International Research Journal of Human Resource and Social Sciences
ISSN(O): (2349-4085) ISSN(P): (2394-4218)
Impact Factor 7.924 Volume 13, Issue 03, March 2026
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Effectiveness of Multi-domain Interventions on Improving Intrinsic Capacity in Older Adults: A Systematic Review

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Abstract

Background and Objective: This systematic review evaluates the effectiveness of multi-domain interventions in enhancing the intrinsic capacity (IC) of older adults aged 65 and above.

Methods: Following the PRISMA 2020 guidelines, a systematic search was conducted across six electronic databases for randomized controlled trials published between 2020 and 2025. Nine studies involving 4,723 participants were included.

Results: The findings indicate that multi-domain interventions significantly improved overall IC for older adults. Physical activity (aerobic and resistance exercise) enhanced locomotor capacity, including muscle strength, balance, and gait. Cognitive training improved executive function and attention. Nutritional supplementation (e.g., high protein, Omega-3), combined with exercise, effectively increased muscle mass and reduced fall risks. Additionally, health education and empowerment strategies bolstered health literacy and exercise motivation.

Conclusion: Intervention efficacy depends on participant adherence, program complexity, and baseline IC scores. Future research should standardize IC assessment tools and integrate community-based empowerment strategies to ensure sustainable outcomes.

Keywords: intrinsic capacity; multi-domain intervention; older adults; systematic review

Introduction

With the rapid acceleration of population aging, maintaining the function and health of older adults has become a global challenge (Sum et al., 2022). Centered on the concept of "healthy aging," the World Health Organization (WHO, 2017) introduced the framework of intrinsic capacity (IC), which encompasses six domains: cognition, locomotion, sensory (vision and hearing), nutrition (vitality), and psychological. These capacities influence functional ability and are closely related to interactions with the environment (WHO, 2017). To promote healthy aging, the WHO proposed the Integrated Care for Older People (ICOPE) framework. This person-centered care model integrates medical, community, and social services to assist healthcare professionals in the early identification of high-risk older adults and the provision of appropriate medical and social support (WHO, 2024).

Research indicates that multi-domain interventions contribute to maintaining and enhancing intrinsic capacity, as well as preventing and delaying disability (Hsueh et al., 2024; Sum et al., 2022; Zhou & Ma, 2022). However, assessment standards for ICOPE vary across countries, and most studies do not provide comprehensive composite scores for intrinsic capacity. Furthermore, the diverse and complex nature of these interventions poses challenges for clinical application. Therefore, this study employs a systematic review to explore the effectiveness of multi-domain care interventions in enhancing the intrinsic capacity of older adults and to analyze the impacts of various intervention strategies, aiming to provide a reference for care practices in preventing and delaying disability.

Methods

The literature search and screening process of this study were conducted in accordance with the Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines.

1. Search strategy

A comprehensive search was performed across electronic databases including PubMed, Embase, Medline, JBI, Cochrane Library, and Airiti Library, covering the period from January 1, 2020, to April 20, 2025. The search strategy was developed based on the PICO (Population, Intervention, Comparison, Outcome) framework using both Chinese and English keywords:

(1) Population: "Aged"[Mesh] OR "Aged, 80 and over"[Mesh] OR "older people"[tw] OR elderly[tw] OR "older adult".
(2) Intervention: "Interdisciplinary Communication"[Mesh] OR "Multifactorial Intervention*"[tw] OR "combined intervention*"[tw] OR "Multiple Component Intervention"[tw] OR "Long-Term Care"[Mesh] OR method* OR "Diet Therapy"[Mesh] OR "Diet"[Mesh] OR "High-Intensity Interval Training"[Mesh] OR "Resistance Training"[Mesh] OR "Exercise"[Mesh] OR "Psychosocial Intervention"[Mesh] OR "Cognitive Behavioral Therapy"[Mesh] OR "Cognitive training"[tw] OR "Hearing Aids"[Mesh] OR "hearing therapy*"[tw] OR "Vision rehabilitation"[tw] OR "Visual Training".
(3) Outcome: "Activities of Daily Living"[Mesh] OR "intrinsic capacity"[tiab] OR "IC"[tiab].
(4) Study Type: Randomized controlled trial.

