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EFFECTIVENESS OF RESISTANCE EXERCISE ON COGNITIVE FUNCTION AND BEHAVIOR ASPECTS IN PEOPLE WITH COGNITIVE IMPAIRMENT: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Trabalho de conclusão de curso apresentado ao Departamento de Fisioterapia da Universidade Federal de Sergipe como um dos requisitos para graduação em Fisioterapia.

Orientadora: Lavinia Teixeira-Machado

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Trabalho de conclusão de curso apresentado ao Departamento de Fisioterapia da Universidade Federal de Sergipe como um dos requisitos para graduação em Fisioterapia, sob a orientação da Prof.ª Dr.ª Lavínia Teixeira-Machado.

Lagarto, _28_de __Julho__de 2022.

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ABSTRACT

EFFECTIVENESS OF RESISTANCE EXERCISE ON COGNITIVE FUNCTION AND BEHAVIOR ASPECTS IN PEOPLE WITH COGNITIVE IMPAIRMENT: A SYSTEMATIC REVIEW AND META-ANALYSIS. FRANCIELY OLIVEIRA DE ANDRADE SANTOS; IANA ALVES ANDRADE, LAGARTO-SE, 2022.

INTRODUCTION: We performed a systematic review and meta-analysis of randomized clinical trials that reported the influence of resistance exercise (RE) training on cognitive function and behavior aspects for people with mild cognitive impairment (MCI), dementia and Alzheimer's Disease (AD). METHODS: Six databases were used: PUBMED, PEDro, SCOPUS, PsycINFO, Web of Science, EBSCO and gray literature. RESULTS: We included 15 studies with 1,019 participants (699 women and 279 men). The pooled estimates showed that RE couldn't improve global cognitive function (95%CI, 0.30 [-0.01, 0.60], p=0.06), but could improve executive function (95%CI 0.40 [0.14, 0.66], p=0.003) and memory (95%CI, 0.35 [0.05, 0.66], p=0.02). DISCUSSION: RE performed more than twice a week can impact in global cognitive function and memory in individuals with cognitive impairment, however, few studies with low risk of bias have been performed, which makes it difficult this proposal indication. Systematic Review Registration: PROSPERO, identifier CRD42018107792.

Key-words: Resistance Training; Cognitive Impairment; Cognitive Function; Memory; Behavior.

RESUMO

EFICÁCIA DO EXERCÍCIO DE RESISTÊNCIA SOBRE A FUNÇÃO COGNITIVA E ASPECTOS COMPORTAMENTAIS EM PESSOAS COM COMPROMETIMENTO COGNITIVO: UMA REVISÃO SISTEMÁTICA E METANÁLISE. FRANCIELY OLIVEIRA DE ANDRADE SANTOS; IANA ALVES ANDRADE, LAGARTO-SE, 2022.

INTRODUÇÃO: Realizamos uma revisão sistemática e meta-análise de ensaios clínicos randomizados que relataram a influência do treinamento de exercícios resistidos (ER) na função cognitiva e aspectos comportamentais de pessoas com comprometimento cognitivo leve (CCL), demência e doença de Alzheimer (DA). MÉTODOS: Foram utilizadas seis bases de dados *PUBMED*, *PEDro*, *SCOPUS*, *PsycINFO*, *Web of Science*, *EBSCO* e literatura cinzenta. RESULTADOS: Foram incluídos 15 estudos com 1.019 participantes (699 mulheres e 279 homens). As estimativas combinadas mostraram que o ER não obteve melhora na função cognitiva global (IC 95%, 0,30 [-0,01, 0,60], p=0,06), mas pode melhorar a função executiva (IC 95%, 0.40 [0.14, 0.66], p=0.003) e memória (IC 95%, 0,35 [0,05, 0,66], p=0,02). DISCUSSÃO: Os ER's realizados mais de duas vezes por semana podem impactar a função executiva e a memória em indivíduos com déficit cognitivo, entretanto, poucos estudos com baixo risco de viés foram realizados, o que dificulta a indicação desta proposta. Registro de Revisão Sistemática: PROSPERO, identificador CRD42018107792.

Palavras-chave: Treinamento Resistido; Comprometimento Cognitivo; Função Cognitiva; Memória; Comportamento.

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SUMMARY

1. INTRODUCTION

Cognitive capacities decline during the progression of age. Although aging is a natural process, it is associated with cognitive decline, functional and social impairments [1]. The decline in memory, judgment, language, and attention can progress to mild cognitive impairment (MCI), defined as the prodromal stage that is not severe enough to require help with the usual activities of daily living [2]. One of the first clinical signs of subtype amnestic MCI is related with memory deficits [4]. Thus the decrease in volume of the hippocampal and entorhinal cortex along with factors such as increasing age, low educational level and evaluative measures can explain and predict its progression [3,5]. Another factor that can be a predictor of progression from MCI to Alzheimer's Disease (AD) is behavioral symptoms such as depression [6].

The increase in population aging and the diversity of disorders in the older adults population is a factor that needs attention for this population, mainly due to a higher prevalence of people with cognitive impairment. [5,7]. Dementia is characterized by disorders related to cognitive function such as aspects of memory, language, problem solving and can also be accompanied by behavioral changes and mood disorders, such as irritability, agitation, apathy, depression and anxiety [5,8,9]. AD is the most common dementia cause in the elderly and it is estimated that AD will become a global epidemic by 2050 [5,7].

AD is a progressive disease that causes deterioration of cognitive function due to the pathological mechanisms of formation of senile plaques and synaptic degeneration, which leads to impairment in the performance of activities of daily living and in the behavioral aspects of people with AD [10]. It represents 60-80% of the causes of dementia and its progression is divided into phases: preclinical AD, mild cognitive impairment (MCI) and finally AD dementia [5]. The rate of progression of the MCI population to AD is about 10-15% and from MCI to dementia between 5 and 20% within a year [6]. Different types of exercise like aerobic, resistance and balance are promising strategies for improving global health by improving cardiovascular function, reducing the risk factors associated with coronary heart disease and fostering psychological well-being [11,12]. Groot *et al*. [13] and Law *et al*. [14] demonstrated that physical exercise has a positive

effect on the rate of progression of cognitive decline. The benefits of physical exercise depend on a combination of factors, such as the number of repetitions and exercises, load, sequence and interval between series and increases through higher intensity, greater frequency, or longer duration [14]. Resistance exercise (RE) aims, especially, to increase muscular strength, muscular power, muscular hypertrophy and physical function [13]. Furthermore, studies showed that RE has a positive impact on cognitive function and leads to functional plasticity in the elderly [15,16]. Also, it can help reduce depression and behavioral problems in patients with dementia through various potential mechanisms, including direct beneficial brain physiological effects, cognitive stimulation, and behavioral aspects [17].

There is growing evidence in the literature showing that certain hormones act peripherally and interfere with memory storage. These hormones are released in response to stress, a certain amount and duration of stress is required. Strength training, as a stressor, operates on the release of these hormones and consequently improves memory [18]. Resistance exercise interventions stimulate the production of peripheral IGF- and brain-derived neurotrophic factor (BDNF), a protein of the neurotrophic family involved in the growth, differentiation and survival of neurons, contributing to improving cognitive function [19].

A previous study indicated that the peripheral level of IGF-1 was positively correlated with cognitive function [20]. Several reviews have already shown the positive effect of physical exercise in people with cognitive impairment and dementia on global cognitive function, and most studies use aerobic exercise to demonstrate such an effect [11,12,21,22]. Furthermore, exercise promotes short- and long-term spatial memory and executive functions in healthy elderly, this can be explained why the exercise induces hippocampal plasticity and changes in frontal lobe structures [23,24]. A recent meta-analysis (MA) demonstrated a positive effect of resistance exercise on global cognitive function in older people with MCI [16]. However, reviews have not investigated the effect of RE on behavioral aspects and on global cognitive function and more detailed, such as memory and executive function, in elderly people with MCI, dementia and AD. Extending the findings from a recent systematic review of resistance exercise in

the elderly with cognitive impairment [21], We performed a systematic review and meta-analysis of randomized clinical trials that reported the influence of RE training on cognitive function and behavior aspects for people with MCI, and older adults with dementia and AD. The focus was on resistance exercise aspects of executive function, memory and behavior.

2. METHODS

2.1. Eligibility criteria

To develop this systematic review, the protocol was submitted to the International Prospective Register of Systematic Reviews (PROSPERO) in 2018 and the registration number is CRD 42018107792. Additionally, the writing of this review followed Preferred Reporting Items for Systematic Reviews and meta-analyses (PRISMA), and had as a question: "Can resistance exercise improve cognitive function and behavioral aspects in people with MCI, and older adults with dementia and AD?", and PICOS strategy, where: P- population, I-intervention, C-intervention of comparison, O - outcomes, type S of study. Details of the PICOS strategy are in table 1.

TABLE 1. Eligibility criteria by PICOS strategy.

Category	**Eligibility criteria**
Population	People with subjective cognitive decline, mild cognitive impairment (MCI), and older adults with dementia and Alzheimer's Disease;
Intervention	Resistance exercise using free weights, pneumatic resistance systems, different elastic resistance bands (all exercises were for lower, upper limbs or both);
Comparator	Aerobic exercise, balancing exercises, no exercises, cognitive therapy and among other exercises than strength training;
Outcome	Cognitive function and behavior;

Study design	Randomized clinical trials (RCT) and quasi-RCT.

