

Evidence-Based Nutritional Interventions for Sarcopenia: A Systematic Review of Randomized Controlled Trials

Putu Prabhawati Dwikrisna¹, Ni Made DwiAsti Lestari²

^{1,2}Department of Clinical Nutrition, RSUD Bali Mandara
E-Mail: prabhaputu@gmail.com

Background: Sarcopenia is a progressive condition characterized by decreased skeletal muscle mass, strength, and function, which impacts the quality of life of the elderly. Nutritional intervention is one potential approach in sarcopenia management, but its effectiveness still shows variable results. **Objective:** To assess the effectiveness of various nutritional interventions on muscle mass, muscle strength, and physical function in individuals with sarcopenia or at risk of developing it. **Methods:** A systematic review was conducted according to the PRISMA 2020 guidelines. A comprehensive literature search was conducted through PubMed/MEDLINE, Science Direct, and Google Scholar databases from inception to January 2025. Inclusion criteria included randomized controlled trials (RCTs), quasi-experimental, or cohort studies evaluating nutritional interventions in populations ≥ 50 years with sarcopenia. Risk of bias was assessed using Cochrane RoB 2 and ROBINS-I. Analysis was conducted narratively and stratified by intervention type. **Results:** A total of 15 studies with a total of 4,319 participants met the inclusion criteria. The majority of studies (73.3%) used a double-blind RCT design, with intervention durations ranging from 8 weeks to 3 years. Supplementation with leucine-enriched protein and vitamin D consistently significantly increased appendicular lean mass (0.17 kg; $P=0.045$). Omega-3 fatty acids were shown to be effective in increasing skeletal muscle mass, muscle strength, and vastus lateralis thickness by up to 3.5%. The combination of nutrition and exercise provided the most optimal results, with significant improvements in grip strength, muscle mass, and physical function. Most interventions were well tolerated without serious side effects. **Conclusion:** Nutritional interventions, particularly protein with leucine, vitamin D, and omega-3, effectively improved sarcopenia parameters. A combined approach with exercise provided the best results in sarcopenia management.

Keywords: sarcopenia, nutritional intervention, protein supplementation

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Corresponding Author:

Putu Prabhawati Dwikrisna
Department of Clinical Nutrition, Bali Mandara Regional Hospital
prabhaputu@gmail.com

1. Introduction

Sarcopenia is a major problem facing the aging population worldwide. The European Working Group on Sarcopenia in Older People defines sarcopenia as a syndrome characterized by a progressive decline in muscle mass, strength, and physical performance, which can lead to various health complications in older adults. This condition has been clinically classified as a disease with the code M62.84 in the International Classification of Diseases, Clinical Modification (ICD-10-CM) since 2016, highlighting the importance of medical attention and research on this phenomenon. To date, advances in diagnostic methods and the discovery of effective therapies are still needed to address sarcopenia (Bauer et al., 2015).

Globally, the prevalence of sarcopenia continues to increase with increasing life expectancy and the aging population. It is estimated that approximately 20% of the world's elderly experience sarcopenia, in both

Caucasian and Asian populations, with differences in incidence influenced by genetic factors, lifestyle, and nutritional intake. In Indonesia, a longitudinal study showed that one in five elderly people have sarcopenia, a warning for public health systems to prioritize early preventive interventions (Jyväkorpi et al., 2021).

Sarcopenia not only causes reduced muscle strength but also impacts mobility, increased risk of falls, and dependence in daily activities. Consequently, this declines the quality of life of older adults and increases the socioeconomic burden. Therefore, nutrition-based interventions and physical activity are crucial in sarcopenia prevention and management strategies (Kang et al., 2023).

Various studies have shown that nutrition, particularly protein, vitamin D, and branched-chain amino acids (BCAAs), plays a crucial role in maintaining muscle mass and preventing sarcopenia. Appropriate supplementation can increase muscle protein synthesis and slow the muscle degradation process that occurs with aging. This has become the basis for the development of nutritional therapies focused on maintaining muscle function (Moriwaki et al., 2019).

One of the largest studies examining the effects of nutrition on sarcopenia is the PROVIDE Study conducted by Bauer and colleagues. This study used vitamin D and leucine-fortified whey protein supplementation in older adults, and the results showed significant improvements in muscle strength, physical function, and muscle mass in the intervention group compared to the placebo group (Bauer et al., 2015). These findings reinforce the importance of the combination of high-quality protein and vitamin D in maintaining muscle health in older adults.

