Archives of Public Health

SYSTEMATIC REVIEW

Open Access

The effectiveness of multicomponent exercise in older adults with cognitive frailty: a systematic review and meta-analysis

Huanhuan Luo[1,2], Zitian Zheng[3,4], Zhe Yuan[5*], Huixiu Hu[2*] and Chao Sun[1,2*]

Abstract

Background Cognitive frailty, intimately tied to adverse outcomes such as falls, early mortality, and hospitalization, represents a dynamic, reversible process. Multicomponent exercise has emerged as one of the most potent means of mitigating cognitive frailty.

Aims This research seeks to quantitively amalgamate the effects of multicomponent exercise on various domains: cognitive function, frailty status, and other health-related outcomes in cognitively frail older adults.

Methods Our methodology entailed a comprehensive review of literature in databases including PubMed, EMbase, CINAHL, Cochrane Library, Web of Science, Wanfang, Sinomed, VIP, and CNKI from the inception of these databases to December 10, 2023. For our statistical analysis, we utilized RevMan 5.3, Stata 17.0 and R 4.3.2 software. Adherence was maintained to the PRISMA checklist, with the study being registered with PROSPERO (CRD42024499808).

Results Our review encapsulated a total of 2,222 participants and 11 trials. The findings intimate that multicomponent exercise enhances cognitive function [MD = 2.52, $p = 0.03$]), grip strength[SMD = 0.39, $p = 0.008$] and lower limb muscle strength[MD = 4.30, $p < 0.001$], while alleviating frailty[MD = -2.21, $p < 0.001$] and depression [MD = -1.20, $p = 0.001$]. However, cogent evidence is still lacking to endorse the positive effects of multicomponent exercises on both ADL($p = 0.19$) and quality of life($p = 0.16$). Subgroup analyses revealed beneficial effects on cognitive frailty for multicomponent exercise whose type of exercise consisted of aerobic, the duration of which exceeded 120 min per week, and whose form of exercise was group exercise.

Conclusion Multicomponent exercises offer significant improvements in cognitive function, muscle strength, and have the added benefit of reducing frailty and depression in older adults. However, these exercises do not appear to influence activities of daily living and quality of life positively.

Keywords Multicomponent exercise, Cognitive frailty, Meta-analysis, Systematic review

*Correspondence:
Zhe Yuan
18810889552@163.com
Huixiu Hu
18610145247@163.com
Chao Sun
sunchaobjyy@163.com
Full list of author information is available at the end of the article

Text box 1. Contributions to the literature

- Multicomponent exercise improves cognitive function, grip strength, and lower limb muscle strength, while reducing frailty and depression in cognitively frail older adults.
- Group-based multicomponent exercise that includes aerobic components and exceeds 120 min per week shows enhanced benefits for this population.
- Further research is needed to confirm the effects of multicomponent exercise on activities of daily living (ADL) and quality of life for cognitively frail older adults.

Introduction

Cognitive frailty (CF) is a heterogeneous clinical phenomenon first proposed by the International Society of Nutrition and Aging (IANA) and the International Association of Gerontology and Geriatrics (IAGG) [1]. It is characterized by the concurrent presence of both physical frailty and cognitive impairment (CDR = 0.5) [2]. According to a meta-analysis of 24 studies conducted by Qiu et al. [3], the overall prevalence rate of CF is 9%. Notably, the prevalence rate increased by 5% between 2018 and 2020 compared to 2012–2015 [3], highlighting CF as a significant public health concern in the aging global population. Additionally, CF is associated with an increased incidence of adverse outcomes. Numerous systematic reviews and meta-analyses have shown that older adults with CF are 2.22, 3.02, 2.06, and 2.01 times more likely to experience disability [4], falls [5], depression [6], and death [7], respectively, compared to older adults without CF. Furthermore, older adults with CF exhibit a higher susceptibility to dementia than those with only physical frailty or mild cognitive impairment (MCI) [8].

Despite the high incidence of adverse outcomes in elderly individuals with CF, it is a dynamic and reversible condition [9]. Early detection and timely intervention can reduce the incidence or severity of CF [10]. Exercise intervention has been proven to be one of the most effective methods for improving the functional status of elderly individuals with cognitive frailty [11]. Multicomponent exercise (ME) refers to a structured physical activity program that incorporates various types of exercise modalities aimed at improving multiple aspects of physical fitness and functional capacity [12]. It has been widely used to enhance physical function and other aspects of health in the elderly. Evidence suggests that ME may offer superior benefits compared to single-type exercise regimens. For instance, a meta-analysis indicated that ME was more effective than resistance or aerobic training alone in improving cognitive function in Alzheimer's patients [13]. Another meta-analysis demonstrated that ME improved muscle strength, endurance, and balance in frail older adults [14]. However, while these studies showed that ME improved the physical and mental state of patients with either cognitive impairment or physical frailty, they did not specifically focus on individuals with CF, who are at a higher risk of adverse outcomes such as dementia and even death. Furthermore, these studies did not address the heterogeneity of clinical trials or possible publication bias. In short, the effects of multicomponent exercise on cognitively frail older adults are currently unknown.

Given this context, the aim of the present study is to systematically review and meta-analyze randomized controlled trials (RCTs) and non-RCTs of ME in cognitively frail older adults. This study seeks to clarify the effects of ME on cognitive function, frailty status, muscle strength, activities of daily living (ADL), depression, and overall quality of life. Additionally, it aims to provide practical recommendations for community medical personnel on guiding elderly individuals in exercise, thereby reducing the impact or incidence of cognitive frailty and promoting healthy aging. Subgroup analyses will be conducted to demonstrate the influence of different exercise volumes, intensities, and other training variables on outcomes in elderly individuals with CF.

Methods

Protocol and registration

Our study was performed following the PRISMA (Preferred Reporting Items for the Systematic Reviews and Meta-analyses) network statement [15] (Supplementary PRISMA 2020 Checklist). The protocol for this study was registered in the International Prospective Register of Systematic Reviews (PROSPERO). The registration number is CRD42024499808.

Search strategy

A comprehensive systematic literature review was performed using several databases, including PubMed, Excerpta Medica, Cumulative Index to Nursing and Allied Health Literature, Cochrane Library, Web of Science, Wanfang, Sinomed, VIP Database for Chinese Technical Periodicals, and CNKI. The review covered studies published from the inception of these databases to December 10, 2023. Using PubMed as an example, this study developed a search strategy based on the PICO framework, which includes four groups of keywords: P (elderly with cognitive frailty), I (exercise), C (unlimited), and O (unlimited). The keywords used are as follows: aged (including aged, elder*, old, senior*, geriatric*, older, aging), frailty (including frailty syndrome, pre-frail*, frail*), cognitive impairment (including cognitive frailty, cognitive impairment, cognitive decline), and exercise (including exercis*, sport*, movement intervention, motor intervention, movement therapy, physical exercise, training). Additionally, the reference lists of studies retrieved from the databases were manually scrutinized for comprehensiveness. Gray literature was further explored through PROQUEST Thesis & Dissertations on the same day. The full search strategy is delineated in Supplementary Table S1.

Inclusion and exclusion criteria

The systematic review embraced studies published in either English or Chinese that met the following criteria:

(1) Population (P): The study participants were older adults, aged 65 years and above, identified with cognitive frailty.
(2) Intervention (I): The intervention involved was multicomponent exercise, which is a structured physical activity program encompassing at least two components from aerobic, strength/resistance, balance, or flexibility exercises.
(3) Control (C): Any control was deemed acceptable, except those incorporating a physical activity component.
(4) Outcome (O): The study outcomes included at least one of the following: cognitive function, frailty status, grip strength, lower limb muscle strength, daily living activities, depression, and health-related quality of life.
(5) Study Design (S): The studies were either randomized controlled trials (RCTs) or non-RCTs.

Study selection

All citations retrieved from the databases were compiled in Endnote X9. Following the removal of duplicates, two researchers(LH and ZZ) independently screened the titles and abstracts based on the defined inclusion criteria. The process involved careful examination of full texts for potential inclusion, sealing the selection of studies for the review. Any doubts or discrepancies arising during the selection process were resolved through discussion with a third author(HH).

Data extraction

Two authors(LH and ZZ) independently extracted data using Microsoft Excel, with any disagreements settled through discourse with a third author. The extracted data encompassed various aspects, including the study's authors, publication year, country of origin, design of the study, characteristics of participants, sample size, mean age, details of the exercise intervention, control intervention, point of assessment, and outcome measures in relation to cognition, physical functioning, ADL, and depression.

