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Exercise and physiotherapy for nursing home residents with dementia: practices and preferences

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Part 1

Chapter 2:

Characteristics and effectiveness of physical therapist supervised exercise interventions for nursing home residents with dementia: a systematic review

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Abstract

Background and Objectives: Although physical therapy, in particular exercise therapy, is widely used in nursing home residents with dementia, the literature on this topic is relatively scarce. This systematic review aimed to summarize the literature on the characteristics and effectiveness of exercise interventions supervised by physical therapists in nursing home residents with dementia.

Research Design and Methods: Six electronic databases were systematically searched for relevant studies up to the 17th of August 2022. Randomized controlled trials (RCTs) comparing exercise interventions supervised by a physical therapist to any other form of intervention or usual care in nursing home residents with dementia were selected. Data were narratively analyzed and forest plots visualizing exercise effects were created.

Results: From the 1377 records retrieved and screened, six RCTs, reported in 11 papers, met the selection criteria. Included studies used multimodal or aerobic exercise interventions, with the frequency, duration and intensity varying across studies. Three of the six studies were at high risk of bias. Due to inconsistency in the findings and variety in outcome measures, results on the effectiveness of the interventions are inconclusive.

Implications: Our review emphasizes the need for more robust studies to offer understanding of the efficacy of exercise interventions supervised by physical therapists for nursing home residents with dementia.

Background and Objectives

Dementia has an estimated prevalence of 48 to 84%[1,2] in nursing home residents in Western countries. Nursing home residents often display multiple geriatric syndromes that result in limited functional performance and mobility and increased care needs.[3] Physical exercise is an important intervention to positively impact their functional capacities, thereby improving daily functional performance.[4]

Exercise guidelines[4–6] have been published for nursing home residents, including those with dementia. Recommendations advocate the use of multicomponent exercise consisting of strength, endurance, and balance exercises to be conducted a minimum of two times per week at moderate intensity, under the supervision of an exercise specialist.[4] In this context, physical therapy services are globally used by 10-67% of nursing home residents.[7] The usage, however, is unevenly spread, with residents without dementia and on temporary stay receiving significantly more physical therapy.[8,9] A rationale for this is unclear, and may result in permanent residents with dementia not receiving sufficient physical therapy.[8]

Of the six known systematic reviews[10–15] on exercise interventions in nursing home residents with dementia, two[10,14] have included studies with physical therapist supervised exercise interventions, while in the other reviews[11–13,15] supervisors were not described. Apart from physical therapists, the interventions were conducted by research assistants,[10,14] occupational therapists,[10,14] psychology students,[10,14] recreational therapists,[10] nurses,[10,14] caregivers[10,14] and an exercise scientist.[14] Furthermore, the characteristics of the included interventions varied widely. Reviews included both traditional physical exercise interventions as well as dance,[10] hand-movement,[10] walking and talking,[10,12,14,15] Tai Chi,[12] and ball-games.[14] This variation in both exercise supervisors and intervention characteristics limits the translation of findings into clinical care.

Regarding the effects of exercise, earlier reviews evaluated the impact of interventions on a wide range of outcomes. While two reviews, specifically targeting depression[12] and cognition,[13] identified potential positive effects, the overall evidence presents conflicting or limited findings on the outcomes independence of daily activities (ADL),[10,15] walking performance and endurance,[10,14,15] cognition,[10] depression,[10,15] behavioral symptoms,[10,15] nutrition,[15] mobility,[10,14] and balance.[14] Explanations for this uncertainty of the effects might stem from methodological flaws of included studies,[14,15] as well as the aforementioned variability in intervention characteristics across studies.[10,13]

A systematic review concentrating exclusively on exercise interventions supervised by physical therapists could reduce the heterogeneity in exercise characteristics. This ap-

proach is more in line with the clinical setting of a nursing home, where physical therapists often oversee exercise programs. In terms of effectiveness, a prior study has shown that the involvement of an exercise specialist improves exercise adherence and intensity, which may potentially lead to better health outcomes for this population.[16]

To summarize, exercise under the supervision of an exercise specialist, such as a physical therapist, is recommended by international guidelines.[4,5] Although physical therapy is frequently used in the treatment of nursing home residents with dementia, its effects are uncertain. Therefore, the aim of the present systematic review was to systematically search the available literature and answer the following questions:

- What are the characteristics of exercise interventions supervised by physical therapists for nursing home residents with dementia as employed in (cluster) randomized controlled clinical trials?
- What is the effectiveness of exercise interventions compared to usual care or any other intervention?

Research design and Methods

Study design

This systematic review was registered in the PROSPERO prospective register of systematic reviews (registration number: CRD42022351596) and is reported according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[17]

Search strategy

The search strategy was designed collaboratively by three authors (DB, TVV, and JS), one of whom is a trained librarian (JS). The search strategy was developed for PubMed/Medline and was then modified for Cochrane Library, Embase, Web of Science, Emcare and the Physiotherapy Evidence Database (PEDro), using MeSH terms and free text. Databases were searched from inception up to the current date (17th of August 2022). Key PI(M)CO-terms included "nursing homes", "dementia", "exercise therapy" and "randomized controlled trials". The full search strategy can be found in the Supplementary materials (see table S1). The database of clinicaltrials.gov was searched for ongoing studies or unpublished data. Previously published systematic reviews and reference lists of the included articles were manually searched to identify eligible articles.

Selection of studies

Retrieved records were exported to the Rayyan review software (Rayyan Systems Inc., Cambridge, United States of America). After elimination of duplicates, selection of studies

was independently performed by two reviewers (DB, CS). Studies were eligible for inclusion if they included nursing home residents with a diagnosis of dementia irrespective of the specific diagnostic criteria. Only (cluster) RCTs were considered in order to reduce the heterogeneity among studies. Studies were included if they compared an exercise intervention (fully or partially supervised by a physical therapist) to any other intervention or no intervention. Articles written in English, Dutch or Spanish were considered. Studies were excluded if they included patients with dementia who temporarily stayed in a nursing home for rehabilitation; included mixed populations of residents with and without dementia and did not report separately on residents with dementia; concerned an intervention where physical therapy was part of a multi-component intervention (for example a fall-risk program with medication provision, exercise therapy and home adaptations). Selection of studies was conducted in two steps. First, titles and abstracts were screened using the abovementioned criteria, and if deemed relevant or when eligibility was unclear, full text papers were obtained. Full-text papers were subsequently assessed for eligibility using the same criteria. A third independent reviewer (TVV) was consulted in case of discrepancies. Study protocols were reviewed to determine if separate articles belonged to the same study.

Data extraction

Two reviewers (DB, SS) extracted all data from eligible studies independently according to a pre-specified data extraction sheet in Microsoft Excel (Version 2202 14931.20626). In a meeting, the two researchers discussed their individual extracted data to reach consensus.

The following study characteristics were extracted: study type, age, sex, type of dementia, the nature of the treatment arms, duration of study/follow-up. Extraction of intervention characteristics was based on two templates for the description of non-pharmacological/exercise interventions, i.e. the CERT template[18] and the TIDieR checklist.[19] The characteristics considered in this review consisted of: exercise type, materials used, procedures, exercise conductors, group size, place of delivery, intervention frequency and duration, tailoring, methods of assessing adherence, adverse events, and study length. Regarding the extraction of outcomes, no primary outcomes of interest were defined for this review. We extracted all outcome data (any measures of effectiveness and/or safety) as presented in the studies, including within group and between group difference, confidence interval, (interquartile) range, standard deviation and/or p-value, where appropriate.

Risk of Bias assessment and assessment of certainty in the evidence

The risk of bias of individual studies was assessed with the most recent version of the Cochrane risk-of-bias tool for randomized trials (RoB 2),[20] or the adapted risk-of-bias tool for cluster-randomized trials (RoB 2 CRT).[21] The RoB 2 tool assesses bias across five do-

mains: randomization; deviations from the intended intervention; missing outcome data; measurement of the outcome; selection of reported results (publication bias). The risk of bias outcome is labeled as "low", "some concerns" or "high". In exercise interventions, it is nearly impossible to blind participants and people who deliver the intervention. Therefore, these criteria were not considered. Two reviewers (DB, CS) independently assessed the risk of bias of included studies. A third assessor (TVV) was available if discrepancies could not be resolved.

The Grading of Recommendations, Assessment, Development, and Evaluations GRADE approach[22] was used to assess the certainty in the evidence of exercise effects on the outcomes reported. The certainty in the evidence was determined for outcomes with a minimum of three studies reporting on it. Certainty was categorized into "High" (high confidence in the found effect), "Moderate" (future research could have an important impact in the estimated effect), "Low" (future research is very likely to have an important effect) and "Very low" (any estimate of effect is very uncertain). According to the GRADE approach, certainty is initially determined by study design (RCTs have a higher initial quality compared to observational studies) and may be affected by factors such as risk of bias, inconsistency, indirectness, imprecision, and publication bias. It can be positively influenced by a large effect, dose response or confounding that reduces the observed effect.