2. Inclusion and Exclusion Criteria

2.1. The inclusion criteria for this review were:

(1) Participants aged 65 years or older without severe cognitive impairment, severe depressive symptoms, or severe disability.
(2) Interventions in the experimental group defined as multi-domain interventions, including exercise, cognitive training, nutritional support, emotional support, or a combination of at least two of these measures. Control groups that received no intervention, maintained a regular lifestyle, used a placebo, received general care, or received only a single-domain intervention (e.g., exercise, cognition, nutrition, emotion, or health education alone).
(3) Outcomes presented as scales or quantitative data to demonstrate the effectiveness of the intervention.
(4) Randomized controlled trials (RCTs) published in Chinese or English.

2.2. The exclusion criteria included:

(1) Participants were children or young adults.
(2) Non-randomized studies, pre-test/post-test studies without a control group, case studies, observational or cross-sectional studies, qualitative research, and conference abstracts.
(3) Articles where the full text was unavailable.

3. Study selection and data extraction

A single reviewer performed literature screening and data extraction. Titles and abstracts were first screened, followed by a full-text review to confirm eligibility. Relevant data, including participant characteristics, intervention components, and outcome measures, were then systematically extracted into a standardized form.

4. *Quality assessment*

The quality of the included randomized controlled trials was evaluated using the Cochrane Risk of Bias 2.0 tool (RoB 2). This tool assesses five domains of potential systematic bias: the randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result (Sterne et al., 2019). Each domain is categorized as "Low risk," "Some concerns," or "High risk," which are then synthesized to determine an overall risk of bias for each study. The evaluation findings are visualized in a risk of bias summary (Figure 2) and a risk of bias graph (Figure 3).

Result

1. *Literature search*

A total of 569 records were initially identified through six electronic databases. After removing 2 duplicate records, 567 records underwent initial screening. In the initial screening, 558 records were excluded for not meeting inclusion criteria: 235 non-randomized controlled trials, 191 single-domain interventions, and 132 participants under age 65. Ultimately, 9 randomized controlled trials met all inclusion criteria and were included in this systematic review (Figure 1).

2. *Study characteristics*

2.1. Research features

The included study designs encompassed multicenter (Giudici et al., 2020; van Dongen et al., 2020; Yıldırım Ayaz et al., 2024), cluster-randomized (Chen et al., 2020; Liang et al., 2024), single-blind (Huang et al., 2021; Sipilä et al., 2021), double-blind (Nilsson et al., 2020), and two-arm trials (Grönstedt et al., 2020). Multi-domain interventions were categorized into four primary components: physical activity, cognitive training, nutritional supplementation, and health education. These components are systematically detailed in Table 1. The following sections evaluate the effectiveness of these multidimensional care strategies on the IC of older adults.

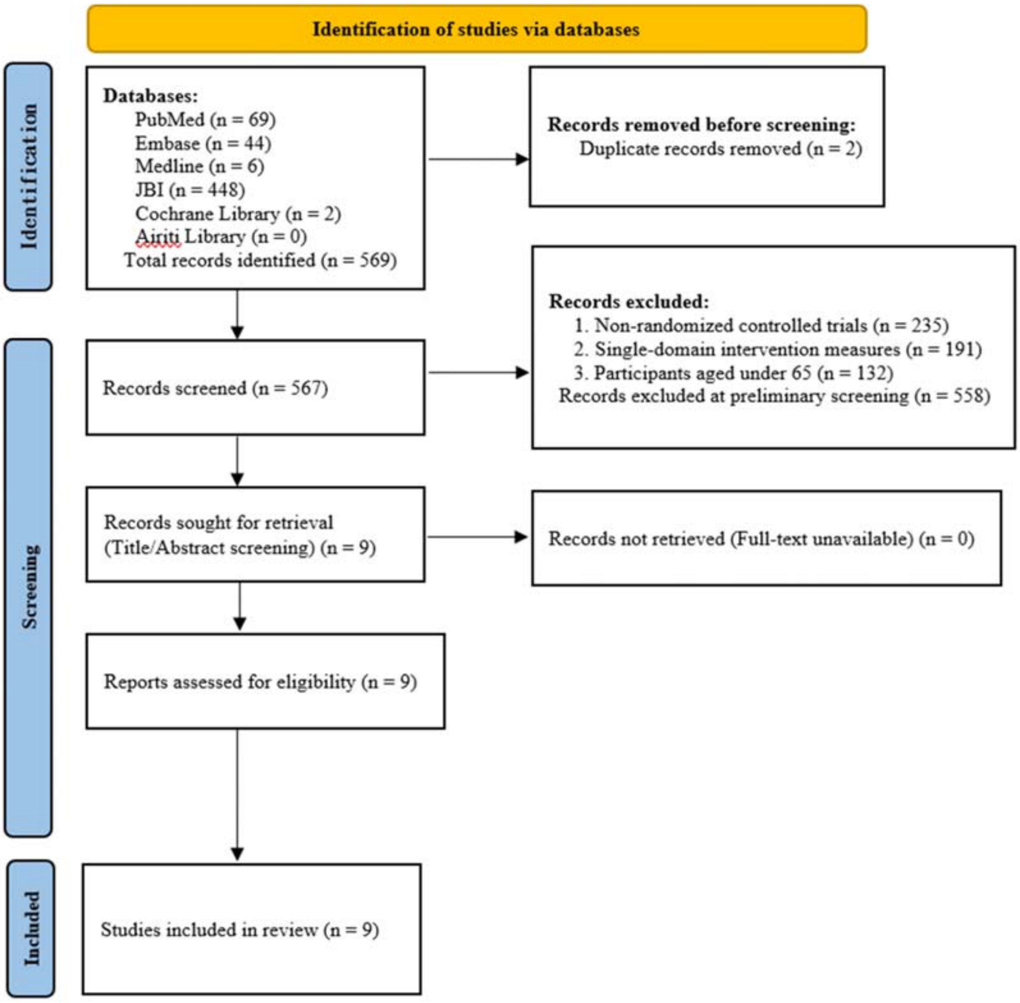
2.2. Multi-domain Intervention Components and Outcomes