A similar intervention was also conducted in the SPRINTT Project, a multi-component study in several European countries. This study emphasized that a strategy combining nutrition, physical activity, and health education can slow the progression of sarcopenia and increase the independence of older adults in the community. The program successfully demonstrated that a comprehensive intervention yielded more optimal results than a single strategy (Jyväkorpi et al., 2021).

In addition to protein and vitamin D, the role of omega-3 fatty acids from fish oil has also attracted attention in recent research. Xu and colleagues found that supplementation with n-3 polyunsaturated fatty acids significantly improved body composition, muscle strength, and physical performance in older adults participating in a regular exercise program (Xu et al., 2022). The combination of nutrition and exercise has been shown to have a synergistic effect on muscle health.

A study by Kang et al. (2023) strengthens this evidence by showing that daily consumption of a vitamin D-fortified protein mix can increase muscle mass, especially in individuals with low serum 25(OH)D levels. This suggests that vitamin D status plays a crucial role in the effectiveness of protein supplementation on increasing muscle mass, making monitoring vitamin D levels an important initial step in managing sarcopenia.

Another study by Moriwaki et al. (2019) showed that hospitalized patients with gait impairment who were given BCAA-rich supplements experienced improved activity-of-daily-living abilities and increased muscle mass. These results indicate that BCAAs can stimulate muscle protein synthesis, particularly in catabolic conditions caused by immobilization.

However, not all nutritional combinations show positive results. Research by Van Vliet et al. (2020) found that the combination of vitamin D with conjugated linoleic acids had no significant effect on muscle protein synthesis in older adults. This indicates that not all forms of supplementation can be used as a therapeutic guide, and further research is needed to determine the most effective formulations (Van Vliet et al., 2020).

Recent research by Khoonin et al. (2023) demonstrated that a complete nutritional beverage enriched with eicosapentaenoic acid (EPA) and BCAAs can improve muscle strength in elderly individuals with low protein

intake. This intervention is considered promising, especially for the elderly population who have limited access to regular high-protein foods (Khoonin et al., 2023).

Efforts to prevent sarcopenia must also be accompanied by a targeted physical exercise program. A study by Wang et al. (2025) showed that a consistent combination of optimal nutrition and resistance training can prevent and even reverse sarcopenia in older adults. This program confirms that a multifactorial strategy involving nutrition, exercise, and health education is the most effective approach (Wang et al., 2025).

Overall, these studies demonstrate that sarcopenia is not an unpreventable condition, but requires a comprehensive, evidence-based approach. A combination of high-quality protein intake, vitamin D, omega-3 fatty acids, and regular physical exercise can maintain muscle mass and improve quality of life for older adults. Therefore, the development of scientifically based nutritional therapies and the integration of public health programs that support active lifestyles are key to combating sarcopenia in the future.

2. Method

This study protocol was developed based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines to ensure transparency and reproducibility of results. Prior to implementation, the protocol was designed in detail, including inclusion and exclusion criteria, search strategy, study selection methods, data extraction, and risk of bias assessment. Only randomized controlled trials (RCTs) in adults ≥ 50 years old with a diagnosis or risk of sarcopenia were included, with interventions consisting of nutritional supplementation such as protein, amino acids, vitamin D, omega-3 fatty acids, and probiotics. Observational studies, case reports, and studies with a duration of less than four weeks were excluded to maintain the strength of the evidence.

A comprehensive literature search was conducted through PubMed/MEDLINE, Embase, Cochrane CENTRAL, and Web of Science for publications from 2015–January 2025. The search strategy used a combination of medical subject headings (MeSH) and free terms such as “sarcopenia,” “muscle strength,” and “nutritional intervention.” Additional searches were also conducted through grey literature and reference reviews of related articles to broaden coverage and avoid publication bias. The study selection process was conducted by two independent reviewers through screening of titles, abstracts, and full-text, with joint discussion or involvement of a third reviewer to resolve disagreements.

Approved data were extracted using a standardized form covering study characteristics, participants, interventions, and primary outcomes. Analysis was conducted narratively, grouped by intervention type and outcome measures, without meta-analysis due to inter-study heterogeneity. Risk of bias was assessed using the Cochrane RoB 2 for RCTs and ROBINS-I for non-randomized studies, while the level of certainty of evidence was evaluated using the GRADE system. This systematic approach is expected to yield accurate and reliable conclusions regarding the effectiveness of nutritional interventions in the prevention and treatment of sarcopenia in the elderly.