Data analysis

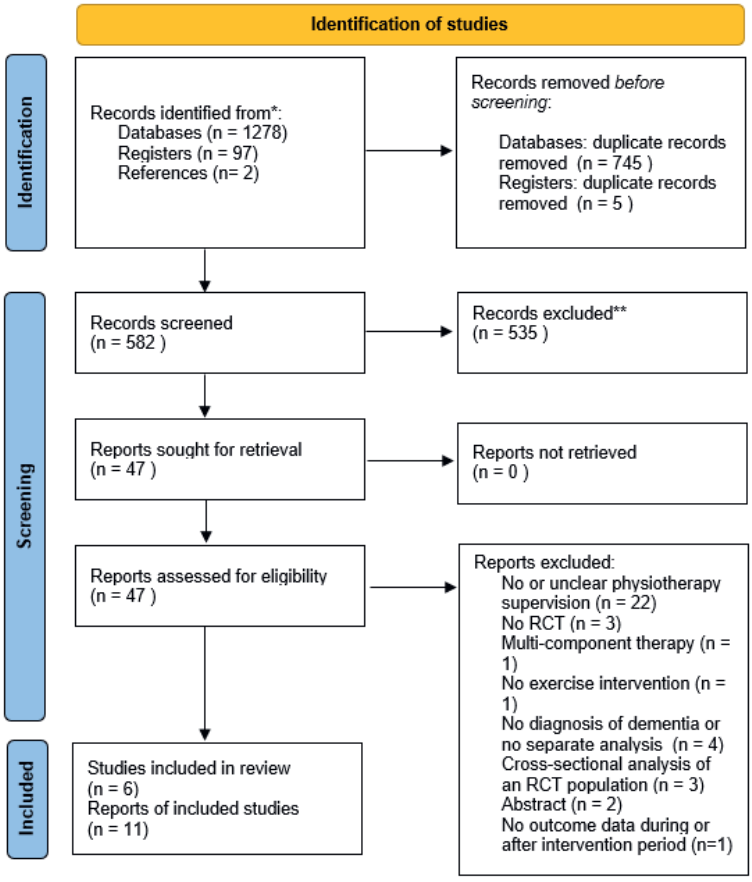
The Synthesis Without Meta-analysis (SWiM) guideline[23] and the Cochrane Handbook for Systematic Reviews of Interventions[24] were used for the narrative synthesis of the data. Due to the high degree of heterogeneity in outcomes and measurements in the studies, a meta-analytic approach was not appropriate. To provide an overview of the results from the individual studies, forest plots with standardized effect sizes were created. The R environment for statistical computing (version 4.2.2) and the package *Metafor*[25] were used to create the forest plots. The mean post-interventions scores of the intervention and control groups and their standard deviations (SD) were used to calculate a standardized mean difference (Hedges G) for each study. In cases where negative mean scores indicated a positive effect, scores were multiplied by −1 to adjust direction of effect in forest plot. If mean post-intervention scores were not available for a study, the change score and corresponding SD were used. If necessary, median and interquartile ranges were converted to means and confidence intervals according to the suggested method in the Cochrane handbook.[26]

Results

Selection of studies

We identified 1278 records from databases, 97 from the clinicaltrials.gov register and 2 after screening the included studies and reference lists of previously published systematic reviews. After removing 750 duplicates, 581 titles and abstracts were screened, resulting in the retrieval of 46 full-text articles. From the 46 full-text articles screened, 11 articles reporting findings from 6 studies were eventually included in this systematic review (Figure 1). Authors of five studies were contacted. One author[27] provided additional information on the type of dementia of the participants, two authors provided[28,29] information on the data analysis and study outcomes. The other two authors[10,30] did not reply or were not able to act to our request for additional information on effect estimates. A list of full-text screened but excluded articles can be found in the Supplementary materials (see table S2).

Figure 1: Flowchart of the selection process of the studies



Study characteristics

The main characteristics of the studies are presented in Table 1. The outcomes of one study were presented in four separate articles.[29,31–33] In two studies, the outcomes were presented in two separate articles each,[34–37] and three studies presented all outcomes in one article.[27,28,30] To ensure clarity in this review, we will cite the first published article when discussing study characteristics. There were two cluster-randomized controlled trials,[28,29,36] and four traditional RCTs.[27,30,34] The intervention length ranged from 12 weeks[34] to 15 months,[30] the number of participants from 24[27] to 191[36] and mean average age from 83[27] to 87 years.[28] One study[34] included two intervention groups that are both included in this review. In three studies[28,29,36] the control group performed light sitting recreational activities, in the other three studies[27,30,34] the control group received usual care.

Characteristics of interventions

Table 2 presents detailed information on the characteristics of the exercise interventions.

Table 1: Main study characteristics of the six included studies

	Study design	Number of Participants	Age, mean (SD)	Duration of study	No (%) Female	Baseline cognitive function, mean (SD)	Baseline physical independence, mean (SD)	Number and nature of treatment arms
Toots et al.[29,31,32], Bostrom et al.[33]	Cluster RCT	IG: 92; CG: 92	Total: 85.1 (7.1); Intervention: 84.4 (6.2) Control: 85.9 (7.8)	4 months	Total: 141 (75.8%) Intervention: 70 (75.3%) Control: 71 (76.3%)	MMSE (0-30) Total: 14.9 (3.5) Intervention: 15.4 (3.4) Control: 14.4 (3.5)	Barthel Index (0-20) Total: 10.9 (4.4) Intervention: 10.7 (4.5) Control: 11.0 (4.4)	Intervention: high-intensity functional weight-bearing exercise program. Control: Sitting activities (conversing, singing, picture viewing, listening to readings or music)
Brett et al. [34,35], Australia	RCT	Intervention 1: 17; Intervention 2: 19; Control: 19	Total: 85 (range 58–100) Intervention 1: 86 Intervention 2: 84 Control: 86	12 weeks	Total: 36 (66%); Intervention 1: 13 (76%) Intervention 2: 13 (68%) Control: 10 (53%)	-	-	Intervention 1: multimodal exercise intervention; Intervention 2: short-duration, high-frequency multimodal exercise intervention; Control: Usual care
Cancela et al.[30] ,Spain	RCT	Intervention: 73; Control: 116	Intervention: 80.63 (8.32); Control: 82.90 (7.42);	15 months	Intervention: 81%; Control: 44%	MMSE (0-30) Intervention: 14.9 (2.4) Control: 15.2 (2.5)	Katz Index (0-6) Intervention: 4.3 (0.9) Control: 4.3 (1.0)	Intervention: very low resistance aerobic cycling program; Control: usual recreational activities
Littbrand et al.[36], Conradsson et al.[37], Sweden	Cluster RCT	Intervention: 91 Control: 100	Total: 84.7 (6.5) Intervention: 85.3(6.1) Control: 84.2(6.8)	13 weeks	Total: 139 (73%) Intervention: 67 (74%) Control: 72 (72%)	MMSE (0-30) Total: 17.8 (5.1) Intervention: 17.5 (5.0) Control: 18.0 (5.3)	Barthel Index (0-20) Total: 13.1 (4.2) Intervention: 12.8 (4.5) Control: 13.4 (3.8)	Intervention: high-intensity functional weight-bearing exercise program; Post-intervention: daily functional tasks; Control: Sitting activities (watching films, singing, reading and conversation)

Table 1: Main study characteristics of the six included studies (continued)

	Study design	Number of Participants	Age, mean (SD)	Duration of study	No (%) Female	Baseline cognitive function, mean (SD)	Baseline physical independence, mean (SD)	Number and nature of treatment arms
Telenius et al.[28], Norway	Cluster RCT	Intervention: 87; Control: 83	Total: 86.7 (7.4) Intervention: 86.9 (7) Control: 86.4 (7.8)	12 weeks	Total: 73.6% Intervention: 59 (72%) Control: 61 (75.3%)	MMSE (0-30) Total: 15.7 (5.0) Intervention: 15.6 (5.0) Control: 15.8 (5.0)	Barthel Index (0-20) Total: 13.5 (3.6) Intervention: 13.6 (3.5) Control: 13.4 (3.6)	Intervention: high-intensity functional weight-bearing exercise program; Control: light physical activity, reading, playing games, listening to music and conversations
Venturelli et al.[27], Italy	RCT	Intervention 12; Control: 12	Intervention: 83 (6); Control: 85 (5)	24 weeks	86% (total sample, before exclusion and randomization)	MMSE (0-30) Intervention: 13 (2) Control:12 (2)	Barthel Index (0-100) Intervention: 34 (4) Control:35 (6)	Intervention: supervised walking at fastest possible pace; Control: Usual care

Notes: CG = control group; IG = intervention group; MMSE = Mini-Mental State Examination; RCT = randomized controlled trial; SD = standard deviation

Table 2: Intervention characteristics of the six included studies based on the CERT and TIDieR templates