2.2. Information sources

We searched the following six databases PUBMED, PEDro, SCOPUS, PsycINFO, Web of Science, SPORTDiscus with full text (EBSCO). To search gray literature, we used the National Guideline Clearinghouse of the Agency for Healthcare Research and Quality, National Institute for Health and Care Excellence (NICE) databases, during April to June 2021. We manually collected relevant studies from the reference lists of systematic reviews with similar themes found while searching the databases and from the included studies.

2.3. Search strategy

We made specific systematic searches for each database involving key terms that met the eligibility criteria such as “resistance exercise”, “strength training”, “resistance training”, “weight training”, “neurocognitive disorder”, “cognitive impairment”, "dementia”, “Alzheimer’s disease”, “behavioral symptoms” and “cognitive function”. Changes were made to the search strategies for each database (See details of search strategy in appendix 1).

2.4. Selection process

Two researchers (FOAS and IAA) independently checked titles and abstracts found during the search through the Rayyan online manager [24]. We included studies that contemplated the above mentioned PICOS strategy (Table 1). We excluded duplicates and studies that did not meet the eligible criteria. A third researcher (LTM) resolved the disagreement. We used the Kappa test to verify Inter-examiner reliability, where values > 0.81 as almost perfect, between 0.61-0.80 is a substantial concordance, 0.21–0.40 is regular, values below that indicate no or slight concordance, requiring a repetition of the assessment [25]. After inclusion from titles and abstracts, the next step was to read the full text of the included studies. The third researcher resolved the disagreement.

2.5. Data collection process

Two researchers (FOAS and IAA) extracted the information and relevant data from the selected studies at the end of the selection and if there were any doubts or discrepancies, a third researcher (LTM) resolved the outstanding issues. To perform this step, a specific extraction form was used to remove the information and we transported data to a Windows Excel® form to organize the data of the studies: participants and assessments; study and outcome; follow up; the risk of bias. These tables contain the following information: name of the first author, year of publication, country of origin, sample size (control group and intervention group), population characteristics (sex, age, mental state, classification, groups), protocols and interventions (dose, duration, equipment, outcome measures and results). If data were not available in the table or results section or did not report relevant numerical outcome data in the text, the authors of these studies were contacted by email or we extracted the data from figures and graphs, when possible.

2.6. Study risk of bias assessment

Two researchers (FOAS and IAA) independently performed the Cochrane Risk of Bias tool for randomized trials. This tool consists of seven domains identified based on both empirical evidence and theoretical considerations. The seven domains are random sequence generation, concealment of allocation, the concealment of participants and personnel, the concealment of results evaluation, incomplete results data, selective outcomes, and other biases. This tool classifies domains as low, unclear or high risk of bias.

2.7. Synthesis methods

For the MA, we used the free and open statistical software Review Manager [26] [Computer program]. The MA calculated the treatment effects of the experimental group (RE) versus the control group (aerobic exercise, no exercise, simulated exercise) on cognitive and behavioral aspects using measures such as mean, standard deviation and number of participants in each group of each clinical trial.

The included studies show variations in intervention time, outcome measure, intervention assessments, and population with cognitive impairment, therefore, we used a random-effects model with standardized mean difference (SMD) using 95% confidence intervals (CIs) [27]. The criterion adopted to compute the weights for each study in the MA is the inverse variance, which for the random-effects model considers both individual standard deviations and between-studies variance, usually calculated using the DerSimonian-Laird method [27]. After analysis, the data were grouped into a table and the results are represented in a forest plot.

To perform the MA, some adaptations were necessary, such as follows:

1. To assess outcomes such as global cognitive function, memory, and executive function was used standardized mean difference (SMD), as it is impossible to perform direct calculations using just the mean difference. SMD standardizes the mean differences to a single scale, as well as in the computation of study weights [27].

2. For global cognitive function, a simple inversion of data from the control group to the experimental group of studies that used the Alzheimer's disease assessment scale (ADAS- cog) was performed [28,29,30], as it presents it results inversely to the other used assessments, Mini Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA). Borenstein *et al.* [27] portray that in cases like this, the inversion can be performed conveniently to resolve the difference. The same inversion was made for the cognitive function analysis with the study that used Trail Making Test Part B [29]. For the variables of executive function and memory we performed the conversion of several scales using the Z-score in three studies [28,30,31].

3. The Singh *et al.* [28] study presented their results in mean and confidence interval, so the conversion in mean and standard deviation was performed using RevMan software, version 5.4.

4. We conducted a quantitative analysis for behavioral aspects using a fixed-effect model, as only two studies reported this outcome. This model was

used because the studies assume that the same true effect is estimated [32].

We performed the heterogeneity analysis using the Higgins index (I^2) and results with an I^2<40% indicate non-significant heterogeneity; I^2 between 30 and 60% may represent moderate heterogeneity; I^2 values between 50 and 90% can show substantial heterogeneity; I^2 between 75 and 100% a significant heterogeneity [33]. For this MA, we used the chi-square test and the Higgins index (I^2), and p-values lower than 0.05 and I^2 >50% we considered significant heterogeneity. For the overall effect we assessed by Z-value.

2.9 Reporting bias assessment

We analyzed the scatter of the intervention effect estimates from individual studies against some measure of each study's size or precision, in which the outcome (intervention effect) was plotted on the vertical axis and the covariate (study size) was plotted on the horizontal axis through a funnel plot in which the precision of the estimated intervention effect increased as the size of the study increased.

3. RESULTS

3.1. Study Selection

We identified 3,357 potentially relevant studies in six databases. We did not find reports in gray literature. We removed duplicates (n=382) totaling 2,975 studies. During the reading of titles and abstracts, excluded 2,954 studies, and selected 21 studies for full reading. The Tsai *et al*. [19] study was not found for full reading and we requested the text to the corresponding author, who sent the article to read. After reading, we excluded six studies for not meeting eligibility criteria, two were not a randomized clinical trial [21,34] three did not report resistance exercise protocol [35,36,37], and one did not target global cognitive function [14]. The remaining 15 studies met the inclusion criteria [19,28,29,30,31,32,37,38,39,40,41,42,43,44,45]. The inter-examiner reliability assessed by the Kappa test (1.0 in the first step and 1.0 in the second step) indicates an almost perfect agreement between researchers. Details of the study selection process are shown in figure 1. We excluded four studies for meta-

analysis as the required information was missing despite efforts to contact the corresponding authors [39,40,44,46].

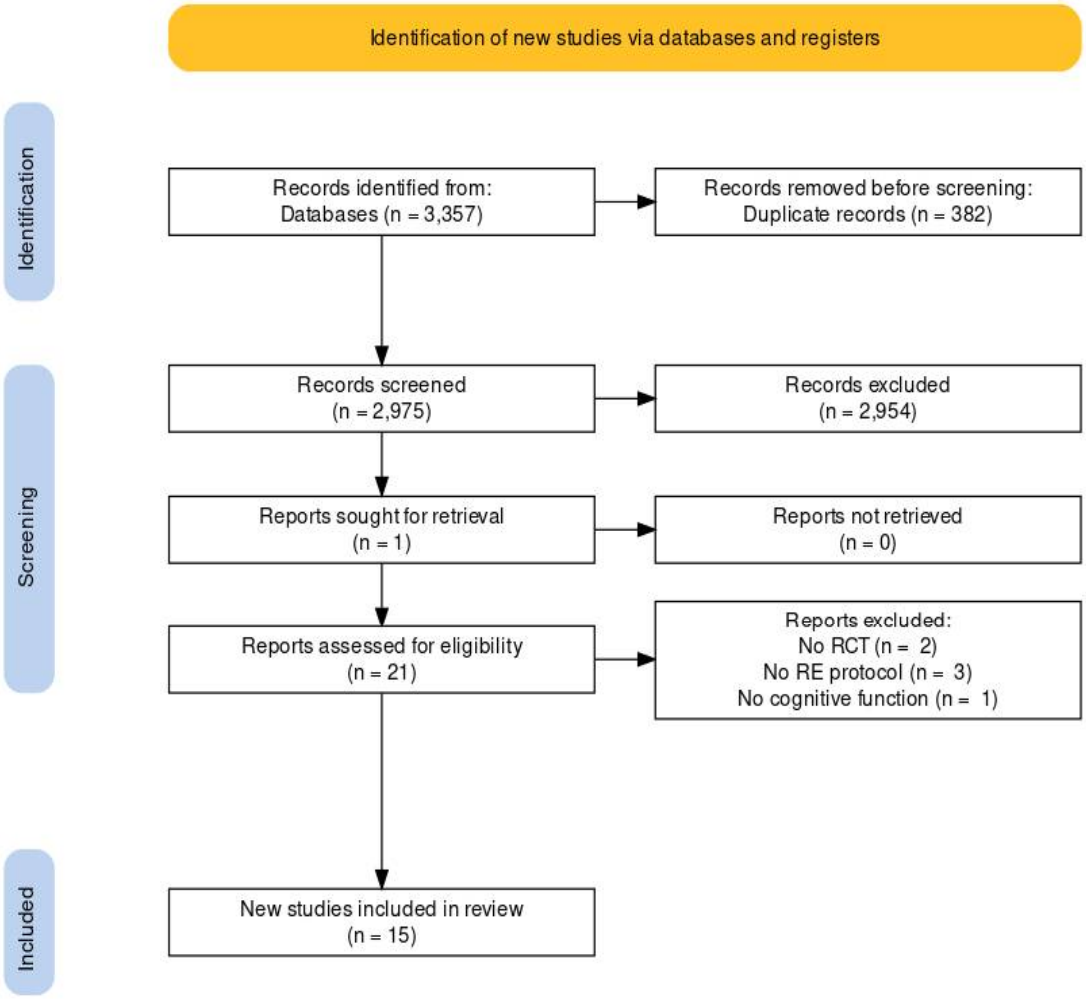


Figure 1. Study flow diagram. Abbreviations: RCT: randomized clinical trial; RE: Resistance exercise.