For each chosen outcome, the mean and standard deviation of the pertinent metrics were extracted from all available data sets. In cases where the studies delivered medians and interquartile ranges, an initial assessment was conducted to detect significant skewness. If none was found, these values were transformed to means and standard deviations as per previously reported methods. Standard errors and 95% confidence interval were converted to mean ± standard deviation using the Revman 5.3 software calculator.

Risk of bias assessment

Risk of bias for RCTs and non-RCTs was evaluated independently by two evaluators(LH and ZZ) using the Cochrane Risk of Bias tool [16] and the Risk of Bias in Non-Randomized Studies (ROBINS-I) tool [17], respectively. According to the Cochrane Handbook for the Evaluation of Intervention Systems, RCTs are assessed across seven key dimensions of bias including allocation concealment, incomplete data reporting, blinding, selective reporting, and other ancillary biases. The ROBINS-I tool presents seven domains for bias evaluation: confounding bias, selection bias in participant recruitment, intervention classification bias, bias from intended interventions, bias due to missing data, bias in outcome measures, and bias in selecting reported outcomes. Any arising disagreements were settled through a consultative process involving a third researcher(HH).

Statistical analysis

The meta-analysis was conducted using Review Manager Version 5.3, Stata 17 and R 4.3.2. Means and 95% Confidence Intervals (CI) were computed to establish the pooled effect size for continuous data. For outcomes measured with distinct tools, the Standardized Mean Difference (SMD) with a 95% CI was employed to express the pooled effect size. Following guidelines from the Cochrane Handbook, the SMD is equivalent to the effect size. It's further categorized as mild (<0.2), small (0.20 to 0.49), moderate (0.50 to 0.79), or large (≥ 0.80) [18]. Heterogeneity was examined using the I^2 statistic. If I^2 was greater than 50%, indicating significant heterogeneity, a random-effects model was implemented; otherwise, a fixed-effects model was utilized. Subgroup analyses were controlled for intervention characteristics such as the inclusion of aerobic exercise, weekly exercise duration (≤ 120 min or >120 min), and the form of exercise (group or individual). We also used Stata 17 for meta-regression. Sensitivity analyses were also performed by sequentially excluding each included study to re-compute the pooled effects of the remaining studies. The potential for publication bias was evaluated using Egger's test [19].

Results

Study selection

The search resulted in a total of 2,743 articles, as depicted in Fig. 1. Following the removal of duplicates, the remaining 1,782 articles underwent title and abstract screening. A meticulous review of the full text of 71 articles culminated in the inclusion of 11 articles, nine of which were found suitable for meta-analysis.

Characteristics of included studies

This review comprises seven RCTs [20–26] and four non-RCTs [27–30] published between the years of 2007 and 2023. A collective total of 2,222 subjects participated in these studies, with the average age of subjects ranging from 72.09 to 86.9 years. The studies were distributed internationally with six conducted in China [20, 25–28, 30], two in Spain [21, 24], and one each in the United States [23], Austria [22], and Singapore [29]. Five studies prominently targeted older adults residing in nursing homes, four recruited community-living older adults, and two focused on older adults in hospital settings. The follow-up durations in the included studies varied from 8 weeks to 6 months. Comprehensive details are documented in Table 1.

Characteristics of the interventions

The intervention groups' exercise regimens primarily consisted of strength/resistance and balance training. Endurance/aerobic exercises were incorporated in six studies [23–27, 29], and flexibility exercises were included in five studies [21, 23–25, 30]. The duration of each intervention ranged from 30 to 70 min, with the most common frequency being three times per week over a total duration of 12 weeks. Control interventions typically comprised usual care, health education about a healthy diet, sleep, the importance of regular exercise, and its scientific aspects. Six studies [20–22, 27–29] conducted the intervention exercises in small groups. Typically, the intervention intensity was low to moderate, with exercise intensity gauged using Borg's scale of self-perceived exertion, HRmax, and heart rate. Detailed characteristics are available in Table 2.

Risk of bias in included studies

The risk of bias assessment for the included RCTs and non-RCTs was carried out employing the Cochrane Risk of Bias tool (RoB) and the ROBINS-I Tools, respectively. The RoB assessment revealed that selection bias (allocation concealment), performance bias (blindness of investigators and participants), and detection bias (blinding of outcome assessment) were the primary risk sources in the seven RCTs [20–26]. In the four non-RCTs [27–30],

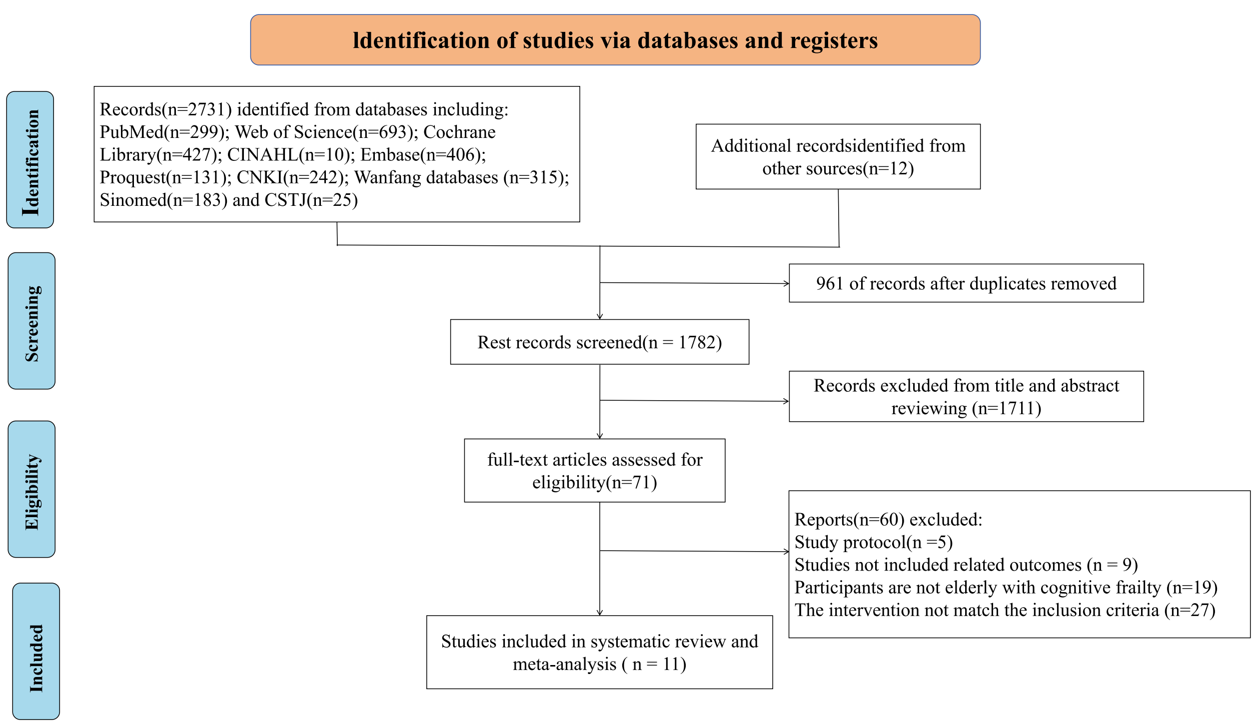

Fig. 1 Flow diagram for searching and selection of the included studies (Up to December 2023)

Table 1 Characteristics of the included studies (Studies from Inception to December 2023)

