NKR 53 Demens og adfærdsforstyrrelser PICO 3 aerob træning vs. ingen aerob træning

Review information

Authors

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Characteristics of studies

Characteristics of included studies

Aguiar 2014

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention ● *Age, y (SD)*: 78.6 (8.4) Control ● *Age, y (SD)*: 74.7 (7.4) **Included criteria:** a) age >= 55 years, b) diagnosis of AD, c) the same caregiver for at least three months, d) no previous use of cholinesterase inhibitors for AD, e) stable systemic blood pressure **Excluded criteria:** a) MMSE score superior to 12, b) inability to follow simple commands, c) have undergone physiotherapy, occupational therapy and/or systematized physical activity in the previous two months, d) psychiatric illness, e) orthopedic, neurological limitations, behavioral or other conditions that could prevent the practise of exercise, f) severe visual or auditory deficits that could preclude the appilication of the program

Interventions	**Intervention Characteristics** Intervention ● *Description*: Initial treatment of RTP (dose of 4.6 mg/day) for two months. Therafter the dose was increased to up to 9.5 mg/day. 40 programmed training performed twice a week, 40 minutes per section. The training program consisted of aerobic activity, flexibility, strength and balance exercises. ● *Duration (weeks)*: 24 ● *Length of follow-up after end of treatment*: None Control ● *Description*: Initial treatment of RTP (dose of 4.6 mg/day) for two months. ● *Duration (weeks)*: 24
Outcomes	*Kognition_MMSE_final_mean SD* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Scale**: MMSE ● **Direction**: Higher is better ● **Data value**: Endpoint *ADL_ADL-Q, higher=worse_final_mean SD* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Scale**: ADL-Q ● **Direction**: Lower is better ● **Data value**: Endpoint *Serious adverse events* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Data value**: Endpoint *Dropouts in absolute numbers* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported

	● **Direction**: Lower is better ● **Data value**: Endpoint
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Judgement Comment: Patients were randomly assigned into two groups using a computer program.
Allocation concealment (selection bias)	Low risk	Judgement Comment: Group allocation was kept in an opaque envelope and sealed until the study was completed.
Blinding of participants and personnel (performance bias)	Unclear risk	Judgement Comment: Blinding of the participants and personnel has not been described in sufficient details
Blinding of outcome assessment (detection bias)	Low risk	Judgement Comment: The investigator who assessed outcomes was blinded
Incomplete outcome data (attrition bias)	High risk	Judgement Comment: 5 out of 22 participants from the intervention group dropped out during the intervention, whereas the control group only 1 out of 18 dropped out.There were no intention-to-treat-analysis. Systematic differences between groups in withdrawals from a study has not been assessed.
Selective reporting (reporting bias)	Low risk	Judgement Comment: The pre-specified outcomes were registred at ClinicalTrials.gov under the number NCT01183806, and seems free of reporting bias
Other bias	Low risk	Judgement Comment: The study seems to be free of other sources of bias

Arcoverde 2014

Methods	
Participants	
Interventions	
Outcomes	
Notes	Data obtained from: Groot C, Hooghiemstra AM, Raijmakers PGHM, van Berckel BNM, Scheltens P, Scherder EJA, van der Flier WM, Ossenkoppele R. The effect of physical activity on cognitive function in patients with dementia: A meta-analysis of randomized controlled trials. Ageing Research Reviews 2016; 25: 13-23.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Reference: Groot et al., 2016
Allocation concealment (selection bias)	Low risk	Reference: Groot et al., 2016
Blinding of participants and personnel (performance bias)	High risk	Reference: Groot et al., 2016
Blinding of outcome assessment (detection bias)	Low risk	Reference: Groot et al., 2016
Incomplete outcome data (attrition bias)	Low risk	Reference: Groot et al., 2016
Selective reporting (reporting bias)	Low risk	Reference: Groot et al., 2016
Other bias	Low risk	Reference: Groot et al., 2016