3.2. Study characteristics

For this review, RCTs that considered RE as a primary outcome on cognitive function and behavioral aspects as a secondary outcome were considered. This review included 15 RCT studies published in journals that were conducted from 2012 to 2020. All the included studies were in English. The total number of participants was 1,019 (72.62%women and 27.38% men). Two studies included only women in their RCT [39,41]. Of these 1,019 participants, 916 with MCI, 69 participants with dementia, and 34 participants with AD. The sample

size of participants in the included studies ranged from 34 to 100. The mean age of participants ranged from 58.68 to 95.55 years, and the treatment duration ranged from 4 to 28 weeks. Three studies had follow-up after 78 weeks [28,30,46]. The participants characteristics of the included studies are summarized in table 2.

All included studies reported the inclusion and exclusion criteria for participant selection. For the mental state, six studies included participants rated at a level with mild or moderate impairment assessment on the MMSE [19,29,32,39,40,41,42,44,45,46]. Six studies included participants with a MoCA score <26 (mild or moderate impairment assessment) [29,31,32,39,41,43]. Two studies included the MCI Peterson Criteria [28,30]. One study included older adults diagnosed with Alzheimer's and MMSE levels <20 [38]. Only four studies reported the educational level [19,29,38,45], three studies described the years of education [19,29,38], and one study described educational level as levels as uneducated, basic education, elementary school, high school, undergraduate and graduate [45].

According to the country where included studies were developed, four studies were conducted in Australia [28,30,40,46], three studies in Korea [41,43,44], two studies in Brazil [31,38], two studies in China [29,32], and the remaining four studies were conducted in Portugal [42], Taiwan [19], Spain [45] and Canada [39].

TABLE 2. Characteristics of participants.

1st Author (year)	Country	Participants							
		N	F	M	Age (Mean (SD))	Mental State	Education (years)	Groups	Assessment
Vital (2012)	Brazil	34	27	7	TG= 78.2 (7.3); SGG= 77.6 (6.5)	Moderate or severe cognitive impairment MMSE <20	TG= 5.4±3.6; SGG= 5.2±3.8	TG (n=17); SGG (n=17)	MMSE; Verbal Fluency Test
Broadhouse (2020)	Australia	84	58	26	69.5 (6.6)	MMSE >24	-	PRT+CCT (n=20), PRT+ShamCCT (n=19), CCT+ShamPRT (n=21) and ShamPRT+ ShamCCT (n=24)	ADAS-Cog
Cardalda (2019)	Spain	77	54	23	TG= 85.54 (8.09); MG= 83.76 (8.33); Control= 88.17 (7.38)	Moderate cognitive impairment	Without studies (%) 45.50 Primary 28.60 Secondary 13.00 University 13.00	TG (n=25), MG (n=23); Control (n=29)	MMSE; Pfeiffer test

Cavalcante (2020)	Brazil	67	52	15	71 (6)	MoCa <26	-	RE (n= 23); REI (n= 22); Control (n = 22)	MoCA
Chupel (2017)	Portugal	46	33	13	ST= 83.5 (5.13); Control= 82.12 (6.41)	Mild or moderate impairment MMSE	-	ST (n=24); Control (n=22)	MMSE
Hong (2017)	Korea	22	16	6	MCIcontrol= M 78.33 (5.5), F 75.11 (4.45); MCIexercise= M 78.33 (3.21), F 77.71 (3.40)	MoCA<23	-	MCI (Control=10, Exercise=12) ;	MoCA-K; Stroop Test; Ray-15 item (recall and recognition); Digit span test
Liu (2020)	China	69	11	50	Intervention = 86.77 (6.99); Control= 84.68 (6.74)	MMSE <24; MoCA<23	-	SG (n=35); AG (n=34)	MMSE, MoCA
Lu (2015)	China	45	32	13	DTG= 69 (3.83); Control = 70.43 (5.53)	MMSE>24; MoCA<26	DTG= 9.82 (2.75); Control= 9.52 (2.61)	DTG (n=22); Control (n=23)	ADAS-Cog; TMT-B The Digit Span Test – forward
Mavros (2017)	Australia	100	68	32	≥55	MCI Peterson criteria	-	PRT (n=22); PRT+CT (n=27); CT (n=24); Sham-Sham(n=27)	ADAS-Cog; WAIS III;

Nagamatsu (2013)	Canada	86	86	0	RT=73.9 (3.4); AT=75.6 (3.6); BAT= 75.1 (3.6)	MMSE>24; MoCA<26	-	RT (n=28); AT (n=30); BAT (n=28)	The Rey Auditory Verbal Learning Test
Singh (2014)	Australia	100	68	32	70.1 (6.7)	MCI Peterson criteria	-	PRT (n=22); CT (n=24); Combined (n=27); Control (n=27)	ADAS-cog; Memory: ADAS-Cog List Learning Memory Sum, Logical Memory I (immediate), Logical Memory II (delayed)
Suo (2016)	Australia	100	68	32	70.1 (6.7)	MMSE>24	-	PRT+ CCT(n=27), PRT+Sham(n=22), CCT+Sham(n=24), Sham+ sham(n=27)	ADAS-cog; Memory Awareness Rating scale; Memory Complaint Score
Tsai (2019)	Taiwan	66	38	17	AE= 66 (7.68); RE= 65.44 (6.76); Control= 65.17 (7)	MMSE >24	AE= 11.63±3.37; RE= 11.72±3.51; Control= 11.83±2.98	AE (n=22); RE (n=22); Control (n=22)	Rey 15-Item memory test; MMSE

Yoon (2016)	Korea	58	58	0	HSPT= 75 (3.46); LSST= 76 (3.94); Control= 78 (2.77)	MMSE <24; MoCA<23	-	HSPT (n=20); LSST (n=19); Control (n=19)	MMSE, MoCA-K
Yoon (2018)	Korea	65	30	13	Intervention = 73.82 (4.37); Control= 74.03 (4.27)	MMSE >22	Intervention= 8.09 ± 3.50; Control= 9.77 ± 4.44	Intervention (n=32); Control (n=33)	Rey 15-Item memory test; TMT A&B; Digit Span test; FAB

Abbreviations: F= Female; M= male; TG = Training Group; SGG = Social Gathering Group; RT = Resistance Training; AT = Aerobic Training; BaT =Balance Training; PRT = Progressive Resistance Training; CT = Cognitive Training; DTG = Dumbbell Training Group; HSPT = High Power Speed Training; LSST = Low Speed Strength Training; RE Resistance Exercise; REI= RE with Instability; AE = Aerobic Exercise; ADAS- Cog= Alzheimer's Disease Assessment Scale–Cognitive Subscale; MCI = Mild Cognitive Impairment; TMT = Trail Making Test (A&B); FAB = Frontal assessment battery; MoCA = Montreal Cognitive Assessment; MMSE = Mini mental State Examination; MoCA-K = Korean version of Montreal Cognitive Assessment; WAIS III = Wechsler Intelligence Scale for Adults.

We judged four studies with a small population (n<50) [29,38,43,42] and eleven studies with a large population (n>50) [19,28,30,31,32,39,40,41,44,45,46]. Protocol interventions included different types of RE (table 3). The types commonly used were training with a pneumatic resistance system and free weights [19,28,29,30,31,32,38,39,40,45,46], and training with an elastic band [41,42,43,44].

Only six studies reported how RE intensity was measured, from the one-repetition maximum (1RM) test [19,30,31,32,43,46]. Two studies reported how the high-intensity exercise was performed, but did not report how the measure was performed [28,40]. Two studies reported that the exercise intensity was based on the rate of perceived exertion according to repetitions (12-13 "somewhat hard" repetitions and 15-16 "hard" repetitions) [41,44]. Chupel *et al.* [42] applied the Perceived Exertion Scale (PES) test to observe the intensity. The other studies did not report how the exercise intensity was measured [29,38,39,45]. The number of sessions varied between 20 and 68 sessions. Frequency varied 2-5 times a week, training consisted of 2-3 sets of 6-15 repetitions, and the intervention duration between 45 and 100 min per session. One study did not report the intervention duration per session [32].

A limited number of studies addressed that the sessions were conducted by physical educator and physical therapists [28,40,46], exercise instructor/coach/fitness trainer [30,32,41,44], and one study was supervised by physical educator students [29]. Regarding the attendance rate, the studies reported attendance rate were greater than 70%. Yoon *et al.* [41] study reported 59% attendance rate, Chupel *et al*. [42] 66.66%, Yoon *et al.* [44], 68.75%, and Broadhouse *et al.* [46], 68.42%. Among the 15 included studies, five studies did not apply any type of physical activity or continued regular lifestyle routine in the control group [29,38,42,43,45], three studies continued regular lifestyle routine and/or stretching [19,31,44], three studies compared RE with aerobic exercise [32,39,41], and four studies compared RE with sham computerized cognitive training and sham exercise [28,30,40,46].