	Exercise type	Materials	Procedures and processes	Supervisors	Individual or group	Place of delivery	Frequency and duration	Tailoring	Method of measuring adherence	Method of measuring intensity	Method of measuring adverse events
Toots et al.[29,31,32], Bostrom et al.[33]	Strength, balance	Weighted (safety) belts, steps, chairs, cushions, mattresses, balls, bean bags	Five-minute warmup for upper and lower extremities while sitting, at least two lower-limb strength exercises and two balance exercises in two sets	Two physical therapists	Group; three-eight participants. Individually supervised sessions for participants unable to attend the group sessions	16 residential care facilities in Sweden	Five sessions of 45 minutes per two weeks.	Yes	Evaluated after each session on a predefined scale[28]	Evaluated after each session on a predefined scale[28]	Active monitoring after each session: (1) minor and temporary; (2) serious symptoms; (3) manifest injury or disease; (4) death[28]
Brett et al.[34,35]	Strength, balance, endurance, flexibility	Hand weights, balls, cones, and static pedals.	Warming up, strength, balance, aerobic exercises, cooling down.	One physical therapist	Group; maximum of five participants.	Two nursing homes in Australia; intervention was held in a noise-adjustable sitting room	Frequency: intervention 1: one 45 min session /week; intervention 2: three 15 min sessions/week.	Yes	Observation of slight breathlessness	Not reported	Not reported

Table 2: Intervention characteristics of the six included studies based on the CERT and TIDieR templates (continued)

	Exercise type	Materials	Procedures and processes	Supervisors	Individual or group	Place of delivery	Frequency and duration	Tailoring	Method of measuring adherence	Method of measuring intensity	Method of measuring adverse events
Cancela et al.[30]	aerobic	Recumbant bicycle geared to low resistance	Minimum of 15 minutes exercise on self-selected pace on very low resistance	Physical therapist	Individual or in pairs	Elderly home-care facilities in Galicia (Spain); intervention took place in the gymnasium	Daily for a minimum of 15 minutes	Yes	Physiotherapist monitored each session and registered the time each individual exercised	Not reported	Not reported
Littbrand et al.[36], Conradsson et al.[37]	Strength, balance After group intervention: physical tasks integrated into daily life	Weighted (safety) belts, steps, chairs, cushions, mattresses, balls, bean bags	Five-minute warmup for upper and lower extremities while sitting, at least two lower-limb strength exercises and two balance exercises in two sets	Two physical therapists	Group; three to nine participants	Nine residential care facilities in Sweden	Frequency: five sessions of 45 minutes per two weeks.	Yes	Not reported	Evaluated after each session on a predefined scale [28]	Not reported

Table 2: Intervention characteristics of the six included studies based on the CERT and TIDieR templates (continued)

	Exercise type	Materials	Procedures and processes	Supervisors	Individual or group	Place of delivery	Frequency and duration	Tailoring	Method of measuring adherence	Method of measuring intensity	Method of measuring adverse events
Telenius et al.[28]	Strength, balance	Weighted (safety) belts, steps, chairs, cushions, mattresses, balls, bean bags	Five-minute warmup for upper and lower extremities while sitting, at least two lower-limb strength exercises and two balance exercises in two sets	One physical therapist per three participants	Group; three to six participants.	18 nursing homes in Norway	Frequency: two sessions of 50-60 min per week	Yes	Not reported	Physical therapists documented the intensity after each session	Not reported
Venturelli et al.[27]	Aerobic	At the end of the session, cookies were offered to the nursing home resident and caregiver.	Some minutes of informal chatting before the start of the exercise	Caregivers (staff and family)	Individually, guided by a caregiver	Alzheimer Care Unit in Italy; walking sessions were conducted in the hallway.	Frequency: minimum of 30 minutes, 4 times/week.	Yes	Walking times and distance were recorded and checked before and after each visit.	Walking on the participant's own but fastest pace	Not reported

Type, materials used and procedures

In four studies[28,29,34,36] multimodal exercise interventions (interventions comprised of more than one exercise type) and in two studies[27,30] aerobic exercise interventions were used. Regarding multimodal exercise interventions, three studies[28,29,36] employed the same HIFE program.[38] The HIFE program is a high intensity multimodal group exercise intervention that, after a warming up, focusses on lower-limb strength and balance exercises. The program uses weighted (safety) belts, steps, chairs, cushions, mattresses, balls and bean bags. In another study[34] the intervention comprised strength, balance, endurance and flexibility exercises and used static bike trainers, hand weights, balls and cones as materials. Participants performed a warming up and cooling down before and after each exercise session. In the study by Venturelli et al.[27] the intervention comprised an aerobic type of exercise intervention in the form of supervised walking. In their study procedure, cookies were offered to the resident and caregiver after the exercise session as a positive psychological reinforcement. In the study by Cancela et al.,[30] recumbent stationary bicycles were used, where participants performed aerobic exercise in the form of cycling on a very low resistance.

Exercise supervisors and group size

Four studies[28,29,34,36] evaluated small-group exercise interventions supervised by one or two physical therapists. Individual sessions for participants unable to attend the group sessions were offered in one[29] of those studies. In another study[30] participants performed exercises individually or in pairs, supervised by a physical therapist. In the study by Venturelli et al.[27], the intervention comprised individual walking sessions provided by caregivers (nursing staff and family caregivers) with the physical therapist giving instructions regarding walking speed, intensity and distance. Family caregivers were not involved in any other studies.

Place of delivery and tailoring

All interventions took place in long-term care facilities, described as nursing homes,[28,34] residential care facilities,[29,36] elderly home care facility,[30] or Alzheimer care unit.[27] In two studies it was specified where the intervention took place (noise-adjustable sitting room[34] and gymnasium)[30]. All six studies reported tailoring the exercises to the participants functional capacities.

Intervention frequency and duration

The study by Brett et al.[34] included two intervention groups: one group exercised once per week for 45 minutes, while the other group exercised three times per week for 15 minutes per session. In two studies,[29,36] the exercise group exercised five times per two weeks, with sessions lasting 45 minutes. In another study[28] the exercise group exercised two times per week for 50-60 minutes per session. In the study by Cancela et al.[30] partici-

pants exercised daily for a minimum of 15 minutes, and in the study by Venturelli et al.[27] the participants exercised at least four times per week, with sessions lasting a minimum of 30 minutes.

Methods of measuring adherence, intensity and adverse outcomes

The measurement of adherence was reported in two studies.[27,29] One study[29] referred to a predefined scale,[38] while in the other study adherence was monitored by recorded walking times and distance.[27] Regarding exercise intensity, in three studies[28,29,36] the exercise intensity was evaluated on a scale that distinguished high, moderate and low. Another study[34] described that intensity was monitored by observing if participants experienced slight breathlessness. One[29] of the six studies described the methodology for defining and monitoring adverse events. That study referred to a protocol[38] in which adverse events were actively monitored during and after each session, whereas the severity of any occurring event was categorized into minor and temporary, serious symptoms (potential risk of severe injury or life-threatening), manifest injury or disease, or death.

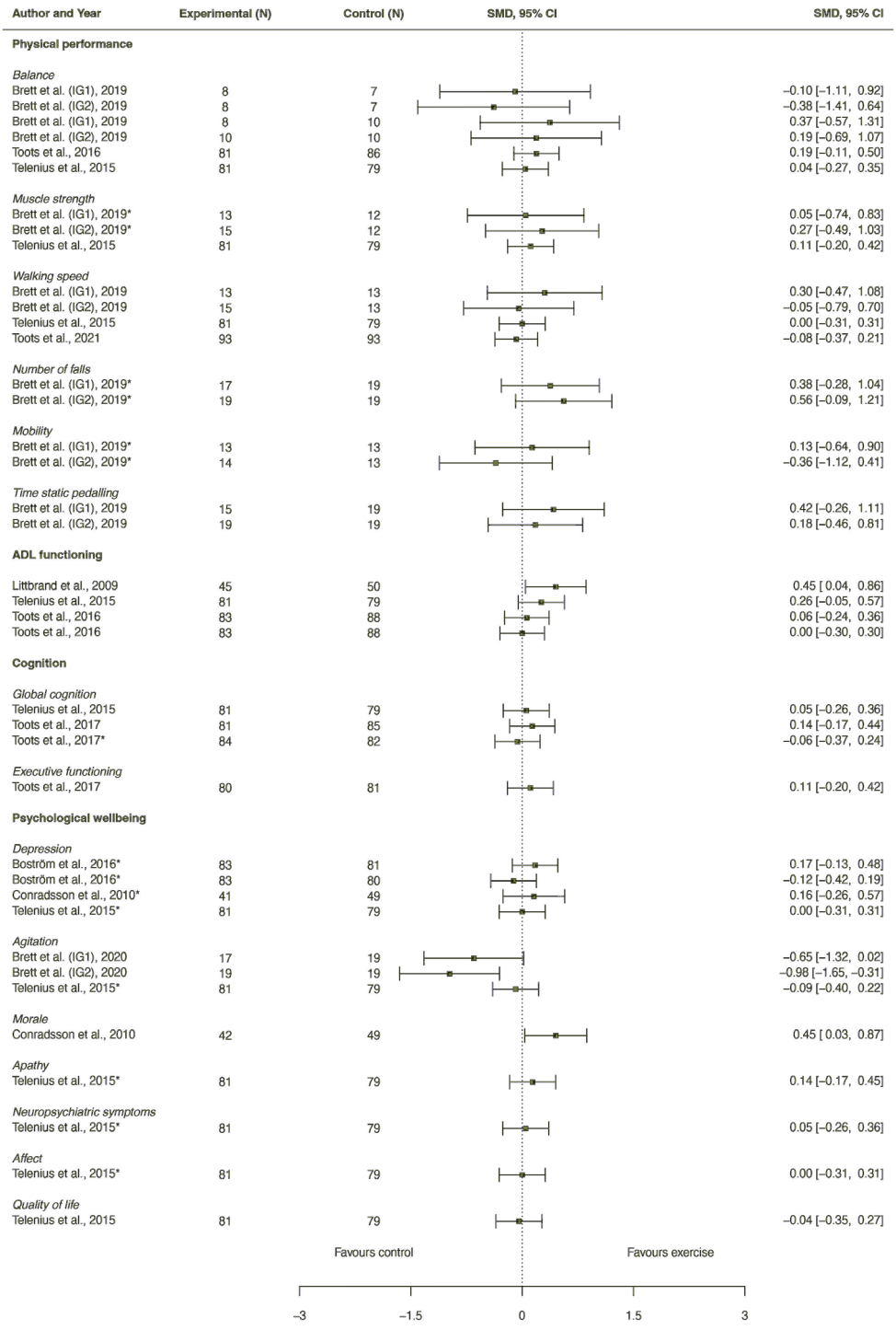
Results of exercise adherence, intensity and adverse outcomes