The design of multi-domain care interventions is informed by the ICOPE assessment framework. Current RCTs primarily focus on physical activity, cognitive training, nutritional supplementation, and health education. These components are implemented through various combinations to enhance intervention efficacy and clinical applicability.

2.2.1. Physical Activity Training

Physical activity is identified as the most significant intervention for enhancing intrinsic capacity. Evidence from the reviewed literature consistently demonstrates its effectiveness in improving physical function, specifically regarding muscle strength (Chen et al., 2020; Liang et al., 2024; Sipilä et al., 2021), lower limb function (Grönstedt et al., 2020; Huang et al., 2021; Nilsson et al., 2020; van Dongen et al., 2020; Yıldırım Ayaz et al., 2024), balance and gait performance (Chen et al., 2020; Giudici et al., 2020; Liang et al., 2024; van Dongen et al., 2020). Furthermore, targeted training has been noted to enhance cardiorespiratory fitness, including endurance and overall cardiovascular health (Chen et al., 2020; Huang et al., 2021; Sipilä et al., 2021; Yıldırım Ayaz et al., 2024).

Figure 1. Prisma flow diagram of literature search.



The research also highlights important synergistic effects, where multi-domain models that combine exercise with nutritional supplementation prove more effective than solitary exercise in enhancing mobility and maintaining muscle mass (Sipilä et al., 2021; van Dongen et al., 2020). The integration of physical activity with other domains varied across studies, three studies combined exercise with nutritional support (Grönstedt et al., 2020; Nilsson et al., 2020; van Dongen et al., 2020); one studies integrated cognitive training (Sipilä et al., 2021); one study included educational components (Liang et al., 2024); and two studies implemented comprehensive interventions encompassing all four domains: physical activity, nutrition, cognition, and education (Chen et al., 2020; Giudici et al., 2020).

While physical activity is foundational, some studies suggest that isolated training may offer limited benefits for overall intrinsic capacity, advocating for a multi-modal approach to achieve comprehensive health gains (Huang et al., 2021; Yıldırım Ayaz et al., 2024). Crucially, the success of these interventions is heavily dictated by adherence and participation levels, emphasizing the vital importance of fostering regular activity habits and long-term engagement to sustainably improve the intrinsic capacity of older adults (Chen et al., 2020; Grönstedt et al., 2020; Huang et al., 2021; Sipilä et al., 2021; van Dongen et al., 2020).This underscores the vital importance of maintaining regular activity habits and long-term engagement to effectively sustain and improve the intrinsic capacity of older adults.

2.2.2. Cognitive Function Training

Cognitive function training within the reviewed studies encompasses both digital and traditional modalities, including the use of specialized cognitive training software (Sipilä et al., 2021) and paper-based assessments focused on memory, reasoning, and attention (Chen et al., 2020; Giudici et al., 2020; Liang et al., 2024). Specifically, Sipilä et al. (2021) utilized the "iPASS" web-based cognitive training program to target executive functions (EFs) in older adults, focusing on inhibitory control, shifting, and updating abilities within working memory. Their findings indicated that while cognitive training effectively improved inhibitory control, its integration with physical activity did not yield a statistically significant increase in overall intrinsic capacity scores (Sipilä et al., 2021).