Bossers 2015

Methods	
Participants	
Interventions	
Outcomes	

Notes	Data obtained from: Groot C, Hooghiemstra AM, Raijmakers PGHM, van Berckel BNM, Scheltens P, Scherder EJA, van der Flier WM, Ossenkoppele R. The effect of physical activity on cognitive function in patients with dementia: A meta-analysis of randomized controlled trials. Ageing Research Reviews 2016; 25: 13-23.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Reference: Groot et al., 2016
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Blinding of participants and personnel (performance bias)	High risk	Reference: Groot et al., 2016
Blinding of outcome assessment (detection bias)	Low risk	Reference: Groot et al., 2016
Incomplete outcome data (attrition bias)	Low risk	Reference: Groot et al., 2016
Selective reporting (reporting bias)	Low risk	Reference: Groot et al., 2016
Other bias	Low risk	Reference: Groot et al., 2016

Bossers 2016

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention ● *Age, y (SD)*: 85.5 (5.4) ● *MMSE (mean)*: 15.3 (4.8) Control ● *Age, y (SD)*: 85.7 (4.8) ● *MMSE (mean)*: 15.9 (4.3) **Included criteria:** Eligibility criteria were aged 65 andolder, diagnosis of dementia reported in the individual'smedical file

	by a Dutch dementia diagnosis team or a med-ical specialist, no history of alcoholism, no severe vision orhearing problems, native Dutch speaker, and absence ofserious health problems (e.g., heart failure, terminal can-cer, chronic obstructive pulmonary disease), as determinedby a geriatrician. Additional inclusion criteria were aMini-Mental State Examination (MMSE) score between 9 and 23 and ability to complete the Timed Up and Go Test as determined by a trained research assistant.
Interventions	**Intervention Characteristics** Intervention ● *Description*: Aerobic Exercise. Aerobic exercise consisted of moderate- to high-intensitywalking sessions in the corridors of the nursing home oron paved outdoor walking paths near the nursing home. Ifa participant requested rest, an appropriate rest periodwas included in the 30-minute session. As soon as the par-ticipant recovered, walking resumed. ● *Duration (weeks)*: 9 ● *Length of follow-up after end of treatment*: None Control ● *Description*: Social Intervention. The social group received 30-minute one-on-one socialvisits. Activities during social visits were small talk whilesitting in a chair. ● *Duration (weeks)*: 9 ● *Length of follow-up after end of treatment*: None
Outcomes	*ADL_Katz ADL, proxy, higher=better_final_mean SD* ● **Outcome type**: ContinuousOutcome *Serious adverse events* ● **Outcome type**: DichotomousOutcome *Dropouts in absolute numbers* ● **Outcome type**: DichotomousOutcome
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "After baseline measurements were made, partici- pants were randomly assigned to one of three groups using numbered containers stratified according to nursing home, sex, and MMSE score (allocation ratio 1:1:1). A scientist unrelated to the study performed the procedure."
Allocation concealment (selection bias)	Low risk	Quote: "A scientist unrelated to the study performed the procedure."
Blinding of participants and personnel (performance bias)	Unclear risk	Quote: "ADL assessors were blinded to participant group assign- ment." Judgement Comment: Participants or personnel could not be blinded to treatment
Blinding of outcome assessment (detection bias)	High risk	Quote: "A nurse who worked closely with the participant filled in a proxy Katz index questionnaire at baseline and 9 weeks. For practical reasons, the nurse was not blinded."
Incomplete outcome data (attrition bias)	Low risk	Quote: "Missing data were addressed using multiple imputation in SPSS." Judgement Comment: Similar rate of dropout accross the groups with reasons given.
Selective reporting (reporting bias)	Low risk	Quote: "Details and full descriptions of the cognitive and motor tests have been published previously. " Quote: "(Project 1003– 76, trial registration Nederlands Trial Register, Trial 2269)." Judgement Comment: The authors state that they performed posthoc comparisons/analyses, and otherwise the study seems free of bias in relation to selective outcome reporting. The protocol can not be detected, but all ADL outcomes appear to be reported. Other outcomes are reported elsewhere
Other bias	Low risk	Quote: "Nederlands Trial Register, Trial 2269). Conflict of Interest: All authors certify that there is no conflict of interest regarding the material discussed in the manuscript. Author Contributions: All authors: study" Judgement Comment: The study seems free of other sources of bias.