Adherence was reported in all studies and ranged from 72%[36] to 93.4%[27] in the intervention group, and from 69%[28] to 70%[34] in the social activities control groups. Regarding the intensity of exercise, three studies[28,29,36] included exercises at a high intensity level, one study[34] employed exercises at moderate intensity, one[30] at very light intensity, and one[27] at the participant's own, but fastest, pace. Regarding adverse events, one study[29] reported that all adverse events were minor and temporary, two studies[27,30] reported that no adverse events were related to the exercise program, the other three studies reported that there were no adverse events[28,34] or that no adverse event resulting in injury, disease or death.[36]

Outcomes of multimodal exercise interventions

Exercise effects of multimodal exercise interventions were evaluated on a total of 25 different outcomes which we categorized in "physical performance", "activities of daily living (ADL) functioning", "cognition", and "psychological well-being". Figure 2a, in the form of a forest plot, provides a visual summary of the effect sizes and confidence intervals of individual studies that employed multimodal exercise interventions for all study outcomes. Further details on the outcomes can be found in Supplemental Table S3.

Figure 2a: visual summary of the effect sizes and confidence intervals of individual studies that employed multimodal exercise interventions for all study outcomes



Physical performance

Three studies[28,29,34] evaluated the effects on physical performance outcome measures. Outcome measures and the number of studies that reported on physical functioning were: balance (three studies),[28,29,34] falls (one study),[34] mobility (one study),[34] muscle strength (two studies),[28,34] timed static pedaling (TSP)(one study),[34] and walking speed (three studies).[28,32,34] Two studies[28,29] found a significant positive effect of multimodal exercise on balance, when compared to sitting recreational activities, one[34] study found a significant positive effect on falls, when compared to usual care. No significant effects were found on mobility, muscle strength, TSP and walking speed.

ADL functioning

Three studies evaluated the effects on ADL functioning.[28,29,36] All studies used the Barthel Index (BI), one study[29] additionally used the Functional Independence Measure (FIM). One study[36] reported a positive exercise effect compared to sitting recreational activities, while two studies[28,29] found no effect.

Cognition

Two studies[28,31] evaluated the effects on cognition. Outcome measures and the number of studies reporting on it were global cognition (two)[28,31] and executive functioning (one).[31] Both studies compared multimodal exercise to sitting recreational activities and found no significant effects.

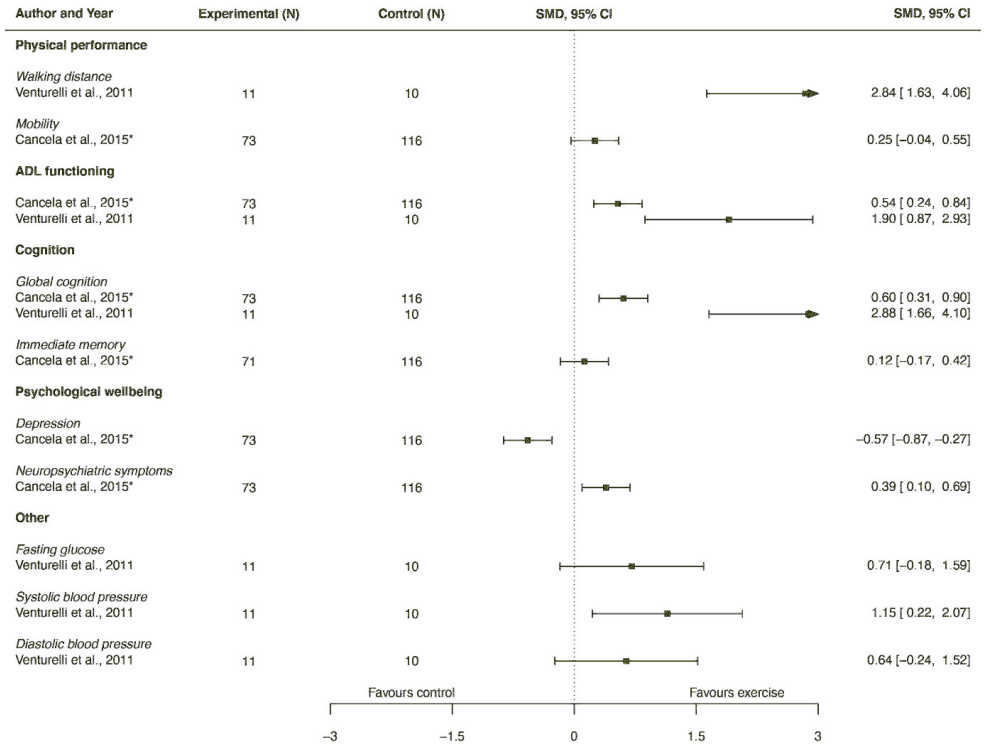
Psychological well-being

Four studies[28,33,35,37] evaluated the effects on psychological well-being. Outcome measures and the number of studies were depression (three),[28,33,37] agitation (two),[28,35] morale (one),[37] apathy (one),[28] behavioral and neuropsychiatric symptoms (one),[28] affect (one),[28] and quality of life (one).[28] Positive effects were found on the outcomes morale[37] and apathy[28] compared to sitting recreational activities. No effect was found on other outcomes.

Outcomes of aerobic exercise interventions

Aerobic exercise effects were evaluated on a total of 11 different outcomes which were categorized in "physical performance", "activities of daily living (ADL) functioning", "cognition", "psychological well-being" and "others". Figure 2b, in the form of a forest plot, provides a visual summary of the effect sizes and confidence intervals of individual studies that employed aerobic exercise interventions for all study outcomes. Further details on the outcomes can be found in Supplemental Table S3.

Figure 2b: visual summary of the effect sizes and confidence intervals of individual studies that employed aerobic exercise interventions for all study outcomes.



Physical performance

Two studies[27,30] evaluated the effects on physical performance. One study[30] evaluated the effect of aerobic exercise on mobility, the other on walking distance.[27] In both studies significant positive effects were found.

ADL functioning

Two studies evaluated the effects on ADL functioning with one study using the Katz Index[30] and one study using the Barthel Index.[27] In both studies significant positive effects were found.

Cognition

Two studies[27,30] evaluated the effects on cognition. One study[30] measured global cognition and immediate memory, one study[27] measured global cognition only. Positive effects were found on global cognition,[27,30] and on immediate memory.[30]

Psychological well-being

One study[30] evaluated the effects on psychological well-being. It evaluated the effects on depression and neuropsychiatric symptoms. No significant effects were found.

Others

One study[27] evaluated the effects on the outcomes glycemia and blood pressure (systolic and diastolic). No significant effects were found.

Risk of bias

Assessment of the risk of bias in the six included studies is presented in Table 3. Three of the six studies[27,30,34] were considered to be at high risk of bias. Causes of a high risk of bias were regarding an inappropriate analysis,[27,34] missing outcome data,[30,34] no assessor blinding,[27,30,34] and the selection of the reported result.[27,30] One study[28] had some concerns regarding risk of bias due to missing outcome data. Two studies[29,36] were considered at a low risk of bias. Additionally, of the risk of bias screening, sources of funding for the included studies were investigated. No conflicting interests were found.