While most research supports the benefits of cognitive training for enhancing intrinsic capacity in the elderly, some conflicting evidence exists. For instance, Giudici et al. (2020) found that neither solitary Omega-3 supplementation nor a comprehensive multi-domain intervention—combining physical activity, cognitive training, and nutritional support—demonstrated a significant effect in preventing the decline of intrinsic capacity.

2.2.3. Nutritional Supplementation

Among the studies focusing on nutritional supplementation, three utilized protein supplementation (Grönstedt et al., 2020; Nilsson et al., 2020; van Dongen et al., 2020), two employed Omega-3 fatty acid supplementation (Giudici et al., 2020; Nilsson et al., 2020), and one incorporated vitamin and mineral supplementation (Nilsson et al., 2020). These interventions were predominantly implemented through nutritional education and behavioral strategies, such as individualized guidance from dietitians (van Dongen et al., 2020) or group-based classes designed to enhance health literacy and self-management skills among older adults (Giudici et al., 2020). Additionally, some researchers utilized tools like dietary logs to monitor adherence, ensuring participants followed their prescribed plans while allowing for timely adjustments based on individual progress (Nilsson et al., 2020; van Dongen et al., 2020).

Following the nutritional interventions, most participants demonstrated improvements in body composition, physical function, and cognitive performance. Specifically, increases in muscle mass and reductions in body fat percentage highlighted the positive impact of high-protein supplementation (Grönstedt et al., 2020; Nilsson et al., 2020; van Dongen et al., 2020). These changes were accompanied by enhanced muscle strength, improved exercise performance and endurance (Grönstedt et al., 2020; Nilsson et al., 2020; van Dongen et al., 2020), and better balance and gait stability, which collectively contributed to a lower risk of falls (Nilsson et al., 2020; van Dongen et al., 2020). However, Giudici et al. (2020) found that while Omega-3 fatty acid supplementation benefited metabolic health, its effectiveness in preventing or reversing cognitive decline and intrinsic capacity deterioration was not significant. Consequently, future research is encouraged to investigate more robust interventions, such as intensive dietary control, to better support the long-term health of older populations.

2.2.4. Health Education

Health education interventions within the reviewed studies primarily focus on the prevention and management of chronic conditions and common geriatric syndromes, including diabetes, hypertension, cardiovascular diseases, dementia, sarcopenia, and osteoporosis (Chen et al., 2020;

Giudici et al., 2020; Huang et al., 2021; Liang et al., 2024; Yıldırım Ayaz et al., 2024). Furthermore, researchers utilized individualized counseling and group-based lectures to provide guidance on healthy eating and nutritional intake, emphasizing the vital role of regular exercise habits and a healthy lifestyle (Chen et al., 2020; Yıldırım Ayaz et al., 2024). Notably, two studies integrated health education with nutritional support (Huang et al., 2021) and physical activity training (Yıldırım Ayaz et al., 2024) to enhance health literacy, self-care capabilities, and intervention adherence among older adults.

Beyond structured educational sessions, Chen et al. (2020) incorporated competitive activities and community engagement strategies rooted in the concept of empowerment. This approach aimed to strengthen participants' intrinsic motivation for autonomous exercise, ultimately leading to significant improvements in walking speed, physical performance, cognitive function, and memory.

2.3. Intrinsic Capacity Assessment Tools

According to the six domains of IC proposed by WHO, commonly utilized assessment tools include the Short Physical Performance Battery (SPPB), Chair-to-Stand Test (CST/STS), Mini-Mental State Examination (MMSE), Mini Nutritional Assessment-Short Form (MNA-SF), and the Geriatric Depression Scale (GDS-15). The following sections detail the assessment tools identified in the included literature across four primary IC domains: locomotion, cognitive function, nutrition and vitality, and psychological.