Cancela 2016

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group

Participants	**Baseline Characteristics** Intervention ● *Age, y (SD)*: 80.63 (8.32) ● *MMSE (mean)*: 15.16 (2.54) Control ● *Age, y (SD)*: 82.90 (7.42) ● *MMSE (mean)*: 14.95 (2.44) **Included criteria:** (a) over 65 years of age, (b)diagnosis of dementia according to Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition criteria, (c)able to stand and walk for 30 m without shortness of breath,(d) able to walk safely without assistance, and(e) resident of an elderlyhome-carefacility in Galicia (northwest region of Spain). **Excluded criteria:** (1) individuals with a history of major psychiatric illness, serious neurologic, cardiovascular or musculoskeletal disorders limiting the understanding and/or performance of the necessary intervention tasks and (2) refusal by the individual and/or their primary caregiver/closest of kin.
Interventions	**Intervention Characteristics** Intervention ● *Description*: The aerobic physical activity program consisted of daily cycling sessions during 15 months.The participants attended the gymnasium daily and cycled continuously alone, or in pairs, in a recumbent bicycle geared to a very low resistance. They were instructed to pedal for a minimum of 15 min at a constant self-selected pace. A physiotherapist monitored each session registering the amount of time that each individual exercised each day as well as their adherence to the program. ● *Duration (weeks)*: 60 ● *Length of follow-up after end of treatment*: None Control ● *Description*: Non-physical distractive recreational activities as usual and of their choice (for example, card-playing, reading, craftwork, etc.). ● *Duration (weeks)*: 60 ● *Length of follow-up after end of treatment*: None

Outcomes	*ADL_Katz ADL, proxy, higher=better_change mean CI* ● **Outcome type**: ContinuousOutcome ● **Scale**: Katz ADL, proxy ● **Direction**: Higher is better ● **Data value**: Change from baseline *Serious adverse events* ● **Outcome type**: DichotomousOutcome *Dropouts in absolute numbers* ● **Outcome type**: DichotomousOutcome *BPSD_NPI, proxy_change_mean CI* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Scale**: NPI, proxy ● **Direction**: Lower is better ● **Data value**: Change from baseline *Kognition_MMSE_change_mean CI* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Scale**: MMSE ● **Direction**: Higher is better ● **Data value**: Change from baseline *Depression_CSDD_change mean CI* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Scale**: CSDD ● **Direction**: Lower is better ● **Data value**: Change from baseline
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Group allocation was performed by an independent researcher blinded to baseline interview data. Computer-generated random numbers were assigned to the participants. SPSS ® Statistics 19.0 was used to generate the random numbers from a normal distribu- tion with a mean and a standard deviation of any specified variable."
Allocation concealment (selection bias)	Unclear risk	Quote: "Computer-generated random numbers were assigned to the participants. SPSS ® Statistics 19.0 was used to generate the random numbers from a normal distribu- tion with a mean and a standard deviation of any specified variable." Judgement Comment: Insufficient information on allocation concealment
Blinding of participants and personnel (performance bias)	High risk	Quote: "Sample data information of the functional mobility was recorded and coded by physiotherapists who were not blind to randomiza- tion. The participants were aware of group identity."
Blinding of outcome assessment (detection bias)	High risk	Quote: "deviation of any specified variable. Sample data information of the functional mobility was recorded and coded by physiotherapists who were not blind to randomiza- tion. The participants were aware of group identity. Once baseline data were collected, the"
Incomplete outcome data (attrition bias)	Low risk	Quote: "The first was based on an intention-to-treat methodology and" Judgement Comment: Droputs accounted for.
Selective reporting (reporting bias)	Low risk	Judgement Comment: There is no reference to study protocol, but seems to be free of selective outcome reporting bias.
Other bias	Low risk	Judgement Comment: The study appears free of other sources of bias.

deSoutoBarreto 2017

Methods	**Study design:** Cluster randomized controlled trial **Study grouping:** Parallel group