Table 3: Description of protocol studies.

			Intervention						
1st Author (year)	**Study Design**	**Time points measured**	**Modality**	**Intervention duration**	**Frequency (days/ week)**	**Session (min)**	**Training session**	**Types of Control**	**Outcome**
Broadhouse (2020)	RCT	3 points: Baseline, 26 weeks and 78 weeks follow up	Pneumatic resistance system	26	2 to 3	90	5-6 exercises, 3 sets, 8 repetitions	Sham cognitive and sham exercise	RE improved global cognitive function and executive function in older adults with MCI
Cardalda (2019)	RCT	2 points: Baseline and post intervention	Lower limbs	12	2	60	2-3 sets, 10-15 repetitions	Not follow any type of physical activity	RE significant improvements in cognitive state
Cavalcante (2020)	RCT	2 points: Baseline and post intervention	Free-weights and machines	12	3	60	7 exercises, 3 sets, 10–15 repetition maximum (RM);	Health education seminars or stretching and relaxation classes	RE did not significantly improve performanc in any cognitive domain (Executive and memory function)
Chupel (2017)	RCT	2 points: Baseline and post intervention	Yellow and red elastic bands	28	2 for 16 weeks and 3 for 12 weeks	45	1/2 sets, 10-12 repetitions of 8-10 exercises	Not follow any type of exercise program	RE significant improved cognitive function in older with MCI
Hong (2017)	RCT	2 points: Baseline and post intervention	Elastic bands of different elasticities	12	2	60	(65%-1RM), 15-repetition maximum	Regular lifestyle routine	No significant improvement on cognitive function,

									changes observed only working memory
Liu (2020)	RCT	2 points: Baseline and post intervention	Isotonic weight training machines	4	5	over the course of 1 day	(40%-50% of 1-repetition maximum); 2 sets of 12 repetitions	Aerobic training	There was improvement on cognitive function, but was not improvement on behavior aspects.
Lu (2015)	RCT	2 points: Baseline and post intervention	Handheld dumbbell-spinning exercises with two built-in eccentric pendulums	12	3	60	Exercise lasted 1–2 minutes with repetitions set at 4–5 minutes	Regular lifestyle routine	RE improved global cognitive function in older with MCI
Nagamatsu (2013)	Sinngle-Blinded RCT	Baseline, mid-point, and trial completion	Keiser® Pressurized Air system and free weights	26	2	60	2 sets of 6–8 repetitions	Aerobic training (AT) and Balance and tonne training (BAT)	RE improved better performance in associative memory and executive function
Mavros (2017)	Double-blind, Double-sham RCT	3 points: Baseline, 26 weeks, and 78 weeks	Keiser pneumatic resistance machines	26	2 Follow-up over 78 weeks	60 to 100	3 sets of 8 repetitions of each of 5–6 exercises/session	Sham cognitive and sham exercise	RE improved cognitive function in people with MCI
Singh (2014)	Double-blind and double-sham RCT	Baseline, 26 weeks, and 78 weeks	Keiser® Pressurized Air system	26	2	60 to 100	3 sets of 8 repetitions of each of 5-6 exercises	Sham cognitive and sham exercise	RE improved global cognitive function in older with MCI

Suo (2016)	Double-blind RCT.	2 points: Baseline and post intervention	Pneumatic resistance machines	26	2	90	3 sets of 8 repetitions of each of 5–6 exercises/session	Sham cognitive and sham exercise	RE improved global cognitive function in older with MCI
Tsai (2019)	RCT	2 points: Baseline and post intervention	Free-weights and bodybuilding machines	16	2	60	60-75% of 1RM, 3 sets of 10 repetitions	Static stretching, three times a week	RE improves cognitive performance
Vital (2012)	Clinical trial	2 points: Baseline and post intervention	Peck Deck, Pull Down, Leg Press, Triceps Pulley	16	3	60	3 sets of 20 repetitions	Not follow any type of physical activity	No significant differences of strength training on memory and cognition in elderly with AD
Yoon (2016)	RCT	2 points: Baseline and post intervention	LSST: Blue color elastic bands; HSPT: Green color elastic bands	12	2	60	HSPT: 2/3 sets,12–15 repetitions; LSST: 2/3 sets, 8–10 repetitions	Aerobic training	RE improved cognitive function in older with MCI
Yoon (2018)	RCT	3 points: Baseline, 8 weeks and 16 weeks	Blue elastic bands	16	3	60	2-3 sets,12-15 repetitions	Regular lifestyle routine, static and dynamic stretching per once a week	RE improvement cognitive function in older with MCI, but no significant changes in memory, cognitive flexibility or working memory

Abbreviation: RCT = randomized clinical trial; RE = resistance exercise; MCI = mild cognitive impairment; CON= control

3.3. Risk of bias of included studies

We judged all RCTs as high, unclear, or low risk of bias in different domains according to the Cochrane recommendation [47]. Figure 2 summarizes the assessment. All studies presented a high risk of bias in at least one domain. Of the 15 studies, six studies described the process of generating a random sequence for participants randomization [28,29,31,40,45,46], three studies mentioned how the groups were allocated, and how this process of selection of participants for each group was [28,29,45]. The Liu *et al*. [32] study addressed the allocation process, thus characterizing a selection process with an unclear risk of bias. Just Vital *et al*. [38] study did not report the randomization and allocation process, which characterized it as a high risk of bias.

The blinding participants domain had the largest number of studies (n=11) with a high risk of bias because as it is an exercise intervention, it is impossible or difficult to blind them. However, three studies [28,30,31] were able to perform blinding and obtained a low risk of bias in this domain. One study was uncertain, as it did not report how they conducted this topic [40].

Regarding detection bias, nine studies showed a lack of clarity in the description of blinding to assess the outcome [19,30,39,41,42,43,44,45,46], and one study presented a high risk, because blinding was not performed in the outcome assessment [31].

Ten studies obtained in their analysis a high risk of bias in the attribution, as they presented incomplete data due to a significant loss of participants, and because they did not perform the necessary analysis to address such losses [19,29,30,38,39,41,42,43,44,46]. The other studies performed intention to treat (ITT), justifying their low risk of bias [28,31,32,40,45]. Most studies showed a low risk of bias in the data reporting domain. Only Broadhouse *et al*. [46] and Nagamatsu *et al*. [39] studies did not report all the outcome measures mentioned in the study.

We defined as other risks of bias studies that did not present limitations or did not report the protocol that was necessary to perform the study. Thus, four studies

[28,39,42,40] were analyzed as high risk and the rest comprised the low-risk criteria [19,29,30,31,32,38,41,43,44,45,46].