Table 3: Assessment of the risk of bias in the six included studies

	Randomisation process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall
Toots et al.[29,31,32]; Boström et al.[33]						
Brett et al.[34,35]						
Cancela et al.[30]						
Littbrand et al.[36]; Conradsson et al.[37]						
Telenius et al.[28]						
Venturelli et al.[27]						

Low risk of bias
Some concerns
High risk of bias

Certainty in the evidence

Certainty in the evidence was determined separately for multimodal exercise interventions regarding outcomes with a minimum of three studies reporting on it. The outcomes physical performance (balance[28,29,34] and walking speed[28,32,34]), ADL functioning,[28,29,36] and depression,[28,33,37] all had three studies reporting on its respective outcome. For all

outcomes, the certainty in the evidence was determined as very low. Causes for low certainty in the evidence could be attributed to risk of bias (balance, walking speed, ADL functioning, depression), inconsistency in the results (balance, ADL functioning, depression), indirectness in the results (balance, walking speed) and imprecision in the results (balance, walking speed, depression). Table 3 in the Supplementary materials provides more detail on the determination of the certainty in the evidence (see table S3).

Discussion

Summary

Previous systematic reviews[10–15] on exercise interventions for nursing home residents with dementia included all kinds of exercise interventions, regardless of their supervision. Although some previous reviews[10,14] included physical therapist-supervised exercise interventions, none synthesized their characteristics and effectiveness.

Regarding study characteristics, the studies included in our review showed variation in population size, length and composition of the intervention and the outcome measures used. Regarding intervention composition, exercise with strength, balance and aerobic modalities at moderate or high intensity for at least 30-45 minutes, two to three times per week is recommended by dementia organizations and international geriatric working groups.[4–6] None of the interventions in the studies in the present systematic review fulfilled these recommendations. When it comes to study length, in three[28,34,36] of the six studies, the length of the intervention was not longer than 13 weeks. To our knowledge, no minimal duration of exercise length has been determined. However, a review on physical activity, cognition and brain plasticity,[39] has suggested an exercise length of 6 to 12 months to attain cognitive benefits. Indeed, although at high risk of bias, the two in our review included studies[27,30] that lasted at least 6 months did both find positive effects on physical performance, ADL functioning and cognition.

Despite the strong promotion of physical exercise for nursing home residents with dementia,[4–6] our review revealed heterogeneous results on a wide range of outcomes. The larger studies that contained multimodal exercise interventions seem to suggest a positive effect on physical performance[28,29] and ADL functioning,[28,29,36] although not in all studies a significant difference was found. Because of varying outcome measures and a small amount of methodologically sound studies, no effect size could be calculated (Forest plot 2.a). The studies incorporating aerobic interventions[27,30] both found significant positive effects on physical performance, ADL functioning and cognition. However, since our search strategy identified no more than two studies, and both of the studies were at high risk of bias, conclusions about the effectiveness cannot be made.

To some extent, the findings of our review are in line with the existing evidence. A previous systematic review[10] (that included both physical therapists supervised exercise interventions and non-physical therapist supervised exercise interventions) found some positive effects, as well as our review. However, that review did not fully report non-significant findings, and emphasized positive findings. By emphasizing positive findings, the exercise effects might appear larger than they actually are.[17,40]

Regarding the outcome cognition, a prior review[13] identified evidence of a positive effect. Within our review, the two studies[28,31] implementing multimodal exercise interventions did not demonstrate a significant effect. However, the two studies[27,30] that employed aerobic exercise did show a positive effect. The two studies employed aerobic exercise without cognitive tasks, although one study[27] did involve social interaction with a caregiver during walking.

In a previous review[14] on exercise interventions for nursing home residents with dementia, significant issues of bias were identified, similar to those found in our own review. Despite that all the RCTs included in our review were published after, the number of RCTs of satisfactory quality remains insufficient to offer a clearer understanding of the subject. Similar to the review of Littbrand et al.[14] we found a lack of transparency about adverse events and the method of assessing them in our included studies. Incomplete or unclear information on the safety of exercise interventions can be harmful. The study by Brett et al.[34] described that recruitment for their study was difficult, since family caregivers were concerned with the safety of the residents, and thought residents were 'too old' to exercise. Careful consideration and registration of adverse events can help objectify the risks of an exercise intervention, and inform participants and their caretakers about the (absence of) possible harms.

Strengths and limitations

There are some limitations to this systematic review and its evidence base. Due to the risk of bias issues, inconsistency in the findings and a low number of studies, we could not form a conclusion on the effectiveness of physical therapist supervised exercise interventions for this particular population. However, this review does describe the current evidence base and its limitations, and thereby forms clear implications for future research. Furthermore, some studies only provided differences in change scores to estimate the effect of the exercise program. This resulted in slight disparities between the study results as reported in the original studies, and the visual representation of the effects in the forest plots based on the post-intervention scores. Nevertheless, the forest plots illustrate a valuable aspect of our review, namely the incongruity among the findings of the studies. A strength of this review is that it fulfills all quality criteria of the AMSTAR II (A MeaSurement Tool to Assess systematic Reviews).[41] Our review is also at low risk of bias

in the four domains assessed by the Risk of Bias in Systematic reviews (ROBIS)[42] tool. Not fulfilled criteria are 1.5 (language restrictions) and 4.5 (robustness by funnel plot). We applied language restrictions by only including studies written in English, Spanish or Dutch. Since almost all studies are published in English, or later translated to English, we think it is unlikely that we missed eligible studies by our language restrictions. We also did not conduct a funnel plot to assess for publication bias. The small amount of included studies (four studies that used multimodal exercise interventions and two studies that used aerobic exercise interventions) give us legitimate reasons to not create a funnel plot.[24] We did sufficiently screen our studies on selective reporting, to limit the risk of publication bias.

Implications

In conclusion, the literature on the characteristics and the effect of physical therapist supervised exercise interventions in nursing home residents with dementia is heterogeneous and limited. Study length, composition of the intervention and outcome measures used varied. We included four studies that used a multimodal group exercise intervention and two studies that used an aerobic exercise intervention, with three of the six studies at high risk of bias. Exercise effects varied between studies, and were reported on a wide range of health outcomes. No conclusion can be drawn on the effectiveness of exercise interventions based on the studies included in our review. Future studies of high methodological quality can help determine the effects on health outcomes in nursing home residents with dementia.

Translational significance

While exercise therapy, especially under the supervision of a physical therapist, is extensively employed for nursing home residents with dementia, its contents and effects have not been thoroughly investigated. We found six RCTs consisting of multimodal and aerobic exercise interventions targeting a variety of outcome measures. Because of inconsistencies in the results and the presence of bias, a conclusion regarding the effectiveness of the interventions could not be reached. By identifying gaps and emphasizing the need for methodologically robust studies, this review contributes to the development of interventions that can positively impact the well-being of nursing home residents with dementia.

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Conflict of interest

None.

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TABLES

Supplementary material tables

Table S1: Complete Search Strategy

P	("Nursing Homes"[Mesh] OR "Nursing Homes"[tw] OR "Nursing Home"[tw] OR "Care Homes"[tw] OR "Care Home"[tw] OR "Intermediate Care Facilities"[tw] OR "Intermediate Care Facility"[tw] OR "Skilled Nursing Facilities"[tw] OR "Skilled Nursing Facility"[tw] OR "residential care facilities"[tw] OR "residential care facility"[tw] OR "Residential Facilities"[Mesh] OR "Residential Facilities"[tw] OR "Residential Facility"[tw]) ("Dementia"[Mesh] OR "Dementia"[tw] OR "Dementias"[tw] OR "Dement*"[tw] OR "senile"[tw] OR "amentia"[tw] OR "amentias"[tw] OR "Alzheimer Disease"[tw] OR "Alzheimer"[tw] OR "Alzheimers"[tw] OR "Alzheimer*"[tw] OR "Primary Progressive Aphasia"[tw] OR "Primary Progressive Nonfluent Aphasia"[tw] OR "Creutzfeldt-Jakob Syndrome"[tw] OR "CADASIL"[tw] OR "Diffuse Neurofibrillary Tangles with Calcification"[tw] OR "Frontotemporal Lobar Degeneration"[tw] OR "Pick Disease of the Brain"[tw] OR "Primary Progressive Nonfluent Aphasia"[tw] OR "Huntington Disease"[tw] OR "Huntington"[tw] OR "Huntington*"[tw] OR "Kluver-Bucy Syndrome"[tw] OR "Lewy Body Disease"[tw])
I	(("Exercise Therapy"[Mesh] OR "Exercise Therapy"[tw] OR "Exercise Therapies"[tw] OR "Exercise Therap*"[tw] OR "therapeutic exercise"[tw] OR "therapeutic exercises"[tw] OR "Remedial Exercise"[tw] OR "Remedial Exercises"[tw] OR "Rehabilitation Exercise"[tw] OR "Rehabilitation Exercises"[tw] OR "Blood Flow Restriction Therapy"[tw] OR "Continuous Passive Motion Therapy"[tw] OR "Endurance Training"[tw] OR "Muscle Stretching Exercise"[tw] OR "Muscle Stretching Exercises"[tw] OR "Plyometric Exercise"[tw] OR "Plyometric Exercises"[tw] OR "Resistance Training"[tw] OR "Exercise Movement Techniques"[Mesh] OR "Exercise Movement"[tw] OR "Breathing Exercises"[tw] OR "Qigong"[tw] OR "Dance Therapy"[tw] OR "Tai Ji"[tw] OR "Yoga"[tw] OR "Exercise"[Mesh] OR "Exercise"[tw] OR "Exercises"[tw] OR "Circuit-Based Exercise"[tw] OR "Circuit-Based Exercises"[tw] OR "Cool-Down Exercise"[tw] OR "Cool-Down Exercises"[tw] OR "Endurance Training"[tw] OR "Exergaming"[tw] OR "Gymnastics"[tw] OR "High-Intensity Interval Training"[tw] OR "Jogging"[tw] OR "Marathon Running"[tw] OR "Muscle Stretching Exercise"[tw] OR "Muscle Stretching Exercises"[tw] OR "Nordic Walking"[tw] OR "Physical Conditioning"[tw] OR "Plyometric Exercise"[tw] OR "Plyometric Exercises"[tw] OR "Preoperative Exercise"[tw] OR "Preoperative Exercises"[tw] OR "Resistance Training"[tw] OR "Running"[tw] OR "Stair Climbing"[tw] OR "Swimming"[tw] OR "Walking"[tw] OR "Warm-Up Exercise"[tw] OR "Warm-Up Exercises"[tw] OR "psychomotor activation"[tw] OR "psychomotor activat*"[tw] OR "motor activation"[tw] OR "motor activat*"[tw])
M	(randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized controlled trials[mh] OR random allocation[mh] OR double-blind method[mh] OR single-blind method[mh] OR clinical trial[pt] OR clinical trials[mh] OR "clinical trial"[tw] OR "RCT"[tw] OR "trial"[tw] OR ((singl*[tw] OR doubl*[tw] OR trebl*[tw] OR tripl*[tw]) AND (mask*[tw] OR blind*[tw])) OR "latin square"[tw] OR placebos[mh] OR placebo*[tw] OR random*[tw] OR research design[mh:noexp] OR comparative study[pt] OR evaluation studies[pt] OR follow-up studies[mh] OR prospective studies[mh] OR cross-over studies[mh] OR control[tw] OR controll*[tw] OR prospectiv*[tw] OR volunteer*[tw])
C	-
O	-

