally small, and their clinical relevance remains uncertain, highlighting the need for future studies to determine whether these changes correspond to clinically improvements.

Several limitations inherent to the included meta-analyses should be acknowledged. First, the methodological quality of the reviews, as assessed by AMSTAR 2, was predominantly rated as low to critically low, reflecting substantial weaknesses in study design and reporting. Common deficiencies included the absence of preregistered protocols and insufficiently detailed search strategies, both of which increase susceptibility to selective reporting bias. Additionally, some studies failed to adequately address the risk of bias in the original trials or investigate the sources of heterogeneity among studies, thereby undermining the reliability of the evidence. Moreover, subgroup analyses could not be consistently conducted because several pooled outcomes were derived from previously published meta-analyses, and a limited number of primary trials were available for certain outcomes. Potential sources of heterogeneity, including dosage, intervention duration, and participant characteristics, should be further explored in future studies. Second, the overall quality of evidence was predominantly moderate to low. Imprecision was the primary reason for downgrading, driven by wide confidence intervals and, in some cases, nonsignificant pooled estimates.

Moreover, the majority of the included meta-analyses did not restrict the source of n-3 PUFAs when selecting the original RCTs, making it difficult to conduct a detailed discussion distinguishing the effects of marine-derived versus plant-derived n-3 PUFAs. Given that the majority of RCTs included in this review investigated marine-derived n-3 PUFAs, the observed beneficial effects are likely to be primarily driven by EPA/DHA-based interventions. However, due to the limited number of studies on plant-based ALA, a direct comparison between different sources could not be performed.

In addition, the inclusion criteria for the umbrella review and the updated meta-analysis differed. While the reanalysis of RCTs excluded studies combining n-3 PUFAs with exercise or other interventions, several meta-analyses included such combined approaches. This inconsistency may have contributed to discrepancies in findings and may confound the effects of n-3 PUFAs. Furthermore, a high degree of overlap among primary studies was identified, indicating substantial redundancy within the evidence base. This overlap may have inflated the apparent volume of evidence and weakened the robustness of the conclusions. In light of these limitations, the conclusion of this umbrella review should be interpreted with caution. While the accumulated evidence supports a potential role for n-3 PUFAs supplementation as one component of a comprehensive strategy to preserve muscle strength and function in older adults, confirmation through further high-quality, methodologically robust RCTs remains essential. Future research should aim to standardize intervention protocols, clearly distinguish between marine-derived and plant-derived n-3 PUFAs, to improve the precision and clarity of findings.

5. Conclusion

This review synthesized evidence from seven meta-analyses and seven RCTs that investigated the effects of n-3 PUFAs supplementation as a major intervention on muscle-related outcomes in healthy older adults. Current evidence suggests that n-3 PUFAs supplementation may exert beneficial effects on muscle mass, strength and function. Notably, as the majority of included RCTs primarily involved marine-derived n-3 PUFAs (EPA/DHA), these findings are more likely to reflect the effects of EPA/DHA-based interventions. Although the methodological quality of the systematic reviews and the overall certainty of the evidence are limited, future studies with larger sample sizes and higher quality may enhance the robustness of these findings. Because different meta-analyses repeatedly included the same original RCTs, the beneficial effects of n-3 PUFAs may have been overestimated, which could undermine the reliability of the conclusions. This umbrella review provides preliminary supportive evidence for the potential role of n-3 PUFAs, particularly marine-derived PUFAs, in promoting muscle health.

Author Contributions

YS and SY conceptualized and designed the study. YS, SY, JY and YZ conducted the investigation. YS, SY,

and TW performed the formal analysis and data curation. YS, TW, and CZ drafted the manuscript. GS and PF contributed to the critical revision of the manuscript for important intellectual content. All authors contributed to the methodology. All authors contributed to the critical revision of the manuscript for important intellectual content. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agree to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

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Conflicts of 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. Peng Feng and Yajie Zhou are employees of Nanjing Zhongke Pharmaceutical Co. However, the company had no role in the handling or conduct of the study. The authors had full access to all data in the study and take full responsibility for the integrity of the data and the accuracy of the data analysis.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/IJVNR49111.

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