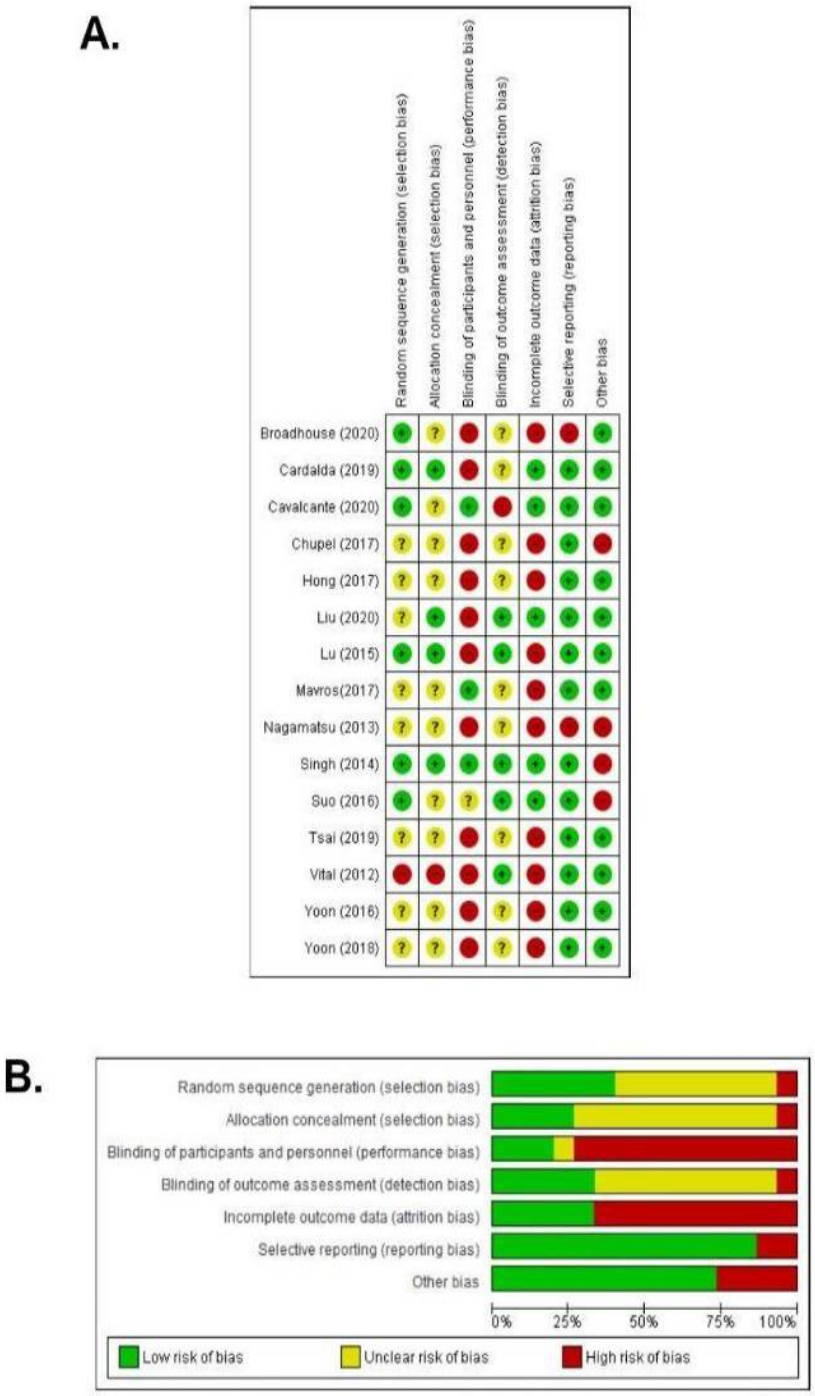


Figure 2. Risk of bias summary and graph: Review the authors' judgments on each risk of bias item for each included study (A) and domain percentages (B) across all included studies.

3.4. Results of individual studies

Global Cognitive Function (GCF)

We included ten studies (383 participants) in the MA for global cognitive function outcome, due to RE pooling data from six studies in machines subgroup (258 participants) [19,28,29,30,31,32,45] and four studies elastic resistance bands subgroup (125 participants) [41,42,43]. We tested the hypothesis that RE is able to promote global cognitive function in participants with mild-to-moderate cognitive impairment. The study by Vital *et al*. [38] with AD participants was excluded from MA because this study was not RCT. Different assessments were used to investigate GCF, such as MMSE, MoCA and Adas Cog. Four studies used the MMSE [19,41,42,45] and three studies used to MoCA assessments [31,32,43] and three studies used the Adas Cog assessment [28,29,30]. The main total results showed heterogeneity, $Tau^2 = 0.13$; $Chi^2 = 19.15$, df=9 (p=0.02); $I^2 = 53\%$. The test for overall effect was Z=1.91 (p= 0.06). Subgroup differences were $Chi^2=0.22$, df=1 (p=0.64), $I^2 = 0\%$. In the subgroup analysis, the subgroup that performed the RE and used the machine had the following main results for heterogeneity $Tau^2=0.18$; $Chi^2=14.14$, df = 5 (p= 0.01); $I^2 = 65\%$, and general effect Z=1.13 (p=0.26). In the elastic bands subgroup, the main result for heterogeneity was $Tau^2=0.07$; $Chi^2 =4.42$, df =3 (p=0.22); $I^2=32\%$, and general effect Z=1.70 (p=0.09).

Concerning the *chi* squared statistic, the first p-value associated with the "Machines" subgroup was lower than 0.05 (p=0.02), which provided evidence of heterogeneity among the studies in this subgroup. This is also reflected in the I^2 statistic (equal to 64%, which is considered moderate/relative high according to the criterion adopted in this work). The second p-value, in turn, which is associated with the "elastic resistance bands" subgroup, is higher than 0.05 (p=0.22), thus not suggesting heterogeneity among the studies in this subgroup (I^2 equal to 32%, a comparatively low value). When taken together, however, both subgroups yield p=0.02 and $I^2=53\%$, indicating that, although there is a significant heterogeneity, it can be considered moderate in this case.

When analyzing the statistics with the forest plot for the "Machines" subgroup, it can be seen that two studies are concentrated on the left side [19,32], whereas four

studies are concentrated on the right side [28,29,30,31]. Considering that the weights associated with each of them are roughly the same, the main source of heterogeneity in this case is assumed to be from the study by Lu *et al.* [29], which is far from the threshold, on the right side. As for the "Elastic resistance bands" subgroup, although the weights from each study vary considerably, all of their confidence intervals intercept, resulting in a comparatively lower heterogeneity. See details in figure 3.A. The funnel plot is in figure 4.A.

As for the Z scores, both individual subgroups (p=0.26 and p=0.09 for the "Machines" and "Elastic resistance bands" subgroups, respectively) and overall analysis (p=0.06) are statistically not significant, that is, none of the interventions could provide significant improvements in terms of global cognitive function. Although the studies show high standard deviations, it is worth mentioning that the final p value is close to the established limit (0.05) and with moderate heterogeneity in the analysis, associated with the fact that the number of samples used in the second subgroup is significantly smaller than the one used in the analysis. Than that of the first group, a more in-depth analysis should be carried out to fully validate these findings considering a larger number of studies, especially based on the same intervention (Figure 3A).

The funnel plot for global cognitive function indicates that most studies are symmetric and concentrated around the central line at relatively low standard errors, indicating that they do not present a high risk of bias. However, for the Lu *et al*. [29]; Yoon *et al*. [41] studies, both SMD and errors increase considerably, moving to the right side of the plot, indicating a possible risk of bias and heterogeneity for these studies (Figure 4A).

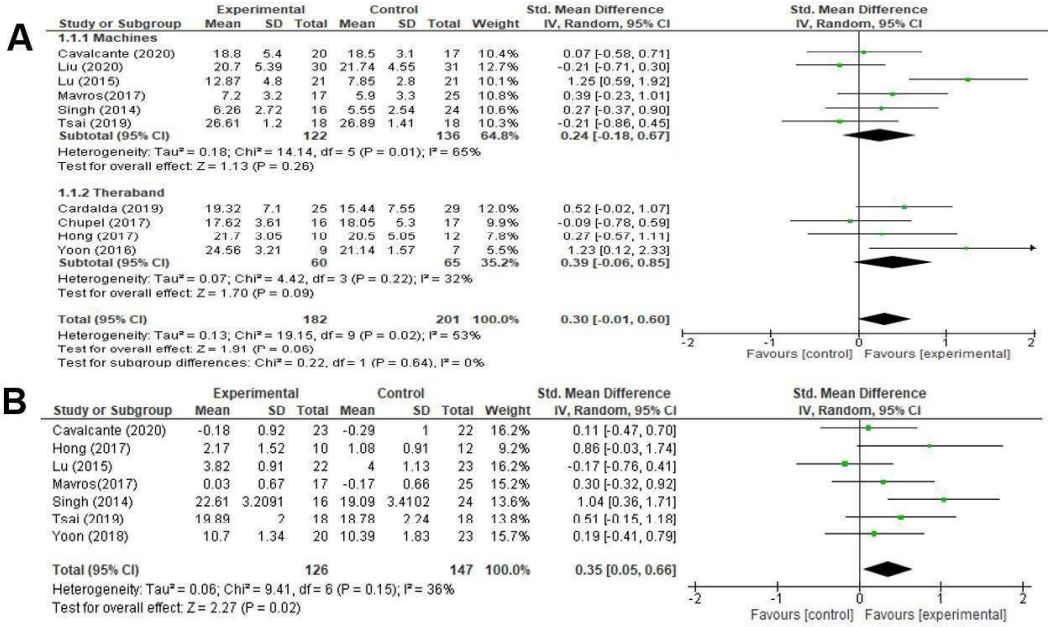


Figure 3. Meta-analysis and forest diagram of the RE effect in participants with mild-to-moderate impairment on global cognitive function (A) and memory (B). Abbreviations: CI: confidence interval, SE: standard error, Std.: standard, IV: inversor variance.

Memory

To observe the effect of RE on memory, seven studies (273 participants) assessed memory [19,28,29,30,31,43,44]. We tested the hypothesis that RE can promote memory improvement in participants with mild-to-moderate cognitive impairment. The main results were heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 9.41$, df=6 (p=0.15); $I^2 = 36\%$ and the test for the overall effect was Z=2.27 (p=0.02). See figure 3B for details. Based on p values (p=0.02), statistical significance was found in this analysis in addition to a good consistency in the results due to a low heterogeneity (I^2=36%). Although the study by Hong *et al*. [43] presents a high standard deviation, (which is likely the reason why its associated weight is low compared to the other studies), the studies by Mavros *et al*. [30], Singh *et al*. [28] Tsai *et al*. [19] and Yoon *et al*. [41] present similarity and favor the experimental group (Figure 3).

Regarding its funnel plot (Fig. 4.B), note that the general behavior of the studies is to concentrate around the central line symmetrically, which indicates a low risk of bias. Two studies [28,43] are relatively distant from the threshold, but since the meta-

analysis provided consistent results in terms of heterogeneity and significance, it can be concluded that the overall risk of bias is not considerable.