3. Results

Study Characteristics

Systematic review This study analyzed 15 studies that met the inclusion criteria (Figure and Table 1), with a total population of 4,319 participants. The majority of studies used a double-blind randomized controlled trial (RCT) design ($n=11$, 73.33%), followed by single-blind RCTs ($n=3$, 20%), and unblind RCTs ($n=1$, 6.67%). Sample sizes ranged from 16 to 1,517 participants, with a median of 80 participants per study. Intervention duration ranged from 8 weeks to 3 years, with most studies lasting 12–24 weeks.

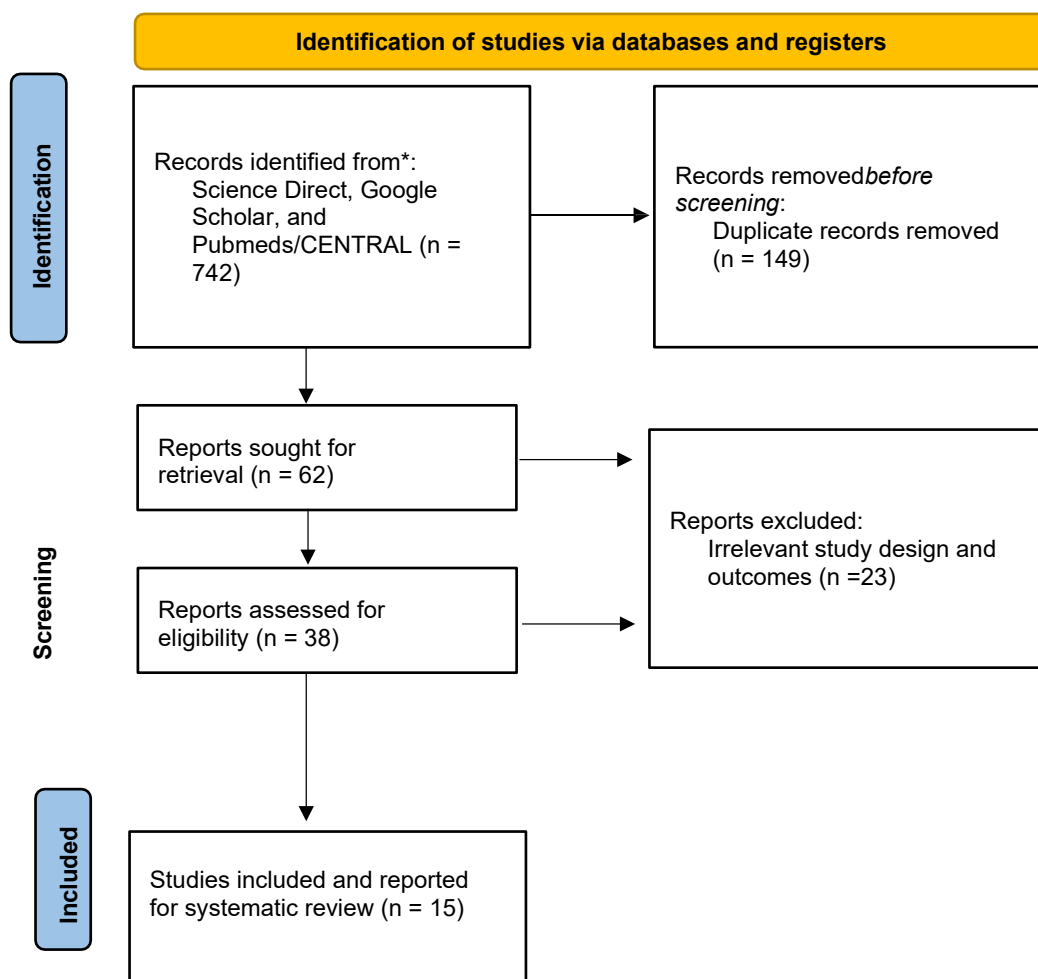


Figure 1. PRISMA Flowchart

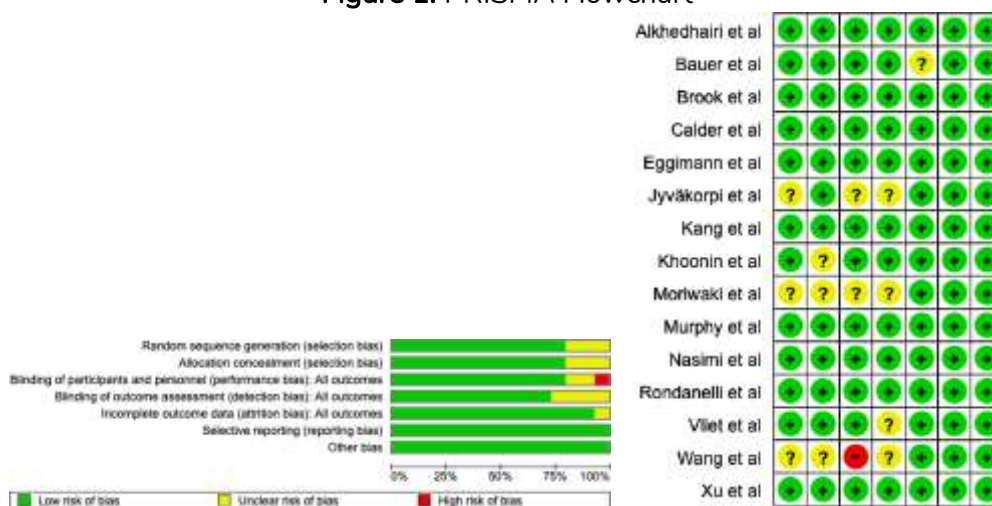


Figure 2. Study Risk of Bias Assessment

Risk of bias assessment using the Cochrane Risk of Bias tool 2 (RoB 2) showed variability in methodological quality among included studies (Figure 2). Most studies showed a low risk of bias for random sequence generation (80%) and selective reporting (100%), indicating adequate randomization and complete outcome reporting. However, there was a significant difference in the blinding of participants and personnel

domain, with 6.67% of studies showing a high risk of bias and 13.3% having an unclear risk, primarily in studies with unblinded or single-blind designs.

Table 1. Characteristics of Studies Included in the Systematic Review

No	Author, year	Study Design	Sample (I/C)	Intervention	Duration	Results
1	Bauer et al, 2015(4)	RCT DB	380 (184/196)	<i>Vitamin D + leucine-enriched whey protein</i>	13 weeks	↑ Appendicular muscle mass (+0.17 kg, p=0.045); ↑ chair-stand test performance
2	Jyväkörpi et al, 2021(5)	RCT SB	1517	Multi-component nutrition	NR	Appropriate intervention allows flexibility for a heterogeneous vulnerable population