Trails	Country	Study design	Participants	Number of participants		Age(years)		Interventions		Intervention duration	Each session	Intervention form	Time point	Outcomes
				TG	CG	TG	CT	TG	CT					
Thomas et al., 2007	Austria	RCT	Frail, cognitive impaired long-term care residents over 75 years old	15	15	86.7 ± 6.1	86.9 ± 5.7	Multicomponent exercise(concluding warm up, strength training, balance training and cool down)	No intervention	10 weeks	50 min	Under the instruction of a sports scientist	baseline and the end of the trial (10 weeks later)	①Cognitive function(MMSE score);②Muscle strength(assessed by a physiotherapist); ③BMI; ④Activities of daily living(Barthel-Index, FIM);⑤Mobility(Tinetti score) ⑥Depression(GDS-15)
Irimia et al., 2019	Spain	Block RCT	Frail institutionalized older adults with mild to moderate cognitive impairment over 75 years old	23	29	83.76 ± 8.33	85.17 ± 7.38	Calisthenics exercises and playful callisthenic games (for improving participants' strength, stamina, speed and flexibility)	Crafts, reading comprehension and cognitive stimulation (no programs related to physical exercise)	12 weeks	60 min	Conducted and controlled by health and fitness professionals specializing in physical activity for older adults	baseline and the end of the trial (12 weeks later)	①Cognitive function(MMSE, Pfeiffer Test); ②Functional(Barthel Index, FTSTS (s)); ③General evaluation of the state of health(SF-12 Physical Health, SF-12 Mental Health); ④Static balance
Liu et al. [23]	America	Multicentrer RCT	Cognitive frailty adults over 70 years old	644	654	78.6 ± 5.2	79.1 ± 5.3	Multicomponent exercise (including walking, strength, flexibility, and balance training)	Health education	24 weeks	65 min	Under the instruction of professionals	baseline and the end of the trial (24 weeks later)	The prevalence of cognitive frailty
Feng et al. [27]	China	Non-RCT	Frail nursing home older adults with cognitive impairment over 65 years old	18		85.94 ± 3.17		Group-based Otago exercise program(concluding warm up, strength training, balance training and walking)		3 months	55 min	Under the instruction of 3 well-trained study research assistants and a physical therapist	baseline and and the end of the trial (3 months later)	①Frailty status(Fried Phenotype) ②Mobility(TUG) ③Lower limb muscle strength (30 s-SST) ④Balance(FSBT)
Chen et al [20]	China	RCT	Participants with cognitive frailty aged 75–92 years	29	30	84.75 ± 5.41	84.59 ± 4.21	Otago exercise program (including warm-up exercise, strength training, balance training, and walking)	Health education	12 weeks	30 min	Guided by a physiotherapist who had clinical experience with older people, and was led by nurses	baseline and 6-week and 12-week follow-up	①Lower limb strength(FTSST),; ②Balance (BBS); ③Functional mobility(TUGT); ④Depression(GDS-15); ⑤The health-related quality of life(SF-12 MCS)

Table 1 (continued)

Trails	Country	Study design	Participants	Number of participants		Age(years)		Interventions		Intervention duration	Each session	Intervention form	Time point	Outcomes
				TG	CG	TG	CT	TG	CT					
Álvaro et al., 2022	Spain	Multi-center RCT	Age > 75 years, pre-frail and frail status according to the Fried criteria	88	100	84.0 ± 4.8	84.2 ± 4.8	Vivifrail multicomponent exercise programme (consisted of resistance/power, balance, flexibility and cardiovascular endurance exercises (i.e. walking))	Usual care	12 weeks	30 min	Under the instruction of family members or caregivers	baseline and the end of the trial (12 weeks later)	①Physical performance(SPPB); ②Cognitive function(MoCA,MEC); ③Activities of daily living(Barthel-Index); ④Handgrip strength(kg); ⑤Quality of Life(QoL); ⑥Depression(GDS-15); ⑦QoL(EQ-VAS)
Zhu et al., 2022	China	Non-RCT	Cognitive frailty adults over 65 years old	35	34	72.66 ± 6.54	72.88 ± 5.78	Group-exergaming exercise (including warm-up, exergaming exercise, cool-down exercise)	Usual care	8 weeks	40 min	Under the instruction of a study research assistants	baseline and the end of the trial (8 weeks later)	①Cognitive function(MMSE); ②Loneliness(the Chinese Version of the Loneliness Scale)
Reshma et al., 2021	Singapore	Non-RCT	Cognitive frailty community-dwelling older adults aged ≥ 60 years	23	69	73 ± 6		Dual-task exercise program called HAPPY (including walking in pairs, resistance training, and circuit training)	Usual care	3 months	60 min	Led by health coaches or volunteers	baseline and and the end of the trial (3 months later)	①Cognitive function(cMMSE, MoCA); ②The prevalence of frailty(The 5-item FRAIL); ③Gait speed; ④Physical performance(SPPB)
Ye et al., 2021	China	RCT	older patients with cognitive frailty	45	45	72.92 + 7.19	72.33 + 6.21	Multi-component exercise (includes aerobic exercise, resistance exercise, balance training and flexibility training)	Health education	6 months	45 min	Under the instruction of geriatric hhysicians and community-based general practitioner	baseline and 3-month and 6-month follow-up	①Frailty(Fried frailty phenotype score); ②Grip strength(kg); ③Gait speed(6-m timed walk); ④Cognitive function(MoCA)
Du [30]	China	Non-RCT	Cognitive frailty community-dwelling older adults aged ≥ 60 years	36	36	72.09 ± 4.21	72.63 ± 4.46	Dual task intervention program of exercise (including warm-up, resistance training, balance training, flexibility training, and stretching)	Community routine nursing	16 weeks	30–45 min	Under the instruction of community nurses	baseline and 8-week and 16-week follow-up	①Frailty(Fried frailty phenotype score); ②Grip strength (kg); ③Gait speed(6-m timed walk); ④Cognitive function(MoCA scale, attention and delayed recall scores) ⑤Tinetti gait and balance test scale

Table 1 (continued)

Trails	Country	Study design	Participants	Number of participants		Age(years)		Interventions		Intervention duration	Each session	Intervention form	Time point	Outcomes
				TG	CG	TG	CT	TG	CT					
Chen et al., 2023 [26]	China	multi-center RCT	Older adults with the risk of functional decline aged 65 years or older	31	38	83(80–87)	86(83–89)	multicomponent exercises (including warm-up, aerobic exercise, progressive resistance training, and balance exercise)	Health education	12 weeks	50–70 min	Under the instruction of professionals	baseline and 6-week and 12-week follow-up	①SPPB ②ADL(IADL, ADL) ③Cognitive function(MMSE) ④Frailty(FRAIL scale) ⑤Balance(Tinetti) ⑥Gait speed(4MGS,6MWD) ⑦Depression(GDS-15) ⑧Grip strength(kg) ⑨Nutritional status(MNA-SF) ⑩QoL(SF-12)

FIM Functional independence measure, *BMI* Body mass index, *FTSTS/FTSST* Five times Sit-to-stand test, *TUG* Time Up and Go test, *30 s-SST* 30 Seconds Sit-To-Stand Test, *FSBT* The Four-Stage Balance Test, *GDS-15* Geriatric Depression Scale-15, *BBS* Berg balance scale, *QoL* quality of life, *SPPB* Short Physical Performance Battery, *EQ-VAS* Visual Analog Scale of the EuroQol Questionnaire, Mini Nutritional Assessment, *6MWD* 6-min walking distance, *4MGS* 4-m gait speed test, Tinetti(Tinetti Balance and Gait Analysis)

Table 2 Protocols of multicomponent exercise(Studies from Inception to December 2023)

Author and years	Types of exercise	Exercise tools	Exercise duration	Exercise frequency	Exercise intensity	Intervention form	Intervention duration	Conductor	Control
Thomas et al., 2007	• warming up 10 min, • strength training 25 min, • balance training 10 min, • cooling down 5 min	• Strength training: elastic resistance bands (thera-bands) and soft weights; • Balance training: exercise balls, balance discs and blocks (20 cm high)	50 min	3 times a week	Not mentioned	Group-based type (7–8 persons per group)	10 weeks	Under the instruction of a sports scientist	Not mentioned
Irimia et al., 2019	Calisthenics exercises and playful callisthenic games (for improving participants' strength, stamina, speed and flexibility)	Not mentioned	60 min	2 times a week (1 session of calisthenics exercises and 1 session of playful callisthenic games)	Not mentioned	Group-based type (8–9 persons per group)	12 weeks	Conducted and controlled by health and fitness professionals specializing in physical activity for older adults	Crafts, reading comprehension and cognitive stimulation
Liu et al. [23]	• aerobics(walking) 30 min, • strength training 10 min, • flexibility 3–5 min, • balance training 10 min	Not mentioned	65 min	5–6 times a week(two center-based visits a week and home-based activity three to four times a week)	The Borg's scale of self-perceived exertion with scores ranging from 6 to 20 (walk at an intensity of 13, lower extremity strengthening exercises at an intensity of 15 to 16)	Individual-based type	24 weeks	Under the instruction of professionals	Health education during the first 26 weeks, and monthly sessions thereafter
Feng et al. [27]	• warm-up exercise 10 min, • strength training 15 min, • balance training 30 min, • aerobics(walking) 30 min at least twice a week	No need	55 min	3 times a week	Not mentioned	Group-based type (6 persons per group)	3 months	Under the instruction of 3 well-trained study research assistants and a physical therapist	No control group
Chen et al. [20]	• warm-up 5 min, • resistance training 10 min, • balance exercise 15 min	0.5 kg sandbags	30 min	3 times a week	Not mentioned	Group-based type	12 weeks	Guided by a physiotherapist who had clinical experience with older people, and was led by nurses	Sleep- and diet-related health education
Álvaro et al., 2022	• resistance training, • balance training, • flexibility exercise, • aerobics(walking)	0.5 kg dumbbells	30 min	5 times a week(resistance, balance, and flexibility exercises 3 days per week and walking 5 days per week)	Not mentioned	Individual-based type	12 weeks	Under the instruction of family members or caregivers	Usual care(their normal ADLs and received habitual outpatient clinical care, including medical treatments and physical rehabilitation when needed)