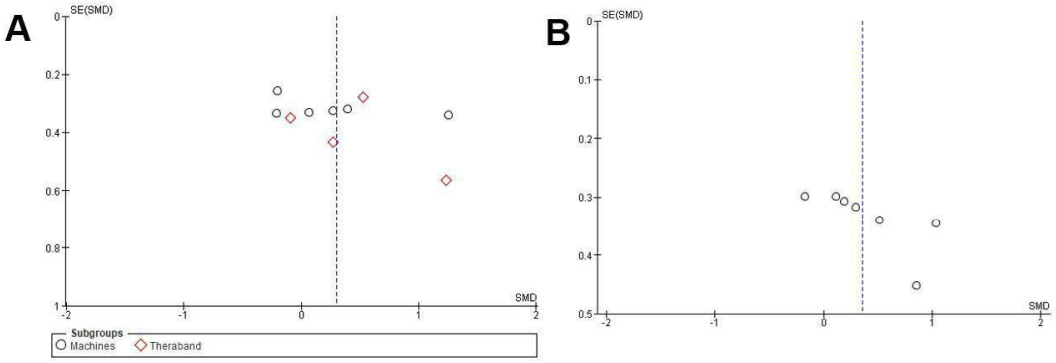
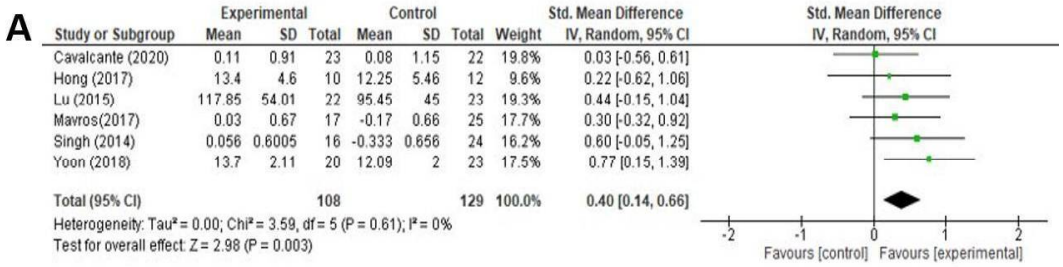


Figure 4. A. Studies distribution to analyze publication bias in global cognitive function by funnel plot. **B.** Studies distribution to analyze publication bias in memory by funnel plot.

Executive function

To test the hypothesis that RE promotes executive improvement in participants with mild-to-moderate cognitive impairment, we selected six studies (237 participants) for executive function assessment [28,29,43,30,44,31]. The analysis showed heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 3.59$, df=5 (p= 0.61); $I^2 = 0\%$ and the test for the overall effect Z=2.98 (p=0.003) (see figure 5A).



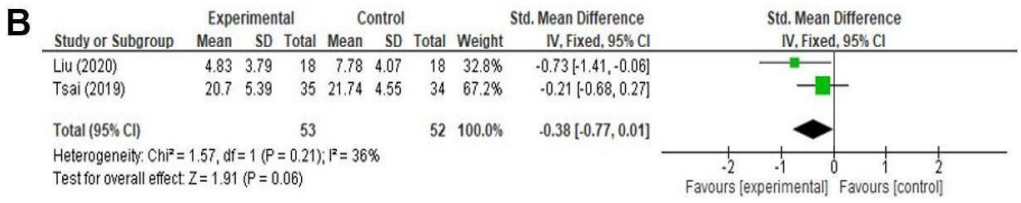


Figure 5. Meta-analysis and forest diagram of the RE effect in participants with mild-to-moderate impairment on executive function (A) and behavior aspect (depression) (B). Abbreviations: CI: confidence interval, SE: standard error, Std.: standard, IV: inversor variance.

The result was significant (p value=0.003), and favored the experimental group (RE) with zero heterogeneity. Only the Cavalcante *et al*. [31] study was between the vertical line with an approximate value of 0 in the forest plot. The other studies are consistent, although Singh *et al*. [28] and Hong *et al*. [43] studies present a high standard error (see funnel plot in figure 6A). The funnel plot indicates that the studies presented a symmetric behavior at relatively low standard errors, which did not suggest a considerable risk of bias.

Behavior aspects

Only two studies [19,32] (105 participants) observed the effect of RE on behavioral aspects, mainly depression. Liu *et al*. [32] used the geriatric depression scale for their analysis, while Tsai *et al*. [19] used the Beck depression inventory (BDI). These studies demonstrated non-significant effects for the variable investigated. Although the number of studies (n=2), MA was performed, which indicated Heterogeneity: $Chi^2=1.57$, df=1 (p=0.21); $I^2=36\%$ and the test for the overall effect was Z=1.91 (p=0.06) (See Fig. 5B).

Despite the small number of studies, interesting results can be observed. The Liu *et al*. [32] study presents a low weight compared to the Tsai *et al*. [19] study, most likely due to the significantly lower number of samples used in this work and slightly higher standard error obtained. Besides, the overall heterogeneity is low ($p > 0.05$ and $I^2=36\%$), and although no statistical significance can be inferred, the p-value is close to the threshold adopted (0.05), and both studies tend to favor the intervention. Thus, it must conduct further investigation into behavior aspects to better assess and validate these results. The same conclusions are before can be drawn from its funnel plot (Fig. 6B).

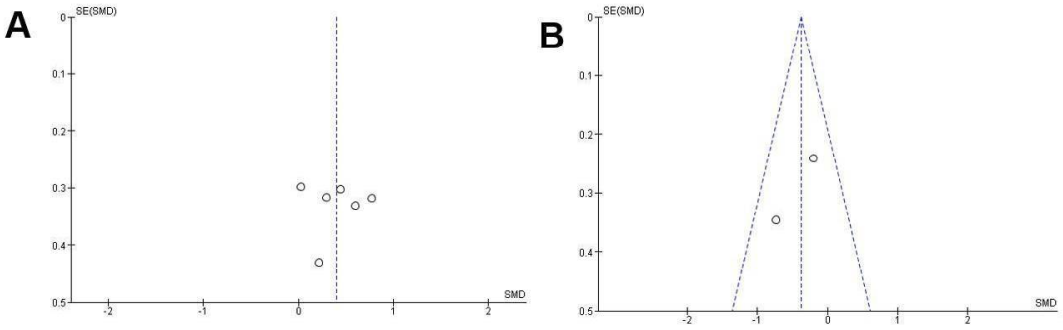


Figure 6. A. Studies distribution to analyze publication bias in executive function by funnel plot. **B.**Studies distribution to analyze publication bias in behavior aspects by funnel plot.

4. DISCUSSION

4.1. Summary of main results

Our systematic review and meta-analysis consisted of 14 RCTs and one quasi-RCT. Most of these studies reported a significant positive association between RE and GCF in people with cognitive impairment [28,29,30,32,34,40,41,42,44,45,46], which corroborates the findings of the previous reviews [16,21,48,49]. Three included studies in this review did not report significant impact of RE on overall cognition. These studies had limitations such as small sample size and did not observe possible variables that can affect cognitive functions such as smoking, physical frailty and alcohol and caffeine consumption, for example [31,38,43].

Previous reviews have addressed the effect of different types of exercise in the cognitive function of elderly people with cognitive impairment, such as aerobic, balance, and strength [21,48,49]. Two systematic reviews and meta-analysis [16,50] have already reported the association of RE and cognition in healthy elderly people. However, our systematic review specified the modality for RE and analysed its effect not only on global cognitive function, but also on memory, executive function, and behavioral aspects in people with MCI, older adults with dementia and AD.

The review conducted by Huang *et al.* [51] found that RE can delay cognitive decline in patients with cognitive impairment. Our review demonstrated that RE had no

significant effect on global cognitive function due to the heterogeneity of the included studies, which can be explained by the fact that our review did not perform sensitivity analysis in relation to sample size, assessment differences and application time.

Sanders *et al.* [52] addressed that shorter session duration and higher frequency of sessions during the week are positive predictors for exercise in people with cognitive impairment. The studies included in our review had a frequency of 2 to 3 sessions per week lasting 40 to 60 min, and had not a positive effect on cognitive function. Vital *et al*. [38] had a frequency of three days per week and did not report any improvement in the participants' cognitive function, but a population with greater cognitive impairment (DA) may have influenced this finding. Liu *et al*. [32] had a weekly frequency of five days a week and reported a good performance in cognitive function in participants with dementia. Cavalcante *et al*. [31] and Lu *et al*. [29] attended three days a week and disagreed with each other. Cavalcante *et al*. [31] did not perform well in cognitive function, while Lu *et al.* [29] performed well. The heterogeneity and the size effect of the included studies in this review made this interpretation difficult. Studies focusing on frequency and duration to promote cognitive benefits in this population are necessary to recommend RE for this outcome, especially in studies in which the population has greater cognitive impairment.

The individual findings of some studies included in this review showed that the RE is related to the increase in circulating levels of IGF-1, the cytokine IL-10, hemoglobin, and hippocampal neurogenesis, increases in the cortical thickness in the posterior cingulate and the formation of patterns of functional plasticity in these brain regions [19,39,40,42]. Aerobic and multicomponent exercise are associated with modest improvements in attention and processing speed, executive function, and memory in both healthy older adults and the cognitively impaired [52]. Furthermore, exercise had a moderate positive effect on global cognition but not on executive function or memory [52]. Our review presented results with a significant effect and with low heterogeneity of RE on function executive and memory.