Participants	**Baseline Characteristics** Intervention ● *Age, y (SD)*: 88.3 (5.1) ● *MMSE (mean)*: 11.4 (6.2) Control ● *Age, y (SD)*: 86.9 (5.8) ● *MMSE (mean)*: 10.8 (5.5) **Included criteria:** Inclusion criteria were a diagnosis of Alzheimer's diseaseor vascular or mixed dementia according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition(DSM-IV); a Mini-Mental State Examination (MMSE)score of 20 or less; age 65 and older; living in the NH forat least 1 month; ability to walk 4 m without human assistance; and ability to rise from a chair with minimal human assistance **Excluded criteria:** Exclusion criteria were terminal illness (lifeexpectancy6 months), Parkinson's disease or dementiawith Lewy bodies, unstable condition precluding participa-tion in exercise, planned transfer from the NH duringintervention period, and participation in another exerciseprogram for two times per week or more in the last 2 months. **Pretreatment:** Gender differences (more women in the intervention group and fewer men).Higher Mini-nutritional assessment score in the intervention group.Higher Neuropsychiatric inventory score in the intervention group
Interventions	**Intervention Characteristics** Intervention ● *Description*: Exercise instructors (3-year university diploma in physicalactivity) had experience working with institutionalizedPWDs. Group-based exercise interventions took place inthe NHs twice per week for 60 minutes per session for24 weeks. The exercise was a multicomponent training:10 minutes of warm-up (e.g., range of motion), 10 min-utes of coordination and balance exercises (e.g., shortwalks with direction changes), 10–15 minutes of musclestrengthening (e.g., weight lifting), 20 minutes of aerobicexercise (mostly walking), and 5–10 minutes of cool-down. Exercise intensity was targeted to be moderate.Instructors endeavored to establish progression individu-ally; visual cues were used, and participants were regularlyencouraged to improve their performance in the absence ofpain or breathlessness. When a subject had improved theexecution of an exercise, a progression was proposed byincreasing exercise difficulty, the number of repetitions tobe performed, or exercise load ● *Duration (weeks)*: 24 ● *Length of follow-up after end of treatment*: None Control

	● *Description*: Social activity interventionists had experience in workingwith institutionalized PWDs. Group-based activities tookplace in the NHs twice per week for 60 minutes per ses-sion for 24 weeks. The selected interventions were newactivities for the residents. No predefined model of socialactivity was established because the same interventionwas not always feasible or available at all participatingNHs. According to availability of interventions near theNHs and NH staff choice, NHs randomized to socialactivity received one of therapeutic music mediation(e.g., relaxation with music, playing percussion instru-ments, singing, light dancing) or arts and crafts (e.g.,painting and drawing alone and in pairs, clay modelling). ● *Duration (weeks)*: 24 ● *Length of follow-up after end of treatment*: None
Outcomes	*Kognition_MMSE_final_mean SE* ● **Outcome type**: ContinuousOutcome *ADL_ADCS-ADL, higher=better_change mean SE* ● **Outcome type**: ContinuousOutcome *Serious adverse events* ● **Outcome type**: DichotomousOutcome *Dropouts in absolute numbers* ● **Outcome type**: DichotomousOutcome
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "A statistician blinded to NH identity and not involved in any other aspect of LEDEN performed ran-domization. Group allocation was stratified according to the median value of dementia prevalence in the NHs and was performed using random permuted block sizes of two within each of the two strata."
Allocation concealment (selection bias)	Low risk	Quote: "Group allocation conceal- ment was guaranteed by using opaque, sealed envelopes until group assignment was revealed to the NHs."

Blinding of participants and personnel (performance bias)	High risk	Quote: "NH staff assessed and recorded outcome measures and data on adverse health events (unblinded to group assignment);"
Blinding of outcome assessment (detection bias)	High risk	Quote: "to group assignment); in practice, outcome assessors were mainly NH nurses, nurses' aides, and coordinating physicians. The research team conducted in-person" Judgement Comment: NH nurses were not blinded
Incomplete outcome data (attrition bias)	Low risk	Quote: "Effi- cacy analyses were performed, as prespecified in the pro- tocol, using a modified intention-to-treat approach including all participants with at least one postbaseline assessment for the ADCS-ADL-sev. Multilevel analyses" Judgement Comment: Drop outs are equally distributed between groups, and reasons for drop outs are provided
Selective reporting (reporting bias)	Low risk	Quote: "clinical trial registry (registration NCT02444078). Participants" Judgement Comment: Outcomes are reported
Other bias	High risk	Judgement Comment: The significant baseline differences between the groups indicate that there has been issues with the randomization. Potentially because the randomization occurred prior to baseline, may indicate a selected group of participants are enrolled.