Table 2 (continued)

Author and years	Types of exercise	Exercise tools	Exercise duration	Exercise frequency	Exercise intensity	Intervention form	Intervention duration	Conductor	Control
Zhu et al., 2022	• warm-up 5 min • exergaming exercise 30 min (upper and lower limb movements for muscular endurance, balance, and stability) • cool-down exercise 5 min	An infrared sensing device and a laptop computer	40 min	2 times a week	Not mentioned	Group-based type (4–6 persons per group)	8 weeks	Under the instruction of a study research assistants	Usual care
Reshma et al., 2021	• walking in pairs, • resistance training • circuit training	Not mentioned	60 min	1–2 times a week	Low to moderate intensity	Group-based type	3 months	Led by health coaches or volunteers	Usual care
Ye et al., 2021	• aerobics 5 min, • strength training 20 min, • balance training 10 min, • flexibility training 10 min	Elastic bands	45 min	3 times a week	RPE 12–14	Individual-based type	6 months	Under the instruction of geriatric hhysicians and community-based general practitioner	Diet-related health education
Du, 2022 [30]	• warm-up 5 min • resistance training 10 min • balance and flexibility training 10 min, • Stretching 5 min	No need	30–45 min	2 times a week	Low to medium intensity training, the exercise intensity was determined by heart rate and the appropriate exercise intensity was no fatigue, the target heart rate = (220—age) × (60% ~ 80%)	Individual-based type	16 weeks	Under the instruction of community nurses	Community routine nursing
Chen et al., 2023 [26]	• warm-up 5–10 min • aerobic exercise 20–40 min, • progressive resistance training, • balance exercise	No need	50–70 min	3 times a week	Low intensity (50%–65% HRmax) and medium intensity (65%–75% HRmax)	Individual-based type	12 weeks	Under the instruction of professionals	Health education about healthy diet, scientific exercise, and the related importance

RPE rating of perceived exertion; HRmax = 211-(0.64 × age) the predominant risk sources were confounding and deviations from intended interventions. Detailed depictions of the bias assessments are provided in Fig. 2.

Effects of ME on cognitive function in older adults with CF

Eight studies [21, 22, 24–26, 28–30] evaluated cognitive function, with six included in this meta-analysis. The impact of multicomponent physical activity on overall cognition in patients with cognitive frailty yielded an effect size (ES) of 2.52 [95% CI (1.05, 2.99), $p=0.03$, $n=521$], accompanied by moderate heterogeneity ($I^2=59\%$) and no signs of publication bias (Egger test $p=0.92$). Subgroup analysis based on the cognitive function evaluation tool was conducted, distinguishing between the Montreal Cognitive Assessment (MOCA) [24, 25, 28, 29] and the Mini-Mental State Examination (MMSE) [21, 22] approaches. Results demonstrated that multicomponent exercise significantly improved cognitive function as assessed by MOCA [MD = 2.50, 95%CI(0.82, 4.18), $p=0.007$, $I^2=75\%$, $n=439$]. However, cognitive function evaluated by MMSE did not exhibit any significant difference [MD = 2.63, 95%CI(-2.56, 7.81), $p=0.81$, $I^2=0\%$, $n=82$]. Additionally, two studies [26, 30] were excluded from the meta-analysis due to their results exhibiting severely skewed distributions that could not be translated into MD. Nevertheless, these studies demonstrated that ME significantly improved cognitive functioning compared to the control group, with the between-group differences reaching statistical significance ($p<0.05$). For further details, see Fig. 3A.

Effects of ME on frailty in older adults with CF

Among the five studies [25–27, 29, 30] addressing frailty, two were incorporated into the meta-analysis. The synthesized effect size indicated that multicomponent exercise significantly impacted frailty [MD = -2.21, 95CI%(-3.73, -0.69), $p<0.001$, $I^2=97\%$, $n=159$]. According to Reshma et al., multicomponent exercise led to a reduction in frailty prevalence from 4 to 2%, and a decrease in prefrailty prevalence from 96 to 38%. For more details, refer to Fig. 3B.

Impact of ME on additional health-related outcomes in older individuals with CF

Impact of ME on muscle strength in older individuals with CF

Six trials [20, 21, 24–26, 30] reported on muscle strength, demonstrating that multicomponent exercise significantly enhanced muscle strength [SMD = 0.59, 95%CI (0.16,1.02), $p=0.007$, $I^2=86\%$, $n=715$]. Subgroup analysis demonstrated a significant enhancement in both upper limb [SMD = 0.39, 95%CI (0.10, 0.67), $p=0.008$, $I^2=49\%$, $n=416$, Egger's test $p=0.69$] and lower limb muscle strength [MD = 4.30, 95%CI (3.43, 5.16), $p<0.001$,

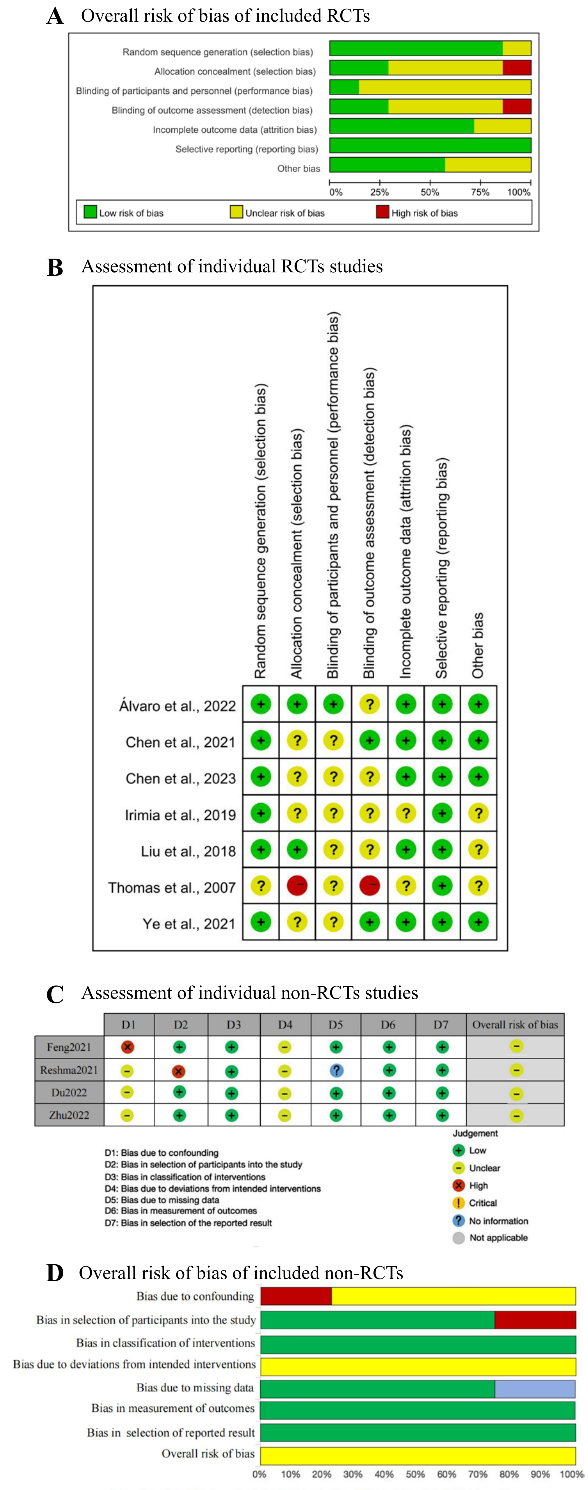

Fig. 2 Risk of bias of included (Studies from Inception to December 2023): **A** overall risk of bias of included RCTs, **B** assessment of individual RCTs studies, **C** assessment of individual non-RCTs studies, **D** overall risk of bias of included non-RCTs