Physical exercise practice significantly reduces behavioral problems. Law *et al*. [12] demonstrated that exercise can induce the release of neurotrophic factor and certain neurotransmitters (norepinephrine, serotonin) and facilitate brain plasticity and

the balance of the neurotransmitter system, which modulate behavioral problems. A study by Chen *et al.* [53] demonstrated that RE program on depression and behavior problems in elderly wheelchair users with dementia improved functional health, sleep quality, and reduced depression. In this review, only two studies with a small sample size observed behavioral aspects [19,32]. These individual studies demonstrated non-significant effects, and in our analysis no statistical significance can be inferred because the p-value is close to the threshold adopted (0.05), although tend to favor the intervention. This result may have occurred because the control group of the studies in question applied aerobic exercise as a control wich can also promote benefits to reduce depression.

4.2. Implications for practice

Physical exercise is essential for physical function, strength gain, risk of falls, and cognitive function. Overall, our review suggests that resistance exercise has positive and significant impacts on global cognitive function, executive function, memory, especially when performed for more than 12 weeks, with a frequency of at least three times per week.

Dementia and AD are neurodegenerative progressive diseases, and MCI can progress to these conditions. RE is a non-pharmacological intervention, with few adverse effects, low cost, and easy to apply, that promotes social/psychological benefits, due to its realization in groups, and biological/structural by releasing neurotrophic factors such as Brain-derived Neurotrophic Factor (BDNF) and decreasing atrophy of the brain's white matter [43,46,54]. Additionally, it has been shown in the literature that one in four people with MCI can develop AD, especially in underdeveloped countries. In this regard, RE can be a effective approach to prevent or avoid progression in individuals with MCI, because it acts on the factors modifiable diseases by improving cognitive function and behavioral health [12,53,54]. However, RE is an understudied resource, especially in low- and middle-income countries, as observed in the studies present in our review, where few included studies were carried out in underdeveloped and developing countries [19,29, 31,32, 38, 41,43,44]. Our review found that exercise with resistance bands performs well on cognitive function, which makes ER a low-cost, easy-access, and high-benefit intervention.

4.3. Implications for research

Research in people with severe dementia and AD performing RE is scarce, particularly to investigate the outcomes of cognitive function and behavioral aspects. For instance, it is difficult for this population to maintain continuity and periodicity during the intervention, due to cognitive fluctuation and advanced age [14,17,54]. Thus, our results were limited to people with mild cognitive impairment and mild or moderate dementia and AD. Only one study reported dementia [32] and one study reported AD [38] for cognitive function.

Our review used only RCT to observe the effect of RE on cognitive function, memory and executive function, as well as behavioral aspects. However, most of the included studies had a high risk of bias, which implies a low methodological quality, being necessary trials that follow the criteria of a good RCT using the current CONSORT statement and guidelines.

It is important to conduct studies with adjusted period of intervention, clearer exercise protocols and description of exercise intensity, plus longitudinal follow-up to observe post-intervention effects on cognitive function and brain protection.

Evidence has shown the impact of behavioral aspects on cognitive impairment [12]. Only two included studies reported RE on behavioral outcomes, which implies the need for more research focused on this aspect in this population, investigating other behavioral changes in neurodegenerative diseases, including depression. In future, research could follow the current recommendations of the harmonized cognitive assessment protocol to improve cognitive assessment tools and thus promote the process of conducting, analyzing, and comparing studies.

4.4. Study limitations and potential biases in the review process

Although we defined the inclusion criteria, the population and intervention were very heterogeneous due to different MCI criteria and intervention time, cognitive and behavioral assessment, and methodological fragility, such as unclear randomization process and blinding of assessors. Another study limitation was the small number of studies that evaluated behavioral aspects, memory and executive function, which made it difficult to delineate the possible benefits of RE in these results. Additionally, many studies had a control group using another type of exercise, which may have hampered and interfered with more positive results regarding resistance exercise.

This systematic review and meta-analysis synthesized studies that revealed important findings about resistance exercise in cognitive function, memory, executive function and depression in people and older adults with MCI, dementia and AD. Our study suggests that resistance exercise had an overall positive effect on executive function and memory. However, it showed no positive effect on global cognitive function and depression. These results should be interpreted carefully, considering that the meta-analysis found moderate heterogeneity of studies that evaluated cognitive function and the limited number of studies that evaluated behavioral aspects.

OTHER INFORMATION

Registration and protocol

The protocol for this review was submitted to the International Prospective Register of Systematic Reviews (PROSPERO), which was approved under the following registration number: CRD42018107792.

Support

This review was developed without financial support.

Competing interests

There were no conflicting outcomes among the review authors.

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APPENDIX

APPENDIX 1- Search strategies

Pubmed

("Neurocognitive Disorders" [MeSH Terms] OR "Cognitive Dysfunction" [MeSH Terms] OR "Memory Disorders" [MeSH Terms] OR Memory Deficits (Text Word) OR Age-Related Memory Disorders (Text Word) OR Memory Deficit (Text Word) OR Mild Cognitive Impairment (Text word) OR cognitive impairment (Text Word) OR Cognitive Decline (Text word) OR "Alzheimer disease"[MeSH Terms] OR Alzheimer disease [Text Word] OR Alzheimer Dementia [Text Word] OR Senile Dementia [Text Word] OR Presenile Dementia [Text Word] OR "Dementia" [MeSH Terms]) AND ((("Resistance training" [MeSH Terms] OR Resistance training [Text Word] OR Strength Training [Text Word] OR ("exercise"[MeSH Terms] OR Exercise [Text Word]) AND program [All Fields] OR Weight Lifting Strengthening Program[Text Word] OR Weight Bearing Strengthening Program [Text Word] OR Weight-Lifting Exercise Program [Text Word] OR Weight-Lifting Strengthening Program[All fields]) OR "Resistance band exercise" [Text Word] OR strengthening Exercises [Text Word])) AND (Cognition [MESH Terms] OR cognition [Text Word] OR cognitive function[Text Word] OR Behavior [MESH Terms] OR Behavioral Symptoms [MESH Terms] OR behavior aspects [Text Word])

Web of science

TS= ("Neurocognitive Disorders" OR "Cognitive Dysfunction" OR "Memory Disorders" OR Memory Deficits OR Age-Related Memory Disorders OR Memory Deficit OR Mild Cognitive Impairment OR cognitive impairment OR Cognitive Decline OR Alzheimer disease OR Alzheimer Dementia OR Senile Dementia OR Dementia) AND
TS= (Resistance training OR Strength Training OR Resistance Exercise OR program Resistance training OR Weight Lifting Strengthening Program OR Weight Bearing Strengthening Program OR Weight-Lifting Exercise Program OR Weight-Lifting Strengthening Program OR "Resistance band exercise" OR "strengthening Exercises") AND
TS=(Cognitions OR Cognitive Function OR Behavior OR Behavioral Symptoms OR b ehavior aspects)

SCOPUS

TITLE-ABS-KEY("Neurocognitive Disorders" OR "Cognitive Dysfunction" OR "Memory Disorders" OR "Memory Deficits" OR "Age-Related Memory Disorders" OR "Mild Cognitive Impairment" OR "cognitive impairment" OR "Cognitive Decline" OR "Alzheimer disease" OR "Alzheimer Dementia" OR "Senile Dementia" OR Dementia) AND TITLE-ABS-KEY("Resistance training" OR "Strength Training" OR "Resistance Exercise" OR "program Resistance training" OR "Weight Lifting Strengthening Program" OR "Weight Bearing Strengthening Program" OR "Weight-Lifting Exercise

Program" OR "Weight-Lifting Strengthening Program" OR "Resistance band exercise" OR “strengthening Exercises”) AND TITLE-ABS-KEY(Cognitions OR "Cognitive Function" OR Behavior OR "Behavioral Symptoms" OR "behavior aspects")

PsycINFO

"alzheimer disease" AND Keywords: "mild cognitive impairment" OR Keywords: dementia AND Title: "resistance training" OR Keywords: "Resistance Exercise" OR Keywords: "Weight training" AND Keywords: "cognition" OR Title: "Behavioral Symptoms"

PEDro

TITLE-ABS Alzheimer disease mild cognitive impairment dementia "resistance training" OR Title: cognit* Behavioral*

EBSCO

Keywords: "alzheimer disease" OR Keywords: "mild cognitive impairment" OR Keywords: dementia AND Keywords: : "resistance training" OR Keywords: "Resistance Exercise" OR Keywords: "Weight training" AND Keywords: "cognition" OR Keywords: : "Behavioral Symptoms"

National Guideline Clearinghouse of the Agency for Healthcare Research and Quality

resistance exercise OR strengh training AND Mild cognitive impairment OR dementia OR alzheimer disease AND cognition

National Institute for Health and Care Excellence (NICE)

resistance exercise AND Cognition AND Mild cognitive impairment OR dementia OR alzheimer disease

ANNEX

ANNEX 1- Journal Rules

Article structure

General Format

- Manuscripts should be typed double-spaced, and numbered, with wide margins. Computer-generated illustrations must be of the high quality of professional line drawings or they will not be accepted.
- The title page should contain: title of paper; author(s); laboratory or institution of origin with city, state, zip code, and country; complete address for mailing proofs; telephone, fax number, and email address (when available, the email address will appear in the correspondence footnote of the published article).
- References, footnotes, and legends for illustrations should be typed on separate sheets, double spaced.
- Illustrations should be identified with figure number and author(s) name; when necessary the top should be clearly marked.
- Each table should be typed on a separate sheet and double spaced.
- All dimensions and measurements must be specified in the metric system. Standard nomenclature, abbreviations and symbols (specified by Royal Society Conference of Editors. Metrication in Scientific Journals. Am. Scient. 56:159-164:1968) should be used throughout.
- Italics should not be used for the purpose of emphasis.