3	Kang et al, 2023(6)	RCT DB	120 (60/60)	<i>Protein mix + vitamin D (2x/day)</i>	NR	↑ Muscle mass in participants with vitamin D deficiency (<20 ng/mL)
4	Moriwaki et al, 2019(7)	RCT unblind	80 (42/38)	BCAA-enriched jellies	NR	↑ Skeletal muscle mass and weight body vs control
5	Vliet et al, 2020(8)	RCT DB PC	32 (24/8)	Vitamin D (2000 IU) ± CLA (4000 mg)	NR	No effect on protein synthesis in muscle vs placebo
6	Khoonin et al, 2023(9)	RCT SB PC	84 (63/21)	EPA (2.2g) ± BCAA (5g) fortified drink	NR	↑ Right arm muscle mass and hand grip strength with EPA+BCAA
7	Wang et al, 2025(10)	RCT SB	46	Combination of nutrition + physical exercise intervention	NR	↑ Handgrip strength, muscle mass upper limbs, motor performance
8	Xu et al, 2022(11)	RCT DB PC	187 (97/90)	<i>Fish oil n-3PUFA (4g/day)</i>	NR	↑ Skeletal muscle mass and muscle strength parameters
9	Brook et al, 2021(12)	RCT DB PC	16 (8/8)	n-3 PUFA during <i>resistance training</i>	NR	Improvement resistance training increases muscle mass
10	Rondanelli et al, 2022(13)	RCT DB	50 (22/28)	<i>Leucine + omega-3 + L. paracase</i> PS23	2 months	↑ Appendicular lean mass, handgrip strength, SPPB; ↓ visceral fat
11	Alkhedhairi et al, 2022(14)	RCT DB	93 (49/45)	Krill oil supplementation	6 months	↑ Knee extensor torque (+9.3%), grip strength (+10.9%), muscle thickness (+3.5%)
12	Nasimi et al, 2021(15)	RCT DB	66 (33/33)	<i>Fortified yogurt</i>	NR	↑ Handgrip strength, gait speed, vitamin D, IGF-1; ↓ malondialdehyde
13	Calder et al, 2017(16)	RCT DB	46 (22/23)	High dose omega-3 + vitamin D + protein	NR	Tolerable well; ↑ BP lipid profile, fatigue due to physical