Table S2: List of excluded studies

	Titel	Authors	Year	Reason
1	Effects of a high-intensity exercise program on well-being among older people with dementia living in care facilities: A cluster-randomized trial	Conradsson, M.; Gustafson, Y.; Holmberg, H.; Lindelof, N.; Littbrand, H.; Nordstrom, P.; Rosendahl, E.	2015	Abstract
2	Can the onset of dependency in activities of daily living (ADLs) be delayed in cognitively impaired older adults with short total sleep time?	Lorenz, R. A.; Richards, K. C.; Rose, K. M.; Cole, C.	2010	Abstract
3	Effect of a high-intensity functional exercise program on functional balance: preplanned subgroup analyses of a randomized controlled trial in residential care facilities	Littbrand, H.; Carlsson, M.; Lundin-Olsson, L.; Lindelöf, N.; Håglin, L.; Gustafson, Y.; Rosendahl, E.	2011	Cross-sectional analysis of an RCT population
4	Is the Effect of a High-Intensity Functional Exercise Program on Functional Balance Influenced by Applicability and Motivation among Older People with Dementia in Nursing Homes?	Sondell, A.; Littbrand, H.; Holmberg, H.; Lindelöf, N.; Rosendahl, E.	2019	Cross-sectional analysis of an RCT population
5	Walking Aids Moderate Exercise Effects on Gait Speed in People With Dementia: A Randomized Controlled Trial	Toots, A.; Littbrand, H.; Holmberg, H.; Nordström, P.; Lundin-Olsson, L.; Gustafson, Y.; Rosendahl, E.	2017	Cross-sectional analysis of an RCT population
6	People living in nursing care facilities who are ambulant and fracture their hips: description of usual care and an alternative rehabilitation pathway	Killington, M.; Davies, O.; Crotty, M.; Crane, R.; Pratt, N.; Mills, K.; McInnes, A.; Kurrle, S.; Cameron, I. D.	2020	Multi-component intervention
7	A high-intensity functional weight-bearing exercise program for older people dependent in activities of daily living and living in residential care facilities: evaluation of the applicability with focus on cognitive function	Littbrand, H.; Rosendahl, E.; Lindelöf, N.; Lundin-Olsson, L.; Gustafson, Y.; Nyberg, L.	2006	No diagnosis of dementia or no separate analysis
8	Evaluating the effects of an exercise program (Staying UpRight) for older adults in long-term care on rates of falls: study protocol for a randomised controlled trial	Taylor, L.; Parsons, J.; Taylor, D.; Binns, E.; Lord, S.; Edlin, R.; Rochester, L.; Del Din, S.; Klenk, J.; Buckley, C.; Cavadino, A.; Moyes, S. A.; Kerse, N.	2020	No diagnosis of dementia or no separate analysis

Table S2: List of excluded studies (*continued*)

	Titel	Authors	Year	Reason
9	Postural stability and quality of life after guided and self-training among older adults residing in an institutional setting	Tuunainen, E.; Rasku, J.; Jäntti, P.; Moisio-Vilenius, P.; Mäkinen, E.; Toppila, E.; Pyykkö, I.	2013	No diagnosis of dementia or no separate analysis
10	A randomized outcome evaluation of group exercise programs in long-term care institutions	Lazowski, D. A.; Ecclestone, N. A.; Myers, A. M.; Paterson, D. H.; Tudor-Locke, C.; Fitzgerald, C.; Jones, G.; Shima, N.; Cunningham, D. A.	1999	No diagnosis of dementia or no separate analysis
11	Why Not a Global Postural Reeducation as an Alternative Therapy Applied to Alzheimer's Patients in Nursing Homes? A Pioneer Randomized Controlled Trial	Todri, J.; Todri, A.; Lena, O.	2019	No exercise intervention
12	The Effects of Exercise on Falls in Older People With Dementia Living in Nursing Homes: A Randomized Controlled Trial	Toots, A.; Wiklund, R.; Littbrand, H.; Nordin, E.; Nordström, P.; Lundin-Olsson, L.; Gustafson, Y.; Rosendahl, E.	2019	No outcome data during or after intervention period
13	A 9-Week Aerobic and Strength Training Program Improves Cognitive and Motor Function in Patients with Dementia: A Randomized, Controlled Trial	Bossers, W. J.; van der Woude, L. H.; Boersma, F.; Hortobágyi, T.; Scherder, E. J.; van Heuvelen, M. J.	2015	No PT
14	A randomised controlled trial testing the impact of exercise on cognitive symptoms and disability of residents with dementia	Stevens, J.; Killeen, M.	2006	No PT
15	Conversation Intervention with Alzheimer's Patients: Increasing the Relevance of Communication	Tappen, R. M.; Williams, C. L.; Barry, C.; Disesa, D.	2002	No PT
16	Effect of Exercise on Behavioral Symptoms and Pain in Patients With Dementia Living in Nursing Homes	Maltais, M.; Rolland, Y.; Vellas, B.; Haÿ, P. E.; Armaingaud, D.; Cestac, P.; Rouch, L.; Cesari, M.; de Souto Barreto, P.	2019	No PT
17	Effect of exercise on mood in nursing home residents with Alzheimer's disease	Williams, C. L.; Tappen, R. M.	2007	No PT
18	Effects of Hand Exercise on Eating Action in Patients With Alzheimer's Disease	Chen, L. L.; Li, H.; Chen, X. H.; Jin, S.; Chen, Q. H.; Chen, M. R.; Li, N.	2019	No PT
19	Effects of Physical Activity in Nursing Home Residents with Dementia: A Randomized Controlled Trial	Henskens, M.; Nauta, I. M.; van Eekeren, M. C. A.; Scherder, E. J. A.	2018	No PT

Table S2: List of excluded studies (*continued*)