2.3.1. Locomotion

The Short Physical Performance Battery (SPPB) was utilized in four studies to assess overall lower-extremity function (Giudici et al., 2020; Nilsson et al., 2020; Sipilä et al., 2021; van Dongen et al., 2020); the Chair-to-Stand Test (CST) was adopted by four separate research teams to measure lower-body strength and endurance (Grönstedt et al., 2020; Huang et al., 2021; Nilsson et al., 2020; Yıldırım Ayaz et al., 2024); the Timed Up and Go (TUG) test appeared in two studies as a measure of dynamic balance and mobility (van Dongen et al., 2020; Yıldırım Ayaz et al., 2024), while gait speed remained the most frequent metric, featured in five different publications (Chen et al., 2020; Huang et al., 2021; Liang et al., 2024; Sipilä et al., 2021; van Dongen et al., 2020).

Several studies used specific tools to assess distinct functional abilities: the IADL scale for complex tasks (Chen et al., 2020), Step-Up Test for muscle power (Nilsson et al., 2020), Shuttle Walking Test for aerobic capacity (Yıldırım Ayaz et al., 2024), and One-Leg Standing Test for static balance (Huang et al., 2021). Yıldırım Ayaz et al. (2024) also evaluated muscle flexibility and cardiorespiratory health. Results showed significant improvements in the intervention group’s Senior Fitness Test, the Cardiovascular Health Study (CHS) frailty scale, and metabolic equivalent (MET) scores, with combined aerobic and resistance training yielding the greatest increases in total IC scores; aerobic exercise alone had no significant effect.

2.3.2. Cognitive function

The Mini-Mental State Examination (MMSE) was utilized in three studies (Giudici et al., 2020; Huang et al., 2021; Yıldırım Ayaz et al., 2024), and the Montreal Cognitive Assessment (MoCA) was also adopted by three studies (Chen et al., 2020; Huang et al., 2021; Liang et al., 2024). Huang et al. (2021) employed a comprehensive battery, including the Wechsler Memory Scale-Revised and WAIS-III; however, the combined exercise group showed no significant IC improvement, likely due to increased task complexity and divided training time. Additionally, Sipilä et al. (2021) utilized the Stroop test and the Consortium to Establish a Registry for Alzheimer's Disease

(CERAD) neuropsychological battery, reporting significant gains in executive function despite no marked improvements in 6-minute walk distance or dual-task performance.

2.3.3. Nutrition and Vitality Assessment

The Mini Nutritional Assessment-Short Form (MNA-SF) was utilized in four studies (Chen et al., 2020; Grönstedt et al., 2020; Liang et al., 2024; Yıldırım Ayaz et al., 2024) , and the Handgrip Strength Test (HGS) was adopted by seven studies (Chen et al., 2020; Giudici et al., 2020; Huang et al., 2021; Liang et al., 2024; Nilsson et al., 2020; Sipilä et al., 2021; Yıldırım Ayaz et al., 2024) , making it the most widely utilized metric for assessing nutritional status and vitality. Beyond these standard measures, Nilsson et al. (2020) conducted a detailed evaluation of body composition and strength—including BMI, waist-to-hip ratio, appendicular skeletal muscle mass, and total lean mass—finding that high-protein supplementation paired with home-based resistance training led to superior muscle mass and strength gains compared to the control group. Furthermore, van Dongen et al. (2020) emphasized that adherence to protein-rich diets and exercise programs is a critical determinant of intervention success, significantly influencing both nutritional recovery and muscle performance in older adults.

2.3.4. Psychological

The Geriatric Depression Scale (GDS-15) was utilized in five studies (Chen et al., 2020; Giudici et al., 2020; Grönstedt et al., 2020; Huang et al., 2021; Yıldırım Ayaz et al., 2024), and the Geriatric Depression Scale-5 Item Version (GDS-5) was adopted by Liang et al. (2024) to evaluate the psychological status of older adults following multi-domain care interventions. Furthermore, Huang et al. (2021) utilized the Generalized Anxiety Disorder 7 (GAD-7) alongside the GDS-15 to assess levels of anxiety and stress. Their findings indicated that while multi-domain care interventions effectively increased total IC scores, the intervention effects showed a tendency to diminish after the program concluded.

Discussion

This systematic review, conducted in accordance with PRISMA guidelines, analyzed nine RCTs from Europe, Asia, and the Americas. Quality assessment using the Cochrane RoB 2 tool identified five studies as "low risk," two as having "some concerns," and two as "high risk," with primary sources of bias arising from deviations from intended interventions, missing outcome data, and measurement bias. Despite these variations, the overall quality of the included literature ranged from moderate to high. High-risk studies were retained to provide a comprehensive evidence base for multi-domain care interventions.