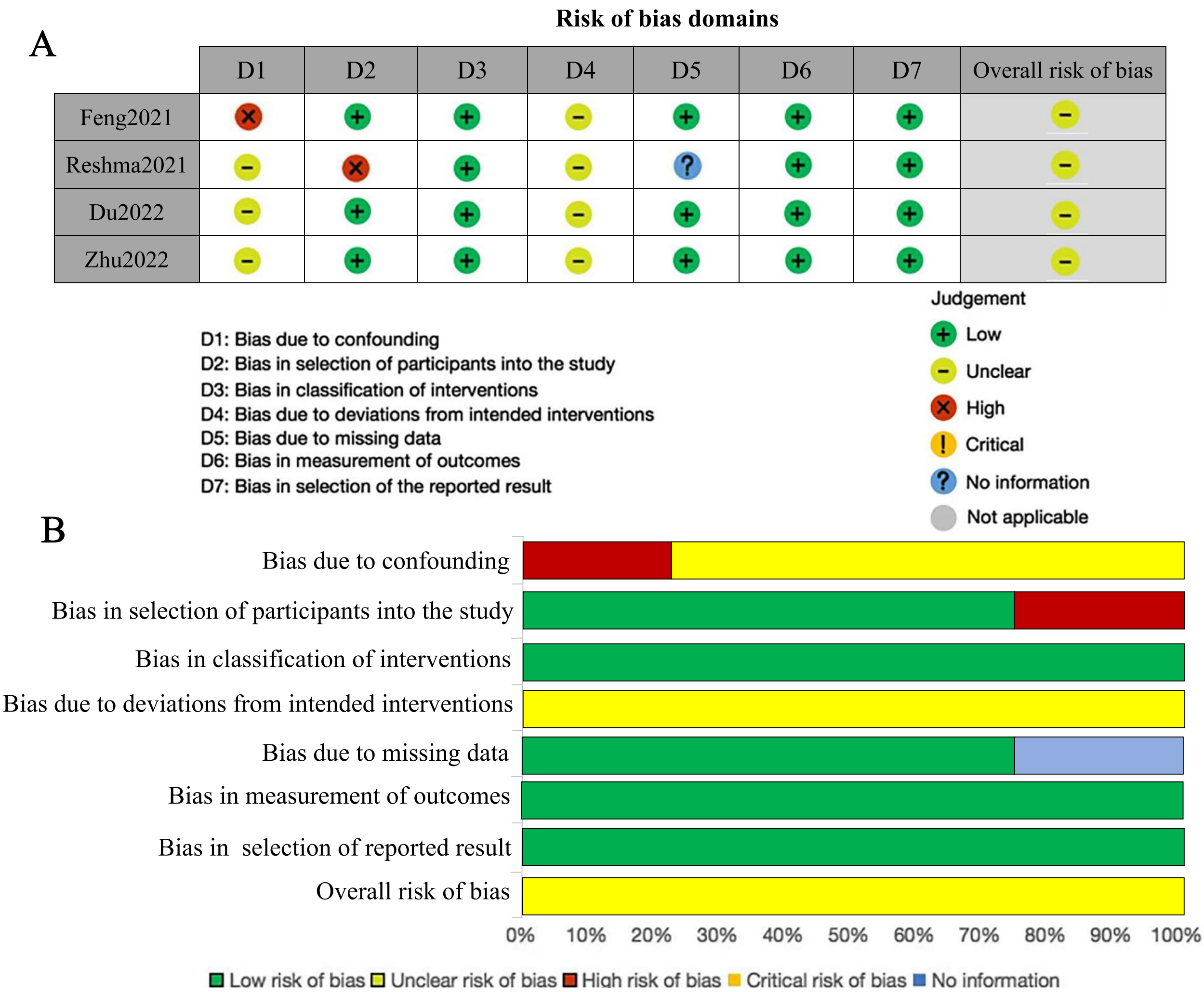

Fig. 3 Forest plot of primary outcomes(Studies from Inception to December 2023): **A** cognitive function and (**B**) frailty

$I^2=0\%$, $n=299$, Egger's test $p=0.71$] (Supplementary Fig. 1A).

Impact of ME on ADL in Older Individuals with CF

Four studies [21, 22, 24, 26], which used Barthel Index and ADL scale to measure ADL, were included in this meta-analysis. Given the high heterogeneity among the studies ($I^2=66\%$), a random effects model was employed to consolidate the data. The results suggested that ME did not significantly improve activities of daily living in older individuals with CF [SMD = 0.28, 95%CI(-0.14, 0.69), $p=0.19$, n = 339, Egger's test $p=0.84$](Supplementary Fig. 1B).

Impact of ME on Depression in Older Individuals with CF

Four studies [20, 22, 24, 26] utilized the GDS-15 measure for depression. The amalgamated effect size demonstrated that multicomponent exercise had a statistically significant impact on depression [MD = -1.20, 95%CI (-1.92, -0.49), $p=0.001$; $I^2=37\%$, n = 346, Egger's test $p=0.12$] (Supplementary Fig. 1C).

Impact of ME on Quality of Life in Older Individuals with CF

Four studies [20, 21, 24, 26] provided data regarding the impact of ME on the quality of life in older individuals with cognitive frailty. The consolidated results indicated that ME did not significantly enhance the quality of life in older individuals with CF [SMD = 0.37, 95% CI(-0.14, 0.87), $p=0.16$, $I^2=80\%$, n = 368, Egger's test $p=0.79$]; these results are depicted in Supplementary Fig. 1D.

Subgroup analysis and sensitive analysis

We implemented subgroup analyses for cognitive function, ADL, depression, and quality of life to scrutinize differential effects across subgroups (Table 3). The analyses revealed that multicomponent exercise regimens

Table 3 Subgroup analysis of exercise type and intervention characteristics (Studies from Inception to December 2023)

Subgroup	Cognitive function				Activities of daily living				Depression				Quality of life			
	Study	SMD/WMD (95%CI)	*P* value	I^2	Study	SMD/WMD (95%CI)	*P* value	I^2	Study	SMD/WMD (95%CI)	*P* value	I^2	Study	SMD/WMD (95%CI)	*P* value	I^2
Exercise type																
Aerobics-including	3	0.42 (0.09, 0.75)	0.01	2%	2	1.22 (-17.56, 20.00)	0.90	0%	2	-1.61 (-2.46, -0.76)	< 0.001	10%	2	8.48 (5.06, 11.91)	< 0.001	0%
Aerobics-excluding	3	0.58 (-0.02,1.17)	0.06	85%	2	0.48(-0.31, 1.27)	0.24	87%	2	-0.65 (-2.18, 0.88)	0.40	45%	2	0.07 [-0.18, 0.31]	0.59	0%
Total minutes of exercise per week																
≤ 120 min	3	0.32 (-0.05, 0.69)	0.09	38%	1	0.10 (-0.45, 0.65)	0.72	NA	1	-1.79 (-2.54, -1.04)	< 0.001	NA	2	0.07 [-0.18, 0.31]	0.59	0%
> 120 min	3	0.66 (0.07, 1.26)	0.03	80%	3	0.33 (-0.24, 0.90)	0.26	76%	3	-0.95 (-1.59, -0.32)	0.003	0%	2	8.48 (5.06, 11.91)	< 0.001	0%
Intervention form																
Group-based type	4	0.32 (0.04, 0.60)	0.03	8%	2	1.22 (-17.56, 20.00)	0.90	0%	2	-1.61 (-2.46, -0.76)	< 0.001	10%	2	8.48 (5.06, 11.91)	< 0.001	0%
Individual-based type	2	0.80 (-0.01,1.61)	0.05	89%	2	0.48(-0.31, 1.27)	0.24	87%	2	-0.65 (-2.18, 0.88)	0.40	45%	2	0.07 [-0.18, 0.31]	0.59	0%

incorporating aerobic exercise fostered superior cognitive function [SMD = 0.42, 95%CI(0.09, 0.75), $p = 0.01$, $I^2 = 0\%$], improved quality of life [MD = 8.48 (5.06, 11.91), $p < 0.001$, $I^2 = 0\%$], and mitigated depression [MD = -1.61, 95%CI(-2.46, -0.76), $p < 0.001$, $I^2 = 10\%$]. Furthermore, interventions involving more than 120 min of exercise per week were associated with enhanced cognitive function [SMD = 0.66, 95%CI(0.07, 1.26), $p = 0.03$, $I^2 = 80\%$], improved quality of life [MD = 8.48, 95%CI(5.06, 11.91), $p < 0.001$, $I^2 = 0\%$], and reduced depression [MD = -0.95, 95%CI (-1.59, -0.32), $p = 0.003$, $I^2 = 0\%$]. Intriguingly, exercises conducted in group settings were found to be more effective than individual home-based exercises, as evidenced by improvements in cognitive function [SMD = 0.32, 95%CI(0.04, 0.60), $p = 0.03$, $I^2 = 8\%$], depression [MD = -1.61, 95%CI(-2.46, -0.76), $p < 0.001$, $I^2 = 10\%$], and quality of life [MD = 8.48, 95%CI(5.06, 11.91), $p < 0.001$, $I^2 = 0\%$].