	Titel	Authors	Year	Reason
20	Exercise or Social Intervention for Nursing Home Residents with Dementia: A Pilot Randomized, Controlled Trial	de Souto Barreto, P.; Cesari, M.; Denormandie, P.; Armaingaud, D.; Vellas, B.; Rolland, Y.	2017	No PT
21	Exercise program for nursing home residents with Alzheimer's disease: a 1-year randomized, controlled trial	Rolland, Y.; Pillard, F.; Klapouszczak, A.; Reynish, E.; Thomas, D.; Andrieu, S.; Rivière, D.; Vellas, B.	2007	No PT
22	Physical and functional implications of aquatic exercise for nursing home residents with dementia	Henwood, T.; Neville, C.; Baguley, C.; Clifton, K.; Beattie, E.	2015	No PT
23	REHABILITATION OF MOBILITY AND MOTOR FUNCTION IN NURSING HOME RESIDENTS WITH DEMENTIA	Aizen, E.; Lubosky, E.; Sobeh, S.; Ibrahim, R.; Pressburger, D.; Oliven, R.	2018	No PT
24	The Effect of Exercise and Social Activity Interventions on Nutritional Status in Older Adults with Dementia Living in Nursing Homes: A Randomised Controlled Trial	Maltais, M.; Rolland, Y.; Haÿ, P. E.; Armaingaud, D.; Cestac, P.; Rouch, L.; de Souto Barreto, P.	2018	No PT
25	The effects of movement stimulation on activities of daily living performance and quality of life in nursing home residents with dementia: a randomized controlled trial	Henskens, M.; Nauta, I. M.; Drost, K. T.; Scherder, E. J.	2018	No PT
26	Therapeutic Effects of Exercise Training on Elderly Patients With Dementia: A Randomized Controlled Trial	Liu, I. T.; Lee, W. J.; Lin, S. Y.; Chang, S. T.; Kao, C. L.; Cheng, Y. Y.	2020	No PT
27	Walking and night-time restlessness in mild-to-moderate dementia: a randomized controlled trial	Eggermont, L. H.; Blankevoort, C. G.; Scherder, E. J.	2010	No PT
28	Walking the line: a randomised trial on the effects of a short term walking programme on cognition in dementia	Eggermont, L. H.; Swaab, D. F.; Hol, E. M.; Scherder, E. J.	2009	No PT
29	Improvement of cognitive function after physical movement training in institutionalized very frail older adults with dementia	Thurm, F.; Scharpf, A.; Liebermann, N.; Kolassa, S.; Elbert, T.; Luchtenberg, D.; Woll, A.; Kolassa, I. T.	2011	No PT
30	"Bring me sunshine, bring me (physical) strength": The case of dementia. Designing and implementing a virtual reality system for physical training during the COVID-19 pandemic	Matsangidou, M.; Frangoudes, F.; Hadjiaros, M.; Schiza, E.; Neokleous, K. C.; Papayianni, E.; Avraamides, M.; Pattichis, C. S.	2022	No PT
31	Effects of a 16-week multimodal exercise program on activities of daily living in institutionalized individuals with dementia A multicenter randomized controlled trial	Bezold, J.; Trautwein, S.; Barisch-Fritz, B.; Scharpf, A.; Krell-Roesch, J.; Nigg, C. R.; Woll, A.	2021	No PT
32	Effect of a comprehensive exercise program on function in nursing home residents with Alzheimer's disease	Tappen, R. M.; Roach, K. E.; Touhy, T. A.	2000	No PT

Table S2: List of excluded studies (continued)

	Titel	Authors	Year	Reason
33	Effect of Centella Asiatica and Aerobic Exercise in Older Women With Dementia: A Randomized Controlled Trial	Fitriana, Lisna Anisa; Irma, Darmawati; Nasution, Lina Anisa; Suci Tuty, Putri; Rohaedi, Slamet; Anggadiredja, Kusnandar; Iwan, Setiawan; Nur, Fauziyah; Adnyana, I. Ketut;	2021	No PT
34	Factors predictive of adherence to a non-pharmacological intervention in nursing home research: a substudy of the LEDEN trial	Chrusciel, J.; Letty, A.; Armaingaud, D.; Barreto, P.; Berrut, G.; Rolland, Y.; Sanchez, S.	2022	No PT
35	Effects of 1 Year of Lifestyle Intervention on Institutionalized Older Adults	Magistro, D.; Carlevaro, F.; Magno, F.; Simon, M.; Camp, N.; Kinrade, N.; Zecca, M.; Musella, G.	2021	No RCT
36	Effects of a multicomponent exercise program in institutionalized elders with Alzheimer's disease	Sampaio, A.; Marques, E. A.; Mota, J.; Carvalho, J.	2019	No RCT
37	Effectiveness of individually tailored exercise on functional capacity and mobility in nursing home residents	Bertoncello, C.; Sperotto, M.; Bellio, S.; Pistellato, I.; Fonzo, M.; Bigolaro, C.; Ramon, R.; Imoscopi, A.; Baldo, V.	2021	No RCT

Table S3: Outcomes, within and between group differences between baseline and follow-up of the six included studies

	Outcome	**Within group differences**	**Between group differences[a]**
Multimodal exercise interventions			
Physical performance			
Brett et al.[34]	Balance ((M)FR)	median (Q1-Q3): IG 1: pre 12 (8–35) post 28 (17–35) p=0.204; IG 2: pre 16 (9–29) post 26 (12–30) p=0.673; CG: pre 21 (18–31) post 27 (24–33) p=0.271	p=0.69
	Balance (FR)	median (Q1-Q3): IG1: pre 12 (0–23) post 18 (11–30) p=0.263; IG2: pre 16 (8–22) post 15 (8–28) p=0.612; CG: pre 15 (12–21) post 13 (7–22) p=0.373	p=0.60
	Falls (Number of falls)	median (Q1-Q3): IG 1: pre 0 (0–1) post 0 (0–2) p=0.496; IG2: pre 0 (0–1) post 0 (0–1) p=1.000; CG: pre 0 (0–2) post 1 (0–4) p=0.011	p=0.02(IG 2 compared to CG)
	Mobility (TUG)	median (Q1-Q3): IG 1 pre 26 (15–36) post 24 (12–29) p=0.045; IG2 pre 26 (17–48) post 27 (19–46) p=0.615; CG pre 23 (17–33) post 21 (16–34) p=0.807	p=0.53

Table S3: Outcomes, within and between group differences between baseline and follow-up of the six included studies (continued)

	Outcome	Within group differences	Between group differences[a]
	Muscle strength (FTCST)	median (Q1-Q3): IG1 pre 27 (17–41) post 18 (13–44) p=0.130; IG2 pre 25 (20–46) post 21 (15–31) p=0.050; CG pre 22 (18–28) post 26 (18–34) p=0.107	p=0.63
	Timed Static Pedalling (TSP)	median (Q1-Q3): IG 1: pre 11 (7–28) post 28 (11–44) p=0.005; IG2: pre 10 (8–29) post 20 (11–34) p=0.040; CG: pre 19 (13–30) post 20 (9–27) p=0.407	p=0.45
	Walking speed (Six meter walk test)	median (Q1-Q3): IG1 pre 0.55 (0.46–1) post 0.67 (0.50–1.20) p=0.161; IG2 pre 0.55 (0.38–0.86) post 0.60 (0.33-0.86) p=0.177; CG: pre 0.60 (0.48–0.86) post 0.55 (0.41–0.93) p=0.724	p=0.53
Telenius et al.[28]	Balance (BBS)	mean + (SD): IG: pre 34.3 (14.5), post 37.2 (14.0). CG: pre 35.4 (13.7), post 36.6 (14.4)	p=0.02
	Muscle strength (CST)	mean + (SD): IG: pre 6.0 (3.1), post 7 (3.3). CG: pre 6.2 (2.9), post 6.6 (3.7)	p=0.11
	Walking speed (Six meter walk test)	mean + (SD): IG: pre 0.5 (0.2), post 0.5 (0.2). CG: pre 0.5 (0.2), post 0.5 (0.3)	p=0.86
Toots et al.[29]	Balance (BBS)	MD + (SE): IG: 2.39 (0.88) CG: -1.82 (0.86)	MD + (95% CI): 4.20 (1.79-6.61) p=<0.001
Toots et al.[32]	Walking speed (Backward walking speed)	MD + (SE): with or without WA: IG: 0.005 (0.013); CG: 0.000 (0.013); without WA: IG: 0.026 (0.018); CG: -0.004 (0.017)	MD + (95% CI): with or without WA: 0.005 (-0.031-0.041) p=0.788; without WA: 0.030 (–0.019, 0.079) p=0.231
ADL functioning			
Littbrand et al.[36]	ADL performance (BI)	MD + (SD): IG: -0.13 (2.11) p=0.67; CG: -1.10 (2.28) p=0.001	MD (95% CI): 1.13 (0.12-2.13) p=0.03
Telenius et al.[28]	ADL performance (BI)	mean + (SD): IG: pre 13.6 (3.5), post 13.7 (3.6); CG: pre 13.4 (3.6), post 12.7 (4.1)	p=0.085
Toots et al.[29]	ADL performance (BI)	MD + (SE): IG: -0.79 (0.31); CG: -1.39 (0.30)	MD + (95% CI): 0.60 (-0.24-1.44) p=0.16
	ADL performance (FIM)	MD + (SE): IG: -3.10 (1.07); CG: -4.44 (1.04)	MD + (95% CI): 1.34 (-1.56-4.25) p=0.36
Cognition			
Telenius et al.[28]	Global cognition (MMSE)	mean + (SD): IG: pre 15.6 (5.0), post 15.5 (5.5); CG: pre 15.8 (5.0), post 15.2 (5.4)	p=0.69
Toots et al.[31]	Global cognition (MMSE)	MD + (SE): IG: –1.15 (0.41); CG: –0.93 (0.4)	MD + (95% CI): -0.27 (-1.4-0.87) p=0.644
	Executive functioning (VF)	MD + (SE): IG: –0.74 (0.32); CG: –0.21 (0.32)	MD + (95% CI): -0.53 (-1.42-0.35) p=0.241