The findings indicate that multi-domain interventions effectively enhance the IC of older adults. Specifically, physical activity training yielded consistent positive effects on muscle strength, gait, balance, and cardiorespiratory endurance (Chen et al., 2020; Grönstedt et al., 2020; Yıldırım Ayaz et al., 2024). Cognitive training improved executive function and attention (Huang et al., 2021; Sipilä et al., 2021), while nutritional support enhanced muscle mass and indirectly strengthened physical function (Nilsson et al., 2020; van Dongen et al., 2020). Crucially, five studies identified participant adherence as a key determinant of success (Chen et al., 2020; Grönstedt et al., 2020; Nilsson et al., 2020; Sipilä et al., 2021; van Dongen et al., 2020), suggesting that empowerment strategies and health education are vital for sustaining behavior change (Liang et al., 2024). However, excessive complexity or insufficient training duration may diminish efficacy (Huang et al., 2021), and effects may fade post-intervention without continued monitoring and support (Grönstedt et al., 2020; Huang et al., 2021; van Dongen et al., 2020).

Limitations

Several limitations warrant consideration. First, there was significant heterogeneity across studies regarding the content, frequency, and duration of interventions. Furthermore, the assessment tools for IC were inconsistent, with most studies evaluating only specific domains, which complicates the comparison and interpretation of results. Second, the factors influencing adherence, such as motivation and social support, were not explored in depth. Finally, the lack of long-term follow-up in most studies limits our understanding of the sustained impact of these interventions on intrinsic capacity.

Conclusion

This review underscores the effectiveness of multi-domain care interventions in improving the intrinsic capacity of older adults, particularly through integrated physical, cognitive, and nutritional strategies. To enhance clinical applicability, future research should prioritize the standardization of assessment tools and incorporate strategies to boost motivation and community resource integration. Developing more practical and sustainable care models will be essential for maintaining the long-term health and independence of the aging population.

Figure 2. Risk of bias summary for included studies.

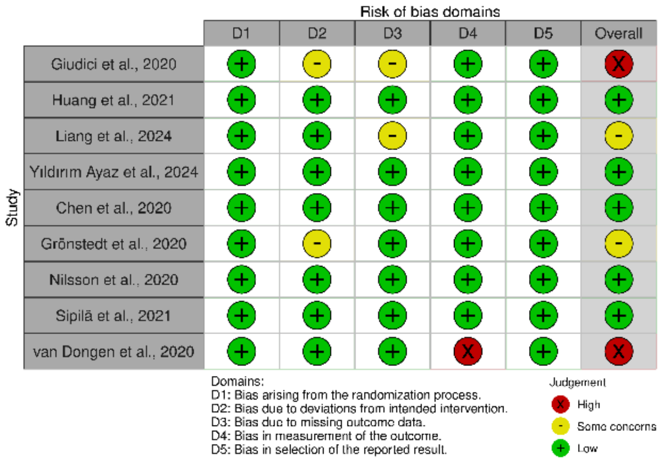


Figure 3. Risk of bias graph for included studies.

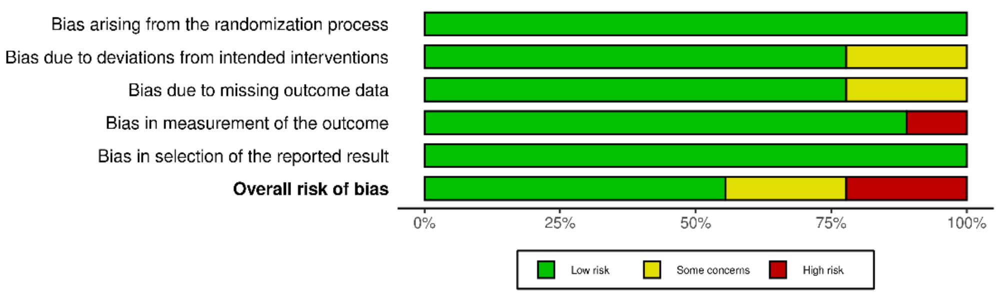


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Table 1. Data Extraction and Summary of Findings for Included Studies