No	Author, year	Study Design	Sample (I/C)	Intervention	Duration	Results
14	Murphy et al, 2022(17)	RCT DB	107 (74/33)	LEU-PRO ± n-3 supplementation	NR	exercise. Inter-individual variability is minimal, most results are below the MCID.
15	Eggimann et al, 2024(18)	RCT DB	1495	Vitamin D (2000 IU) and/or omega-3 (1g)	3 years	There was no significant improvement in the incidence of ALMI or sarcopenia

Information:

- I/C: Intervention/Control group
- RCT: Randomized Controlled Trial; DB: Double Blind; PC: Placebo Controlled; SB: *Single Blind*
- ONS: Oral Nutritional Supplement; SMM: Skeletal Muscle Mass; SPPB: Short Physical Performance Battery
- BCAA: Branched-Chain Amino Acids; EPA: Eicosapentaenoic Acid; CLA: Conjugated Linoleic Acid
- ALMI: Appendicular Lean Mass Index; MCID: Minimal Clinically Important Difference
- ↑: Increase/Improvement; ↓: Decrease/Reduction; NR: Not Reported
- BP: Blood Pressure; IGF-1: Insulin-like Growth Factor-1

Types of Nutrition Interventions

The nutritional interventions studied can be categorized into several main groups. Protein and amino acid supplementation was the most frequently studied intervention (n=7, 36.4%), including leucine- and vitamin D-enriched whey protein, branched-chain amino acids (BCAAs), and protein mixes with various compositions. Omega-3 fatty acid supplementation was the second most common category (n=6, 27.3%), including fish oil, krill oil, and eicosapentaenoic acid (EPA). Combination interventions of vitamin D with various other nutrients were found in 5 studies (22.7%), while probiotic supplementation and other fortified products were each studied in 3 studies (13.6%).

Effectiveness of Intervention on Muscle Mass

Most studies have demonstrated a positive effect of nutritional interventions on increasing muscle mass. Supplementation with leucine-enriched protein and vitamin D consistently demonstrated a significant increase in appendicular lean mass. Bauer et al. (2015) reported an increase in appendicular lean mass of 0.17 kg (95% CI: 0.004–0.338; P = .045) after 13 weeks of intervention. Similarly, Kang et al. (2023) found that supplementation with a protein mix with vitamin D significantly increased lean muscle mass, particularly in participants with vitamin D deficiency (serum 25(OH)D <20 ng/mL).

Omega-3 fatty acid supplementation has also shown promising results. Xu et al. (2022) reported that fish oil-derived n-3 PUFA supplementation (4 g/day) for a specific period effectively improved skeletal muscle parameters, including muscle mass and strength. Alkhedhairi et al. (2022) found that 6 months of krill oil supplementation increased vastus lateralis muscle thickness by 3.5% compared to placebo. However, several studies, such as Vliet et al. (2020), found no independent or combined effect of vitamin D and conjugated linoleic acids on muscle protein synthesis.

Effectiveness on Muscle Strength and Function

Nutritional interventions have shown varying effects on muscle strength and function. Improvements in handgrip strength have been reported in most studies measuring this parameter. Bauer et al. (2015) found a significant improvement in the chair-stand test with a between-group difference of -1.01 seconds (95% CI: -1.77 to -0.19; $P = .018$). Alkhedhairi et al. (2022) reported a 9.3% increase in knee extensor maximal torque and 10.9% increase in grip strength after krill oil supplementation.

Rondanelli et al. (2022) in a study of a novel food containing leucine, omega-3 fatty acids, and *Lactobacillus paracasei* PS23 reported significant improvements in handgrip strength, Tinetti score, and SPPB, accompanied by significant reductions in visceral fat. A study of a combination of nutrition and physical exercise by Wang et al. (2025) showed significant improvements in handgrip strength, upper extremity muscle mass, total muscle strength, and somatic motor performance.

Effectiveness of Combination Interventions

Several studies have explored the effectiveness of combined nutritional interventions with exercise or multiple nutrient supplements. Wang et al. (2025) reported that a combination of nutritional interventions and exercise proved feasible and effective in increasing muscle mass and strength in all three stages of sarcopenia. However, a long-term study by Eggimann et al. (2024) in the DO-HEALTH trial with 1,495 participants over 3 years showed that daily supplementation with vitamin D (2000 IU), omega-3 (1 g), or a simple home exercise program either individually or in combination did not significantly improve ALMI or reduce the incidence of sarcopenia compared to controls in healthy, physically active older adults.