Table S3: Outcomes, within and between group differences between baseline and follow-up of the six included studies (*continued*)

	Outcome	Within group differences	Between group differences[a]
	Global cognition (ADAS-Cog)	MD + (SE): IG: 1.51 (1.06); CG: 2.55 (1.07)	MD + (95% CI): -1.04 (-4-1.92) p=0.491
Psychological wellbeing			
Bostrom et al.[33]	Depression (GDS-15)	IG: MD + (95% CI) 0.03 (–0.53, 0.59) p=0.91; CG MD + (95% CI) 0.08 (–0.49, 0.64) p=0.78	MD + (95% CI) -0.05 (-0.84, 0.75) p=0.91
	Depression (MADRS)	IG: MD + (95% CI) 0.40 (–0.77, 1.57) p=0.50; CG: MD + (95% CI) 0.33 (–0.85, 1.52) p=0.58	MD + (95% CI) 0.06 (-1.60, 1.73) p=0.94
Brett et al.[35]	Agitation (CMAI)	IG 1: pre 28 (9) post 26 (10) p=0.03; IG 2: pre 26 (9) post 24 (8) p=0.23; CG: pre 36 (8) post 32 (8) p=0.02	p>0.05
Conradsson et al.[37]	Depression (GDS-15)	MD + (SD): IG: 0.03 (2.3) p=0.92; CG: -0.10 (1.9) p=0.62	MD + (95% CI): -0.33 (-1.20, 0.55) p=0.46
	Morale (PGCMS)	MD + (SD): 0.35(2.7) p=0.25 CG: 0.02 (2.3) p=0.93	MD + (95% CI): 1.12 (0.09 to 2.16) p=0.03
Telenius et al.[28]	Agitation (NPI-Agitation)	mean + (SD): IG: pre 1.7 (2.1), post 1.5 (2.2); CG: pre 1.3 (1.7), post 1.7 (2.3)	p=0.07
	Apathy (NPI-Apathy)	mean + (SD): IG: pre 0.5 (0.8), post 0.3 (0.6); CG: pre 0.39 (0.7), post 0.4 (0.8)	p=0.048
	Neuropsychiatric symptoms (NPI)	mean + (SD): IG: pre 5.8 (5.9), post 5.1 (6.0); CG: pre 4.8 (4.6), post 5.4 (6.5)	p=0.17
	Affect (NPI-depression and anxiety)	mean + (SD): IG: pre 1.1 (1.4), post 1.0 (1.4); CG: pre 0.8 (1.3), post 1.0 (1.4)	p=0.31
	Depression (Cornell scale)	mean + (SD): IG: pre 4.7 (4.6), post 3.8 (5.2); CG: pre 4.9 (4.3), post 3.8 (3.8)	p= 0.39
	Quality of life (Qualid)	mean + (SD): IG: pre 18.3 (6.1), post 17.1 (7.0); CG: pre 17.7 (5.5), post 17.4 (6.6)	p= 0.97
Aerobic exercise interventions			
Physical performance			
Cancela et al.[30]	Mobility (TUG)	Mean difference + 95%CI: IG: -2.11 (-3.86,-0.36); CG -0.56 (-1.45, 0.33)	p=0.03
Venturelli et al.[27]	Walking distance (6mwt)	mean + (SD): IG: pre 245 (31) post 294 (49) p<0.05 CG: pre 238 (47) post 168 (34) p<0.05	p<0.05
Psychological wellbeing			
Cancela et al.[30]	Depression (Cornell Scale)	Mean difference + 95%CI: IG: 1.84 (-0.80, 4.48); CG: -2.71 (-3.52, -1.91)	p=0.22
	Neuropsychiatric symptoms (NPI)	Mean difference + 95%CI: IG: -0.84 (-3.76, 2.08); CG: 4.60 (1.96, 7.24)	p=0.08

Table S3: Outcomes, within and between group differences between baseline and follow-up of the six included studies (*continued*)

	Outcome	Within group differences	Between group differences[a]
ADL functioning			
Cancela et al.[30]	ADL functioning (Katz Index)	Mean difference + 95%CI: IG: 0.22 (-0.05, 0.49); CG: -0.25 (-0.36, -0.14)	p=0.03
Venturelli et al. (2011)	ADL functioning (BI)	mean + (SD): IG: pre 34 (4) post 42 (4) p<0.05; CG: pre 35 (6) post 32 (6) p>0.05	p=0.003
Cognition			
Cancela et al.[30]	Global cognition (MEC -Spanish MMSE)	Mean difference + CI: IG: 0.09 (-0.32, 0.60); CG: -2.11 (-2.90,-1.32)	p=0.01
	Memory (FOME)	Mean difference + 95%CI: IG: 1.99 (-1.93, 4.33); CG: -1.31 (-3.57, 7.95)	p=0.01
Venturelli et al.[27]	Global cognition (MMSE)	mean + (SD): IG pre 13 (2) post 12 (2) p=>0.05; CG: pre 12 (2) post 6 (2) p<0.05	p<0.001
Others			
Venturelli et al.[27]	(Fasting) Glycemia (mg/dl-1)	mean + (SD): IG: pre 94(5) post 90(3) p=0.784; CG: pre 92(5) post 93(5) p=0.345	p=0.143
	Systolic blood pressure (mmHg)	mean + (SD): IG: pre 132(10) post 126(8) p=0.05; CG: pre 133(6) post 135(7) p=0.368	p=0.108
	Diastolic blood pressure (mmHg)	mean + (SD): IG: pre 84(5) post 82(3) p=0.550; CG: pre 84(3) post 84(3) p=0.334	p=0.376

[a]Mean difference with 95% CI or p-value of test of between group difference if mean difference with 95% CI was not available.

(M)FR=(Modified) Functional Reach test, TUG= Timed Up and Go test, FTSTS= Five-Times-Sit-to-Stand, TSP= timed static pedalling, BBS= Berg Balance Scale, CST= Chair Stand Test (30 sec), MD= Mean difference, WA= walking aid, GDS 15= Geriatric Depression Scale 15-item version, MADRS= Montgomery–Åsberg Depression Rating Scale, CMAI= Cohen-Mansfield Agitation Inventory, PGC-MS= Philadelphia Geriatric Center Morale Scale, BI=Barthel Index, FIM= Functional Independence Measure, MMSE= Mini-Mental State Examination, NPI-Q= The Neuropsychiatric Inventory questionnaire, QUALID= Quality of life in late-stage dementia scale, VF= Verbal fluency, ADAS-COG= Alzheimer's Disease Assessment Scale-Cognitive Subscale, 6mwt= six minute walking test, FOME=Fuld Object Memory Evaluation, mg/dl=milligrams per decilitre, mmHg= millimetre of mercury

Table S4: Certainty in the evidence according to the GRADE approach

Multimodal exercise interventions								
	No of studies	**N total**	**Study design and execution**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**GRADE**
Physical performance								
Balance	3	355	-2 (one study at high risk of bias)	-1 (2 in favor of intervention, 1 no effect)	-1 (differences in intervention duration and frequency, differences in control groups)	-1 (one study with a large confidence interval)	-	Very low
Walking speed	3	387	-2 (one study at high risk of bias)	-	-2 (differences in intervention duration and frequency, differences in control groups. difference in outcome measure)	-1 (one study with a large confidence interval)	-	Very low
ADL functioning								
ADL functioning	3	421	-1 (one study with RoB concerns)	-2 (1 in favor of intervention, 2 no effect)	-	-	-	Very low
Psychological wellbeing								
Depression	3	314	-1 (one study with RoB concerns)	- 1 (different directions of effect)	-	-1 (one study with a large confidence interval)	-	Very low

Table S5: Prisma Chart

Section and Topic	Item	Checklist item	Location where item is reported (Line)
TITLE			
Title	1	Identify the report as a systematic review.	13
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	48
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	107-110
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	111-115
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	139-149
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.	126-129
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Sup 1
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.	138-139
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.	156-171
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.	168-171
	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.	160-167

Table S5: Prisma Chart (continued)

Section and Topic	Item	Checklist item	Location where item is reported (Line)
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.	173-183
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.	203-210
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	197-202
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	203-210
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	207
	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.	199, 200
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	-
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	-
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	-
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	190-194
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.	Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Sup 2
Study characteristics	17	Cite each included study and present its characteristics.	Table 1

Table S5: Prisma Chart (continued)

Section and Topic	Item	Checklist item	Location where item is reported (Line)
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Table 4
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.	Table 3, Figure 2a, 2b
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Table 3, Figure 2a, 2b, Table 4
	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.	Figure 2a, 2b
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	-
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	-
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.	Sup 3
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	434-485
	23b	Discuss any limitations of the evidence included in the review.	487-493
	23c	Discuss any limitations of the review processes used.	496-508
	23d	Discuss implications of the results for practice, policy, and future research.	512-520

Table S5: Prisma Chart (continued)

Section and Topic	Item	Checklist item	Location where item is reported (Line)
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.	120
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	120
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	-
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	523
Competing interests	26	Declare any competing interests of review authors.	526
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.	-