Length of Paper

The Editors insist upon clear, concise statement of facts and conclusions. Fragmentation of material into numerous short reports is discouraged. All accepted papers are subject to editorial revision and copyediting. Authors should avoid redundancy between sections of text and illustrations and text. The Editors may recommend that appendices and tables containing extensive data be published in the electronic version of *Alzheimer's & Dementia* and only referenced in a footnote in the print edition.

Subdivision - numbered sections

Divide your article into clearly defined and numbered sections. Subsections should be numbered 1.1 (then 1.1.1, 1.1.2, ...), 1.2, etc. (the abstract is not included in section numbering). Use this numbering also for internal cross-referencing: do not just refer to 'the text'. Any subsection may be given a brief heading. Each heading should appear on its own separate line.

Appendices

If there is more than one appendix, they should be identified as A, B, etc. Formulae and equations in appendices should be given separate numbering: Eq. (A.1), Eq. (A.2), etc.; in a subsequent appendix, Eq. (B.1) and so on. Similarly for tables and figures: Table A.1; Fig. A.1, etc.

Essential title page information

- ***Title.*** Concise and informative. Titles are often used in information-retrieval systems. Avoid abbreviations and formulae where possible.
- ***Author names and affiliations.*** Please clearly indicate the given name(s) and family name(s) of each author and check that all names are accurately spelled. You can add your name between parentheses in your own script behind the English transliteration. Present the authors' affiliation addresses (where the actual work was done) below the names. Indicate all affiliations with a lower-case superscript letter immediately after the author's name and in front of the appropriate address. Provide the full postal address of each affiliation, including the country name and, if available, the e-mail address of each author.
- ***Corresponding author.*** Clearly indicate who will handle correspondence at all stages of refereeing and publication, also post-publication. This responsibility includes answering any future queries about Methodology and Materials. **Ensure that the e-mail address is given and that contact details are kept up to date by the corresponding author.**
- ***Present/permanent address.*** If an author has moved since the work described in the article was done, or was visiting at the time, a 'Present address' (or 'Permanent address') may be indicated as a footnote to that author's name. The address at which the author actually did the work must be retained as the main, affiliation address. Superscript Arabic numerals are used for such footnotes.

The title should not be longer than 85 characters, including spaces between words. Only the first word of the title should be capitalized.

Highlights

Highlights are mandatory for this journal as they help increase the discoverability of your article via search engines. They consist of a short collection of bullet points that capture the novel results of your research as well as new methods that were used during the study (if any).

Highlights should be submitted in a separate editable file in the online submission system. Please use 'Highlights' in the file name and include 3 to 5 bullet points (maximum 85 characters, including spaces, per bullet point).

Abstract

Each paper submitted must be accompanied by a structured abstract of 150 words or less to appear after the title. The abstract should be suitable for use by abstracting journals and must include the following headings using the IMRAD format (specifically, INTRODUCTION, METHODS, RESULTS, DISCUSSION, using all uppercase letters followed by a colon and space), not exceeding 150 words. A list of 5 to 15 keywords or short phrases suitable for indexing terms should be typed at the bottom of the abstract page accompanying the manuscript. These terms will be printed with the paper following the abstract.

Research in Context

Alzheimer's & Dementia requires a section called "*Research in Context*". Authors must provide a summary, similar to an abstract, for inclusion during the online submission process. In the summary of 150 words or less, authors must place their results or findings into context with previous work. Please refer to the top of the "Guide for Authors" or refer to the editorial for (Volume 8, Issue 3, Page 171, May 2012) for further details.

Figure captions

Ensure that each illustration has a caption. Supply captions separately, not attached to the figure. A caption should comprise a brief title (**not** on the figure itself) and a description of the illustration. Keep text in the illustrations themselves to a minimum but explain all symbols and abbreviations used.

Tables

Number tables consecutively in accordance with their appearance in the text. Place footnotes to tables below the table body. Indicate footnotes in this order: *,†, ‡, §, ¶, #, **, ††,‡‡, §§, ¶¶, ##. Avoid vertical rules. Be sparing in the use of tables and ensure that the data presented in tables do not duplicate results described elsewhere in the article.

References

Citation in text

Please ensure that every reference cited in the text is also present in the reference list (and vice versa). Any references cited in the abstract must be given in full. Unpublished results and personal communications are not recommended in the reference list, but may be mentioned in the text. If these references are included in the reference list they should follow the standard reference style of the journal and should include a substitution of the publication date with either 'Unpublished results' or 'Personal communication'. Citation of a reference as 'in press' implies that the item has been accepted for publication.

Reference links

Increased discoverability of research and high quality peer review are ensured by online links to the sources cited. In order to allow us to create links to abstracting and indexing services, such as Scopus, CrossRef and PubMed, please ensure that data provided in the references are correct. Please note that incorrect surnames, journal/book titles, publication year and pagination may prevent link creation. When copying references, please be careful as they may already contain errors. Use of the DOI is highly encouraged.

Reference links

Increased discoverability of research and high quality peer review are ensured by online links to the sources cited. In order to allow us to create links to abstracting and indexing services, such as Scopus, CrossRef and PubMed, please ensure that data provided in the references are correct. Please note that incorrect surnames, journal/book titles, publication year and pagination may prevent link creation. When copying references, please be careful as they may already contain errors. Use of the DOI is highly encouraged.

A DOI is guaranteed never to change, so you can use it as a permanent link to any electronic article. An example of a citation using DOI for an article not yet in an issue is: VanDecar J.C., Russo R.M., James D.E., Ambeh W.B., Franke M. (2003). Aseismic continuation of the Lesser Antilles slab beneath northeastern Venezuela. Journal of Geophysical Research, https://doi.org/10.1029/2001JB000884. Please note the format of such citations should be in the same style as all other references in the paper.

Web references

As a minimum, the full URL should be given and the date when the reference was last accessed. Any further information, if known (DOI, author names, dates, reference to a source publication, etc.), should also be given. Web references can be listed separately (e.g., after the reference list) under a different heading if desired, or can be included in the reference list.

References in a special issue

Please ensure that the words 'this issue' are added to any references in the list (and any citations in the text) to other articles in the same Special Issue.

Data references

This journal encourages you to cite underlying or relevant datasets in your manuscript by citing them in your text and including a data reference in your Reference List. Data references should include the following elements: author name(s), dataset title, data repository, version (where available), year, and

Data references

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Reference management software

Most Wiley journals have their reference template available in many of the most popular reference management software products. These include all products that support Citation Style Language styles. Using citation plug-ins from these products, authors only need to select the appropriate journal template when preparing their article, after which citations and bibliographies will be automatically formatted in the journal's style. If no template is yet available for this journal, please follow the format of the sample references and citations as shown in this Guide. If you use reference management software, please ensure that you remove all field codes before submitting the electronic manuscript.

Reference style

Text: Indicate references by number(s) in line with the text. The actual authors can be referred to, but the reference number(s) must always be given.
Example: '..... as demonstrated [3,6]. Barnaby and Jones [8] obtained a different result ....'

Reference Listing: Number the references (numbers in square brackets) in the list in the order in which they appear in the text.
Examples:
Reference to a journal publication:
[1] J. van der Geer, J.A.J. Hanraads, R.A. Lupton, The art of writing a scientific article. J Sci Commun 2010;163:51-59.
Reference to a book:
[2] W. Strunk Jr., E.B. White, The Elements of Style, 4th ed. New York: Longman; 2000.
Reference to a chapter in an edited book:

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[2] W. Strunk Jr., E.B. White, The Elements of Style, 4th ed. New York: Longman; 2000.
Reference to a chapter in an edited book:
[3] G.R. Mettam, L.B. Adams, How to prepare an electronic version of your article. In: B.S. Jones, R.Z. Smith (Eds.). Introduction to the Electronic Age. New York:E-Publishing Inc: 2009, p. 281-304
Dataset reference
[dataset] [4] Oguro M, Imahiro S, Saito S, Nakashizuka T. Mortality data for Japanese oak wilt disease and surrounding forest compositions, Mendeley Data, v1; 2015. http://dx.doi.org/10.17632/xwj98nb39r.1.

Journal abbreviations source

Journal names should be abbreviated according to the List of Title Word Abbreviations.

ANNEX 2- Checklist PRISMA

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	-
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	-
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	9
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	11
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	11
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	12
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	12
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	12-13
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	13
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	-
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	-
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	13
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	-
Synthesis	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention	5

methods		characteristics and comparing against the planned groups for each synthesis (item #5)).	
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	5-9
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	14-15
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	14-15
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	14-15
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	14-15
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	15
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	-
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	15
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	15
Study characteristics	17	Cite each included study and present its characteristics.	17
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	26
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	28
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	28
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	28
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	28
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	28
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	-
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	-
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	33

	23b	Discuss any limitations of the evidence included in the review.	37
	23c	Discuss any limitations of the review processes used.	37
	23d	Discuss implications of the results for practice, policy, and future research.	35
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	37
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	37
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	37
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	37
Competing interests	26	Declare any competing interests of review authors.	37
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	-

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71.
For more information, visit: http://www.prisma-statement.org/