Additionally, we performed a sensitivity analysis to assess the consistency of findings across various study designs. We excluded quasi-experimental studies from the meta-analysis, which revealed that multi-component exercise continues to improve cognitive function [MD = 3.40 (1.47, 5.34), $p < 0.001$, $I^2 = 48\%$] (refer to Fig. 2 in the appendix).

Meta regression

We performed meta-regression on cognitive function, depression, ADL, and quality of life based on the study region (China = 0, Spain = 1, other = 2), study design (RCT = 0, quasi-experimental = 1), frailty status of the study population (frailty only = 0, both pre-frailty and frailty = 1), outcome measurement tools, intervention duration (< 12 weeks, ≥ 12 weeks), intervention form (individual-based = 0, group-based = 1), intervention time (≤ 120 min per week = 0, > 120 min per week = 1), and intervention type (aerobics-excluding = 0, aerobics-including = 1). The results showed that the study region explained 94.31% of the heterogeneity in cognitive function ($p = 0.002$), intervention time explained 73.27% of the heterogeneity in depression ($p = 0.021$), study region ($p = 0.007$) and measurement tools ($p = 0.003$) explained 100% of the heterogeneity in ADL, and study region explained 25.93% of the heterogeneity in quality of life ($p = 0.178$). For more details, see Supplementary Table 2–5.

Discussion

To the best of our understanding, the present study represents the first endeavor to quantitatively integrate the impact of multicomponent exercise on the physical and mental facets of functionality within a cohort of cognitively frail older adults. Despite observable heterogeneity across most outcomes, our meta-analysis suggests that multicomponent exercise significantly enhances cognitive functionality, frailty status, grip and lower limb muscle strength, and alleviates symptoms of depression among older adults with cognitive frailty. However, the evidence supporting the effectiveness of multicomponent exercise on ADL and the quality of life remains insufficient. Furthermore, our results indicate the disappearance of these beneficial effects when the exercise regimen does not include aerobic activity, lasts less than 120 min per week, or is conducted individually at home.

Effect of multicomponent exercise on cognitive frailty

Our systematic review and meta-analysis reveal that ME improves overall cognitive function and frailty status among older adults. However, when segregating cognitive function assessments via subgroup analyses, multicomponent exercise did not yield a statistically significant improvement measured by the MMSE, which contradicts the conclusions drawn by Yan et al [31]. Statistical power is influenced by various factors, including sample size and effect size. In our meta-analysis, only two studies utilized the MMSE scale to measure cognitive functioning, with sample sizes of 38 for the experimental group and 44 for the control group. The limited number of studies and small sample sizes may lead to an underestimation of the true effect of multicomponent exercise on cognitive functioning as measured by the MMSE scale, increasing the risk of Type II errors (false negatives). Future studies should aim to increase sample sizes to improve the statistical power of individual studies. Additionally, performing a priori power analyses during the study design phase can help ensure sufficient power to detect significant effects. The inclusion of more high-quality RCTs with larger sample sizes would strengthen the evidence base and provide a more reliable assessment of the effects of multicomponent exercise.

Exercise reinforces cerebrovascular function via mechanisms, including angiogenesis promotion, endothelial nitric oxide synthase (eNOS) upregulation, and endothelial progenitor cell production [31–33], potentially delaying cognitive decline associated with aging [34]. The efficacy of multicomponent exercise on frailty is well-documented [35, 36]. A combination of different training modalities, emphasizing resistance and aerobic training, appears to be the preeminent strategy for preserving or enhancing cognitive function [37]. However, additional research is warranted to unravel the underlying physiological mechanisms induced by exercise in frail older adults with MCI.

Impact of multicomponent exercise on muscle strength

Our findings underline the potent effects of ME on muscle strength in older adults with CF. Multicomponent exercise, generally combining resistance and strength training, amplifies muscle strength through fostering muscle growth [38] while minimizing fat infiltration [39, 40]. Notably, multicomponent exercise showed more significant improvements in lower limb muscle strength as opposed to grip strength. This observation might be due to multicomponent exercise protocols emphasizing lower limb muscle training while leaving upper limb muscle exercises underrepresented. Hence, in implementing multicomponent exercise interventions, exploring appropriate duration and intensity of functional upper limb exercises might help optimize upper limb muscle strength enhancement in older adults.

Impact of multicomponent exercise on depression

Multicomponent exercise effectively alleviates depression in older adults with CF. The mechanisms underlying these improvements are complex and involve both psychological and neurobiological factors. Multicomponent exercise enhances and accelerates the upregulation of brain-derived neurotrophic factor (BDNF) [41] and promotes its expression, which is a key component of catecholamine-enhancing, mood-stabilizing antidepressant therapy. Additionally, the aerobic component of multicomponent exercise can alter monoamine neurotransmitters, increase levels of serotonin (5-HT) and norepinephrine, decrease cortisol levels, and elevate β-endorphins, thereby alleviating depressive symptoms [42, 43]. Furthermore, this exercise promotes positive changes in brain structure by reducing stress and inflammation, improving neural network connectivity in various brain regions, including the default mode network (DMN) [44], and enhancing neuroplasticity. It also positively affects oxidative stress, salivary cortisol, and gamma-aminobutyric acid (GABA) [45], thereby improving neural processing, enhancing mood, reducing depression, and delaying cognitive deterioration [43, 46].

Impact of multicomponent exercise on ADL and QOL

Our review shows that the differences in ADL and QOL improvement between the multicomponent exercise intervention group and the control group were not statistically significant. Various factors might explain this unexpected outcome. ADLs encapsulate a broad spectrum of daily tasks, including basic activities like eating, dressing, and bathing, while QOL is a subjective and multidimensional construct, influenced by an array of factors beyond physical health. Therefore, the intricate and diverse nature of these aspects may render a multicomponent exercise program challenged to adequately address each specific aspect. Moreover, considering that the impact of multicomponent exercise on ADLs and QOL represents a long-term process [47], further research is needed to elucidate the time-response relationship of multicomponent exercise interventions on ADL capability and QOL.

Implications for practice and research

This meta-analysis offers a quantitative synthesis of the impacts of incorporating ME interventions in the lives of older adults with cognitive frailty. The evidence obtained suggests that implementing appropriate ME interventions can serve as an effective strategy in geriatric practice to stimulate cognitive function, mitigate frailty and depression, and fortify muscle strength among older adults with cognitive frailty.

Our subgroup analyses indicate that exercise regimens incorporating more than 120 min of activity per week significantly enhance cognitive function, quality of life, and reduce depression symptoms. This aligns with existing research, suggesting that higher volumes of exercise provide more substantial benefits for cognitive and emotional health [48]. Guidelines have shown that a threshold of at least 150 min per week of moderate-intensity exercise is generally recommended for older adults to achieve optimal health benefits [49], which is consistent with our findings. Intensity is another critical factor. Moderate-to-high intensity exercises, particularly aerobic activities, are known to effectively boost cognitive function and alleviate depressive symptoms through mechanisms such as increased cerebral blood flow, enhanced neuroplasticity, and improved neurochemical profiles, including elevated levels of BDNF and reduced cortisol levels [50]. Our findings support this, as aerobic components in multicomponent regimens showed significant improvements in cognitive and emotional outcomes. Moreover, group-based exercises demonstrated superior outcomes compared to individual home-based activities. This could be attributed to the social interaction and motivation provided in group settings, which enhance adherence and engagement, thereby amplifying the psychological and physiological benefits of the exercise. Social support and interaction inherent in group activities may also directly contribute to improved mood and reduced depression through increased socialization and reduced feelings of isolation [51].