Safety and Tolerability

Most nutritional interventions were reported to be well tolerated with minimal adverse effects. Calder et al. (2017) reported that targeted medical nutrition containing high-dose omega-3s, vitamin D, and high-quality protein was well tolerated and improved blood pressure and lipid profiles. There were no reports of serious adverse events associated with the nutritional interventions in the studies analyzed. However, Murphy et al. (2022) noted interindividual variability in response to protein and fish oil supplementation, with most outcomes falling below the minimal clinically important difference.

Heterogeneity of Results

There is considerable heterogeneity in results across studies, likely due to differences in intervention type and dose, study duration, population characteristics, and outcome measurement methods. Some studies show significant effects on certain parameters but not others. For example, Khoonin et al. (2023) found significant improvements in right arm muscle mass and handgrip strength after administration of a complete nutrition drink enriched with EPA and BCAAs, but effects on other parameters were not consistently reported across studies.

Discussion

This systematic review analyzed 15 studies with a total of 4,319 participants and showed that nutritional interventions have a positive effect on sarcopenia management, particularly in improving muscle mass, strength, and physical function. These findings align with the European Society of Clinical Nutrition and Metabolism (ESPEN) recommendations, which emphasize that older adults' diets should provide a minimum of 1.0–1.5 g of protein per kilogram of body weight per day, with 25–30 g of protein distributed per meal to maintain muscle health.

The review results showed that supplementation with leucine- and vitamin D-enriched protein consistently significantly increased appendicular lean mass. This is supported by evidence that leucine plays a key role in

muscle protein synthesis through activation of the mTOR pathway. Furthermore, the effectiveness of omega-3 fatty acid supplementation has been confirmed in various studies showing increases in overall muscle mass and strength, although small sample sizes and heterogeneity between studies limit the generalizability of the results. The mechanisms of action of omega-3 fatty acids involve anti-inflammatory effects, increased skeletal muscle insulin sensitivity, and optimization of muscle protein synthesis. Several studies also highlight that EPA and DHA provide specific benefits to skeletal muscle, particularly in the context of physical activity, obesity, and cachexia.

Furthermore, a network meta-analysis showed that a combination of vitamin D supplementation, protein, and exercise significantly increased handgrip strength and showed a positive trend toward increased muscle mass. These findings are consistent with other systematic reviews that confirmed that the combination of vitamin D and protein can increase muscle strength in patients with sarcopenia, although it does not always improve muscle mass or overall performance. Combination interventions, particularly those combining nutrition with exercise, have been shown to be more effective than either intervention alone. This reinforces the concept that exercise both resistance training and aerobics balanced with adequate protein and energy intake is a key strategy in the prevention and management of sarcopenia.

However, the long-term results of the DO-HEALTH trial in this review showed no significant improvement in appendicular lean mass index (ALMI) or reduction in sarcopenia incidence after three years of vitamin D, omega-3, or exercise intervention in healthy, physically active older adults. These findings underscore the importance of selecting the appropriate target population and intervention duration. The literature also suggests that protein supplementation alone tends to only slow muscle loss, so a multimodal approach integrating nutrition and exercise is necessary to achieve optimal results. A recent meta-analysis also confirmed that the combination of regular exercise and nutritional supplementation is the most effective strategy for preventing and managing sarcopenia in older adults.

4. Conclusion

Nutritional interventions have been shown to play a crucial role in the prevention and management of sarcopenia, particularly through supplementation with leucine-enriched protein, vitamin D, and omega-3 fatty acids. These three components have consistently demonstrated effectiveness in increasing muscle mass, strength, and physical function in individuals with sarcopenia and those at risk. Combining nutritional interventions with physical exercise, both resistance training and aerobic exercise, provides more optimal results than either intervention alone, highlighting the importance of a multimodal approach to maintaining muscle health in older adults.

However, differences in study design, intervention duration, and population characteristics contribute to variations in results between studies. Therefore, further research with more consistent methodology, larger sample sizes, and longer-term follow-up is needed to strengthen the evidence and develop more comprehensive clinical guidelines. It is recommended that future sarcopenia management strategies focus not only on nutritional supplementation but also include nutrition education, increased physical activity, and regular monitoring of muscle health status to achieve sustained effectiveness.

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