Author, Year, Country	Study Design / Follow-up	Multi-domain Intervention Components	Key Findings	Assessment Tools
Giudici et al., 2020, France	Multicenter, placebo-controlled RCT / 3 years	Lifestyle intervention: ● Cognitive: 60 min/week reasoning & memory training. ● Physical: 45 min/week exercise advice & demos. ● Nutrition: 15 min/week counseling. ● Follow-up: Monthly 1-hr sessions from month 3; 2-hr sessions at 12 & 24 months. ● Supplement: Omega-3 (800mg DHA, 225mg EPA daily).	● Omega-3 alone: (–) ● Omega-3 + Multi-domain: (–)	**Cognition:** MMSE **Locomotion:** SPPB **Psychological:** GDS-15 **Vitality:** HGS
Huang et al., 2021, Japan	Single-blind RCT / 1 year (26-week intervention + 26-week follow-up)	**Intervention Group (supervised, heart rate monitored):** ● Group exercise: 60 min, twice/week (warm-up, core, cool-down). ● AT group: 10-15 min stepping/walking. ● RT group: Elastic band & bodyweight resistance training. ● Combined (AT+RT): 20 min each of AT and RT. **Control Group:** Two health promotion lectures.	● AT and RT groups improved at 26 weeks (↑), but effects diminished by 52 weeks after stopping . ● Combined group: (–), likely due to task complexity and divided time.	**Cognition:** WMS-R, CFT/LFT, MMSE, WAIS-III, TMT-A/B **Locomotion:** OLS test, 5-m gait speed, 5-repetition STS **Psychological:** GDS-15, GAD-7 **Vitality:** HGS
Liang et al., 2024, Taiwan	Cluster RCT / 1 year	**Intervention Group:** Standard Intervention (12 weeks): ● Physical: 45 min strength/balance/flexibility. ● Cognitive: 1-hr reasoning/memory training. ● Nutrition: 15 min advice. ● Health Education: Lectures on healthy aging, dementia, sarcopenia. **Control Group:** Monthly health education phone calls.	● Significant prevention of decline in cognition and locomotion after intervention (↑) . ● Efficacy was higher in those with higher baseline IC scores.	**Cognition:** MoCA **Locomotion:** 6-m gait speed **Psychological:** GDS-5 **Vitality:** HGS, MNA-SF **Sensory:** Vision/Hearing self-report

Author, Year, Country	Study Design / Follow-up	Multi-domain Intervention Components	Key Findings	Assessment Tools
Yıldırım Ayaz et al., 2024, Turkey	Multicenter RCT / 3 months (12 weeks)	Green Exercise (Outdoor): ● All: 2-hr health education. ● **Intervention groups:** Weekly 50-min outdoor session + twice-weekly autonomous training. ● **AT group:** 40-min moderate walking. ● **AT+RT group:** 20-min walk + 20-min high/low intensity resistance training.	● Intervention groups: improved muscle strength, mobility, cognition, and psychological status (↑) . ● AT+RT group: significantly improved vitality, nutrition, and total IC scores (↑).	**Cognition:** MMSE **Locomotion:** 8ft-TUG, SWT, SFT, CST **Psychological:** GDS-15 **Vitality:** HGS, MNA
Grönstedt et al., 2020, Sweden	Two-arm RCT / 3 months (12 weeks)	**Intervention Group:** ● Exercise: Sit-to-Stand (STS) 4 times/day, 7 days/week integrated into daily life. ● Nutrition: High-protein oral supplement (2 bottles/day, 36g protein total). **Control Group:** Regular care.	● Intervention group: Improved body composition, nutrition, and weight (↑) . ● No significant change in overall physical locomotion (–).	**Locomotion:** 30s-CST **Psychological:** GDS-15 **Vitality:** MNA-SF, weight, TLM
Chen et al., 2020, Taiwan	Cluster RCT / 3 years (Phase 1: 12m; Phase 2: 10m + 2m empowerment)	1. **Effectiveness Study:** **Control Group:** Routine health education via telephone every 3 months. **Intervention Group:** 12-month program (16 two-hour sessions) including: 45 min physical training (aerobic, resistance, balance, flexibility); 1 hr cognitive training (memory, reasoning, attention); 15 min nutrition/chronic disease education. Quarterly physician-led lectures. 2. **Empowerment Study:** **Control Group:** Same protocol as the Effectiveness intervention group. **Intervention Group:** 10-month curriculum followed by 2 months of motivation-boosting activities, including competitions, community engagement, and use of pedometers/manuals.	1. **Effectiveness Study:** Intervention group showed significant improvements in depression, nutrition, and cognitive attention (↑), with the greatest gains in participants aged 75+. 2. **Empowerment Study:** Enhanced group demonstrated superior locomotor capacity at 6 months (↑) and better cognitive retention/delayed memory at 9 months.	**Cognition:** MoCA **Locomotion:** Gait speed, CHS, MET **Psychological:** GDS-15 **Vitality:** HGS, MNA-SF, IADL