Limitations

Despite offering the latest evidence on the effects of multicomponent exercise on cognitive function and physical performance in older adults with cognitive frailty, our study bears several limitations. Firstly, akin to any review, we might have overlooked relevant studies despite our comprehensive search strategy. Secondly, the language limitation to English and Chinese may have restricted the assortment of studies included. Thirdly, due to the scarcity of high-quality RCTs in this domain, conducting a meta-analysis with only RCTs is insufficient. Therefore, we included both RCTs and quasi-experimental studies in this meta-analysis to more comprehensively synthesize evidence and investigate the multifaceted impacts of multicomponent exercise on cognitively impaired elderly individuals. However, incorporating non-randomized controlled trials may introduce a higher risk of bias. To address this, we used the ROBINS-I tool to thoroughly assess the quality of non-RCTs. After independent assessments by two researchers, all included non-RCTs were deemed to have moderate bias. Additionally, we performed a sensitivity analysis to assess the consistency of the findings across diverse study designs. The results remained robust even after excluding the quasi-experimental studies (see Fig. 2 in the appendix).

Most of our study results exhibited a moderate to high degree of heterogeneity. This heterogeneity can be attributed to several factors. Firstly, although all included interventions were multicomponent exercise programs, they differed in specific variables such as exercise type, intensity, and duration. Additionally, follow-up periods varied significantly, ranging from 8 weeks to 6 months, contributing to the heterogeneity. Secondly, different assessment tools were used across studies; for example, cognitive function was evaluated using either the MoCA or MMSE scales, and similar variations were observed for ADL and quality of life measures. Furthermore, the meta-analysis included studies from various regions, and meta-regression identified study region as a major source of heterogeneity. Lastly, there was some variation in the study populations, with some studies including both frail and pre-frail older adults, and differing levels of cognitive impairment, which also contributed to the heterogeneity.

Conclusion

Multicomponent exercise programs, tailored specifically towards older adults with cognitive frailty, are efficacious in enhancing cognitive functionality, vibrant muscle strength, and reducing indicators of frailty and depression. Nevertheless, the evidence regarding the positive impact of such exercises on ADL and quality of life remains statistically inconclusive. Hence, in the clinical realm, there lies a necessity for the integration of aerobic exercises into the intervention repertoire and organizing moderate-to-high-intensity group exercises for older adults whenever feasible. To better ascertain the effectiveness of multicomponent exercise programs in this context, future studies warranted larger sample sizes, extended follow-up periods, and rigorously structured experimental designs.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13690-024-01441-y.

Supplementary Material 1.

Supplementary Material 2.

Acknowledgements
Not applicable.

Authors' contributions
HHL, TZZ, and XHH developed the study design, search strategy, and ranking criteria, extracted the data, and evaluated the quality of the literature. HHL and TZZ wrote the first draft of the article, and ZY and CS revised and finalized the final version.

Funding
This study was supported by National Natural Science Foundation of China (72474032); the Fundamental Research Funds for the Central Universities (3332023093), National High Level Hospital Clinical Research Funding (BJ-2024-167; BJ-2024-250); National Key R&D Program of China (2020YFC2008504).

Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
CHARLS data has been approved by the Biomedical Ethics Committee of Peking University (approval number: IRB 00001052–11015), ensuring ethical research conduct with informed consent from all participants.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Institute of Geriatric Medicine, Beijing Hospital, National Center of Gerontology, Chinese Academy of MedicalSciences and Peking Union Medical College, Beijing, People's Republic of China. [2]Department of Nursing, Institute of Geriatric Medicine, Beijing Hospital, National Center of Gerontology, Chinese Academy of Medical Science, NO.1 Da Hua Road, DongDan, Beijing 100730, People's Republic of China. [3]Department of Sports MedicineInstitute of Sports Medicine of Peking UniversityBeijing Key Laboratory of Sports Injuries, Peking University Third Hospital, Beijing, People's Republic of China. [4]Engineering Research Center of Sports Trauma Treatment Technology and Devices, Ministry of Education, Beijing, People's Republic of China. [5]Department of Orthopedics, the Fourth Medical Centre, Chineses PLA General Hospital, 51 Fucheng Road, Beijing 100048, People's Republic of China.

Received: 15 March 2024 Accepted: 31 October 2024
Published online: 29 November 2024

References

1. Kelaiditi E, Cesari M, Canevelli M, van Kan GA, Ousset PJ, Gillette-Guyonnet S, Ritz P, Duveau F, Soto ME, Provencher V, et al. Cognitive frailty: rational and definition from an (I.A.N.A./I.A.G.G.) international consensus group. J Nutr Health Aging. 2013;17(9):726–34.
2. Sugimoto T, Arai H, Sakurai T. An update on cognitive frailty: Its definition, impact, associated factors and underlying mechanisms, and interventions. Geriatr Gerontol Int. 2022;22(2):99–109.
3. Qiu Y, Li G, Wang X, Zheng L, Wang C, Wang C, Chen L. Prevalence of cognitive frailty among community-dwelling older adults: A systematic review and meta-analysis. Int J Nurs Stud. 2022;125:104112.