Hoffmann 2016

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention ● *Age, y (SD)*: 69.8 (7.4) ● *MMSE (mean)*: 23.8 (3.4) Control ● *Age, y (SD)*: 71.3 (7.3) ● *MMSE (mean)*: 24.1 (3.8) Overall ● *Age, y (SD)*: 70.5 (7.4) ● *MMSE (mean)*: 24.0 (3.6)

	Included criteria: Inclusion criteria included a Mini Mental StateExamination (MMSE) score >19 (at screening lessthan six weeks prior to baseline visit), age between50–90 years, and a caregiver with regular contact (morethan once a month) who was willing to participate inthe study. If patients received anti-dementia medica-tion or mood stabilizing medication, they had to be ona stable dose for at least three months before inclusion. **Excluded criteria:** Exclusion criteria were 1) presence of cardiac orother medical diseases constituting a contraindicationto physical activity or other neurological diseases caus-ing cognitive decline (including severe cerebrovasculardisease judged from cranial computed tomography ormagnetic resonance imaging); 2) severe psychiatricdisease; 3) alcohol abuse within the last two yearsaccording to the national guidelines; and 4) participa-tion in regular physical activity of high intensity two ormore times weekly. **Pretreatment:** There were no significant differences in base-line characteristics between the intervention group andthe control group in any of the parameters (Table 1).
Interventions	**Intervention Characteristics** Intervention ● *Description*: Three weekly exercise sessions were conducted ina group of 2–5 participants supervised by an experi-enced physiotherapist. The first four weeks of exercise(adaption) emphasized getting used to exercising andbuilding up strength, primarily of the lower extremi-ties (twice weekly). Participants were also introducedto aerobic exercise (once weekly). For the remain-ing 12 weeks, patients performed aerobic exercise ofmoderate-to-high intensity (in total 3×10 min on anergometer bicycle, cross trainer, and treadmill with2–5 min rest between). Average heart rate (HR) was registered using continuous monitoring during aerobicexercise, including the rest intervals. The target inten-sity was 70–80% of maximal HR (220 - the person'sage). To ensure that participants exercised with theintended intensity throughout the training period, aver-age HR was further calculated for three time periods(between weeks 4 to 8, 8 to 12, and 12 to 16) as: (aver-age HR of all sessions in a 4-week period)/(maximalHR) [17]. The training log also included informationabout training instruments and attendance. Attendancerate was defined as: (total number of attended trainingsessions)/(total number of offered training sessions). ● *Duration (weeks)*: 16 ● *Length of follow-up after end of treatment*: None Control ● *Description*: Participants assigned to the control group receivedtreatment as usual with access to memory clinic staffif medical or other needs necessitated contact duringthe study period. In order to increase adherence andpositive expectations to the study, all control group subjects were offered 4 weeks of adaptation exerciseafter the termination of the study.

	● *Duration (weeks)*: ● *Length of follow-up after end of treatment*: None
Outcomes	*BPSD_NPI, proxy_final_mean SD* ● **Outcome type**: ContinuousOutcome *Kognition_MMSE_final_mean SD* ● **Outcome type**: ContinuousOutcome *Depression_Hamilton Depression Rating Scale_final_mean SD* ● **Outcome type**: ContinuousOutcome *ADL_ADCS-ADL, higher=better_final mean SD* ● **Outcome type**: ContinuousOutcome *Dropouts in absolute numbers* ● **Outcome type**: DichotomousOutcome
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Subsequently, participants were randomized in blocks of 4–10 per participating center, using a computerized random- number generator. In the case of an unequal number of participants in one center, randomization was set up to favor the intervention group."
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Insufficient information on allocation concealment
Blinding of participants and personnel (performance bias)	High risk	Quote: "All raters performing the outcome measurements were blinded to group assignment, and patients and caregivers were advised not to disclose group assign- ment during the test sessions." Judgement Comment: Nothing mentioned