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Nilsson et al., 2020, Canada	Double-blind RCT / 1 year (12-week intervention)	**Intervention group:** ● Supplement: 5-ingredient supplement (Muscle5: Whey/Casein protein, Creatine, Vit D3, Omega-3). ● Home-based Exercise: Resistance bands 3 times/week + walking goal (5,000–10,000 steps). **Control Group:** Daily isocaloric placebo (collagen and sunflower oil, matched with M5 for caloric and nitrogen content) + Home-based Exercise.	● Intervention group: Significant increase in LBM, muscle-to-fat ratio, strength, and mobility (↑). ● Control group: Fat mass increased.	**Vitality:** HGS, 1-RM LP, BMI, LBM, TLM, ASM **Locomotion:** SPPB, 6-m gait speed, CST, SUT
Sipilä et al., 2021, Finland	Single-blind, parallel RCT / 1.25 years (12m intervention)	Intervention lasted 12 months with assessments at 0, 6, and 12 months: **Control Group (Physical Training, PT):** ● Supervised Sessions (2x/week): 45-min walking/balance (Borg RPE 13 – 15) and 1-hr resistance training using pneumatic equipment (progressive intensity based on 6RM) . ● Home Exercise (2 – 3x/week): Elastic band strength and balance training; aim for ≥ 150 min/week of moderate aerobic activity. **Intervention Group (PT + Cognitive Training):** ● Combined Protocol: Same PT frequency/intensity as the control group. ● Computerized CT: 15 – 25 min sessions, 3 – 4x/week using the iPASS web-based program to target Executive Functions (EFs), including inhibition, shifting, and updating.	● Both groups: improved 10-m gait speed (↑). ● Ex+Cog group: significantly greater improvements in Executive Function . ● No significant improvement in 6-min walk or dual-task performance (–).	**Cognition:** Dual-task walk, Stroop, TMT, CERAD **Locomotion:** 10-m gait speed, 6MWT, SPPB **Vitality:** HGS, leg strength

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van Dongen et al., 2020, Netherlands	Multicenter RCT / 2 years (24-week intervention)	24-week intervention (12-week intensive + 12-week voluntary moderate). Assessments at 0, 12, and 24 weeks: **Control Group:** Participants maintained their usual lifestyle (resistance exercise < 2 days/week, < 30 min/session) **Intervention Group (Diet + Exercise):** ● **Intensive Phase (Weeks 1 – 12):** Supported by physiotherapists, dietitians, and coaches. - Resistance Training: 2x/week, 60 min/session (warm-up, leg press/extension, lat pulldown, row, chest press, cool-down). Intensity: Weeks 1 (50% 1RM, 3–4 sets of 15); Weeks 7–12 (75%–80% 1RM, 4 sets of 8–12). - Dietary Intervention: Initial consultation with a goal of 25g protein per meal; provision of dairy or high-protein snacks; 3-day dietary logs at weeks 1 and 6. ● **Moderate Phase (Weeks 13 – 24, Voluntary):** - Exercise: 1–2x/week, adding balance and functional training. - Diet: Five 1.5-hour high-protein cooking/tasting classes and bimonthly educational emails.	● Intensive phase: Locomotion and muscle mass significantly increased (↑) . ● Adherence dropped during moderate phase, and mobility decreased in the control group (↓).	**Locomotion:** SPPB, gait speed, TUG, leg strength **Vitality:** LBM, ALM, weight

Abbreviations: ASM: Appendicular Skeletal Muscle Mass; CHS: Cardiovascular Health Study frailty score; CST/STS: Chair-to-Stand / Sit-to-Stand; GDS-15/5: Geriatric Depression Scale (15 or 5 items); HGS: Handgrip Strength Test; IC: Intrinsic Capacity; LBM/TLM: Total Lean Body Mass / Total Lean Mass; MET: Metabolic Equivalent of Task; MNA-SF: Mini Nutritional Assessment-Short Form; MMSE: Mini-Mental State Examination; MoCA: Montreal Cognitive Assessment; SPPB: Short Physical Performance Battery; TUG: Timed Up and Go Test; 1RM: One-repetition maximum

Note: (–) No significant difference; (↑) Significant increase; (↓) Significant decrease.