4. Tang KF, Teh PL, Lee SWH. Cognitive frailty and functional disability among community-dwelling older adults: a systematic review. Innov Aging. 2023;7(1):igad005.
5. Guo X, Pei J, Ma Y, Cui Y, Guo J, Wei Y, Han L. Cognitive frailty as a predictor of future falls in older adults: a systematic review and meta-analysis. J Am Med Dir Assoc. 2023;24(1):38–47.
6. Zou C, Yu Q, Wang C, Ding M, Chen L. Association of depression with cognitive frailty: a systematic review and meta-analysis. J Affect Disord. 2023;320:133–9.
7. Qiu Y, Li G, Zheng L, Liu W, Li X, Wang X, Chen L. Relationship between cognitive frailty and mortality in older adults: a systematic review and meta-analysis. J Am Med Dir Assoc. 2023;24(11):1637–1644.e1638.
8. Shimada H, Makizako H, Tsutsumimoto K, Doi T, Lee S, Suzuki T. Cognitive frailty and incidence of dementia in older persons. J Prev Alzheimers Dis. 2018;5(1):42–8.
9. Panza F, Lozupone M, Solfrizzi V, Sardone R, Dibello V, Di Lena L, D'Urso F, Stallone R, Petruzzi M, Giannelli G, et al. Different cognitive frailty models and health- and cognitive-related outcomes in older age: from epidemiology to prevention. J Alzheimers Dis. 2018;62(3):993–1012.
10. Arai H, Satake S, Kozaki K. Cognitive frailty in geriatrics. Clin Geriatr Med. 2018;34(4):667–75.
11. Liang JH, Xu Y, Lin L, Jia RX, Zhang HB, Hang L. Comparison of multiple interventions for older adults with Alzheimer disease or mild cognitive impairment: A PRISMA-compliant network meta-analysis. Medicine (Baltimore). 2018;97(20):e10744.
12. Yan J, Li X, Guo X, Lin Y, Wang S, Cao Y, Lin H, Dai Y, Ding Y, Liu W. Effect of Multicomponent Exercise on Cognition, Physical Function and Activities of Daily Life in Older Adults With Dementia or Mild Cognitive Impairment: A Systematic Review and Meta-analysis. Arch Phys Med Rehabil. 2023;104(12):2092–108.
13. Hernández SSS, Sandreschi PF, da Silva FC, Arancibia BAV, da Silva R, Gutierres PJB, Andrade A. What are the benefits of exercise for Alzheimer's disease? a systematic review of the past 10 years. J Aging Phys Act. 2015;23(4):659–68.
14. Li Y, Gao Y, Hu S, Chen H, Zhang M, Yang Y, Liu Y. Effects of multicomponent exercise on the muscle strength, muscle endurance and balance of frail older adults: A meta-analysis of randomised controlled trials. J Clin Nurs. 2023;32(9–10):1795–805.
15. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, Clarke M, Devereaux PJ, Kleijnen J, Moher D. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. PLoS Med. 2009;6(7):e1000100.
16. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019;366:l4898.
17. Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, Henry D, Altman DG, Ansari MT, Boutron I, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ. 2016;355: i4919.
18. Erdfelder E, Faul F, Buchner A. Power analysis for categorical methods; 2005. https://doi.org/10.1002/0470013192.bsa491.
19. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ. 1997;315(7109):629–34.
20. Chen X, Zhao L, Liu Y, Zhou Z, Zhang H, Wei D, et al. Otago exercise programme for physical function and mental health among older adults with cognitive frailty during COVID-19: a randomised controlled trial. J Clin Nurs. 2021. https://doi.org/10.1111/jocn.15964.
21. Cardalda IM, López A, Carral JMC. Arch Gerontol Geriatr. 2019;83:223–30.
22. Dorner T, Kranz A, Zettl-Wiedner K, Ludwig C, Rieder A, Gisinger C. The effect of structured strength and balance training on cognitive function in frail, cognitive impaired elderly long-term care residents. Aging Clin Exp Res. 2007;19(5):400–5.
23. Liu Z, Hsu FC, Trombetti A, King AC, Liu CK, Manini TM, Fielding RA, Pahor M, Newman AB, Kritchevsky S, et al. Effect of 24-month physical activity on cognitive frailty and the role of inflammation: the LIFE randomized clinical trial. BMC Med. 2018;16(1):185.
24. Casas-Herrero Á, de Sáez AML, Antón-Rodrigo I, Sánchez-Sánchez JL, Montero-Odasso M, Marín-Epelde I, Ramón-Espinoza F, Zambom-Ferraresi F, Petidier-Torregrosa R, Elexpuru-Estomba J, et al. Effects of Vivifrail multicomponent intervention on functional capacity: a multicentre, randomized controlled trial. J Cachexia Sarcopenia Muscle. 2022;13(2):884–93.
25. Ye M, Li S, Zhu Z, Zhu H. Effect of a multicomponent exercise prescription in elderly patients with cognitive frailty. Chin General Pract. 2021;24(04):460–6.
26. Chen B, Li M, Zhao H, Liao R, Lu J, Tu J, Zou Y, Teng X, Huang Y, Liu J, et al. Effect of multicomponent intervention on functional decline in chinese older adults: a multicenter randomized clinical trial. J Nutr Health Aging. 2023;27(11):1063–75.
27. Feng H, Zou Z, Zhang Q, Wang L, Ouyang YQ, Chen Z, Ni Z. The effect of the group-based Otago exercise program on frailty among nursing home older adults with cognitive impairment. Geriatr Nurs. 2021;42(2):479–83.
28. Zhu YZ, Lin CF, Yang HL, Jin G, Chiu HL. Effects of exergaming on cognitive functions and loneliness of older adults with cognitive frailty. Int J Geriatr Psychiatry. 2023;38(6):e5944.
29. Merchant RA, Chan YH, Hui RJY, Tsoi CT, Kwek SC, Tan WM, Lim JY, Sandrasageran S, Wong BLL, Chen MZ, et al. Motoric cognitive risk syndrome, physio-cognitive decline syndrome, cognitive frailty and reversibility with dual-task exercise. Exp Gerontol. 2021;150:111362.
30. Du J. Effect of dual task training on elderly patients with cognitive frailty in community: Zhengzhou University; 2022. https://doi.org/10.27466/d.cnki.gzzdu.2022.002048.
31. Trigiani LJ, Hamel E. An endothelial link between the benefits of physical exercise in dementia. J Cereb Blood Flow Metab. 2017;37(8):2649–64.
32. Gertz K, Priller J, Kronenberg G, Fink KB, Winter B, Schröck H, Ji S, Milosevic M, Harms C, Böhm M, et al. Physical activity improves long-term stroke outcome via endothelial nitric oxide synthase-dependent augmentation of neovascularization and cerebral blood flow. Circ Res. 2006;99(10):1132–40.
33. Zhang P, Yu H, Zhou N, Zhang J, Wu Y, Zhang Y, Bai Y, Jia J, Zhang Q, Tian S, et al. Early exercise improves cerebral blood flow through increased angiogenesis in experimental stroke rat model. J Neuroeng Rehabil. 2013;10:43.
34. Viboolvorakul S, Patumraj S. Exercise training could improve age-related changes in cerebral blood flow and capillary vascularity through the upregulation of VEGF and eNOS. Biomed Res Int. 2014;2014:230791.
35. Courel-Ibáñez J, Buendía-Romero Á, Pallarés JG, García-Conesa S, Martínez-Cava A, Izquierdo M. Impact of tailored multicomponent exercise for preventing weakness and falls on nursing home residents' functional capacity. J Am Med Dir Assoc. 2022;23(1):98–104.e103.
36. Yi M, Zhang W, Zhang X, Zhou J, Wang Z. The effectiveness of Otago exercise program in older adults with frailty or pre-frailty: a systematic review and meta-analysis. Arch Gerontol Geriatr. 2023;114: 105083.
37. Venegas-Sanabria LC, Cavero-Redondo I, Martínez-Vizcaino V, Cano-Gutierrez CA, Álvarez-Bueno C. Effect of multicomponent exercise in cognitive impairment: a systematic review and meta-analysis. BMC Geriatr. 2022;22(1):617.
38. Kim H, Suzuki T, Kim M, Kojima N, Ota N, Shimotoyodome A, Hase T, Hosoi E, Yoshida H. Effects of exercise and milk fat globule membrane (MFGM) supplementation on body composition, physical function, and hematological parameters in community-dwelling frail Japanese women: a randomized double blind, placebo-controlled, follow-up trial. PLoS ONE. 2015;10(2):e0116256.
39. Cadore EL, Casas-Herrero A, Zambom-Ferraresi F, Idoate F, Millor N, Gómez M, Rodriguez-Mañas L, Izquierdo M. Multicomponent exercises including muscle power training enhance muscle mass, power output, and functional outcomes in institutionalized frail nonagenarians. Age (Dordr). 2014;36(2):773–85.
40. Lin TY, Chen JJ, Lin LL, Ou Yang WT, Chen MY, Tsai YC. Effects of multicomponent exercise training on muscle oxygenation in young and older adults. J Exerc Sci Fit. 2023;21(1):138–46.
41. Ströhle A. Physical activity, exercise, depression and anxiety disorders. J Neural Transm (Vienna). 2009;116(6):777–84.
42. Kvam S, Kleppe CL, Nordhus IH, Hovland A. Exercise as a treatment for depression: a meta-analysis. J Affect Disord. 2016;202:67–86.
43. Schuch FB, Stubbs B. The role of exercise in preventing and treating depression. Curr Sports Med Rep. 2019;18(8):299–304.
44. Eyre HA, Acevedo B, Yang H, Siddarth P, Van Dyk K, Ercoli L, Leaver AM, Cyr NS, Narr K, Baune BT, et al. Changes in neural connectivity and memory following a yoga intervention for older adults: a pilot study. J Alzheimers Dis. 2016;52(2):673–84.

45. Yadav R, Yadav RK, Khadgawat R, Pandey RM. Comparative efficacy of a 12 week yoga-based lifestyle intervention and dietary intervention on adipokines, inflammation, and oxidative stress in adults with metabolic syndrome: a randomized controlled trial. Transl Behav Med. 2019;9(4):594–604.
46. Schuch FB, Deslandes AC, Stubbs B, Gosmann NP, Silva CT, Fleck MP. Neurobiological effects of exercise on major depressive disorder: a systematic review. Neurosci Biobehav Rev. 2016;61:1–11.
47. Romera-Liebana L, Orfila F, Segura JM, Real J, Fabra ML, Möller M, Lancho S, Ramirez A, Marti N, Cullell M, et al. Effects of a primary care-based multifactorial intervention on physical and cognitive function in frail, elderly individuals: a randomized controlled trial. J Gerontol A Biol Sci Med Sci. 2018;73(12):1688–1674.
48. Gallardo-Gómez D, Del Pozo-Cruz J, Noetel M, Álvarez-Barbosa F, Alfonso-Rosa RM, Del Pozo CB. Optimal dose and type of exercise to improve cognitive function in older adults: A systematic review and bayesian model-based network meta-analysis of RCTs. Ageing Res Rev. 2022;76:101591.
49. Izquierdo M, Duque G, Morley JE. Physical activity guidelines for older people: knowledge gaps and future directions. Lancet Healthy Longev. 2021;2(6):e380–3.
50. Schuch FB, Vasconcelos-Moreno MP, Borowsky C, Zimmermann AB, Wollenhaupt-Aguiar B, Ferrari P, de Almeida Fleck MP. The effects of exercise on oxidative stress (TBARS) and BDNF in severely depressed inpatients. Eur Arch Psychiatry Clin Neurosci. 2014;264(7):605–13.
51. Stødle IV, Debesay J, Pajalic Z, Lid IM, Bergland A. The experience of motivation and adherence to group-based exercise of Norwegians aged 80 and more: a qualitative study. Arch Public Health. 2019;77:26.

Publisher's Note