Blinding of outcome assessment (detection bias)	Low risk	Quote: "After screening for eligibility and obtaining informed consent, assessors (blinded to the group assignment throughout the study period) completed the baseline assessments." Quote: "administered to both caregiver and patient [26]. All raters performing the outcome measurements were blinded to group assignment, and patients and caregivers were advised not to disclose group assign- ment during the test sessions. "
Incomplete outcome data (attrition bias)	Low risk	Quote: "possible clustering by training groups. Missing data may have different causes for the two randomization groups and to avoid the associated bias, the measure- ments available at follow-up were weighted by the inverse of an estimate of the probability of still being in the study [27]. These probabilities were estimated from the data in a logistic regression model with the patient's baseline characteristics and the observed outcome at baseline as covariates. In the analysis of secondary outcomes, multiple comparisons were adjusted for by controlling the false discovery rate at 5% [28]. In addition to intention-to-treat (ITT) analyses, we analyzed outcomes in a" Judgement Comment: Dropouts accounted for at evenly distributed
Selective reporting (reporting bias)	Low risk	Quote: "The trial protocol was approved by the Danish National Committee on Biomedical Research Ethics (H-3-2011-128) and" Judgement Comment: No other apparent sources of bias
Other bias	Low risk	Judgement Comment: the study appears to be free of other sources of bias

Miu 2008

Methods	
Participants	
Interventions	
Outcomes	
Notes	Data obtained from: Groot C, Hooghiemstra AM, Raijmakers PGHM, van Berckel BNM, Scheltens P, Scherder EJA, van der Flier WM, Ossenkoppele R. The effect of physical activity on cognitive function in patients with dementia: A meta-analysis of randomized controlled trials. Ageing Research Reviews 2016; 25: 13-23.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Reference: Groot et al., 2016
Allocation concealment (selection bias)	Unclear risk	Reference: Groot et al., 2016
Blinding of participants and personnel (performance bias)	High risk	Reference: Groot et al., 2016
Blinding of outcome assessment (detection bias)	Low risk	Reference: Groot et al., 2016
Incomplete outcome data (attrition bias)	Low risk	Reference: Groot et al., 2016
Selective reporting (reporting bias)	High risk	Reference: Groot et al., 2016
Other bias	Low risk	Reference: Groot et al., 2016

Morris 2017

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention ● *Age, y (SD)*: 74.4(6.7) ● *MMSE (mean)*: 25.8(3.3) Control ● *Age, y (SD)*: 71.4(8.4] ● *MMSE (mean)*: 25.0(3.2) **Included criteria:** Inclusion criteria included MCI or dementia with etiologic diagnosis ofprobable AD based on clinical and cognitive test results using standard criteria;[26, 27] ClinicalDementia Rating (CDR) of 0.5 or 1 (very mild to mild dementia);[28] at least 55 years ofage; sedentary or underactive as defined by the Telephone Assessment of Physical Activity;[29]community dwelling with a supportive caregiver willing to accompany participants to visits asnecessary; adequate visual and auditory ability to perform cognitive testing; stable medicationdose (30 days); and ability to participate in all scheduled evaluations and the exercise program. **Excluded criteria:** Exclusion criteria included clinically significant psychiatric disorder; systemic illness or infectionlikely

	to affect safety; clinically-evident stroke; myocardial infarction or coronary arterydisease in the last 2 years; uncontrolled hypertension in the last 6 months; cancer in the last 5years; drug or alcohol abuse in the last 2 years; insulin dependent diabetes; or significant painor musculoskeletal symptoms that would prohibit exercise. **Pretreatment:** Demographic and baseline characteristics are given inTable 1. Participants in the two groups did not significantly differ in these measures.
Interventions	**Intervention Characteristics** Intervention ● *Description*: InterventionParticipants were asked not to alter current physical activities other than those prescribed bythe study team. The AEx group began the intervention with a weekly goal of 60min in Week1 and increased their weekly exercise duration by approximately 21min per week until theyachieved the current public health recommended target duration of 150min per week, distributedover 3–5 sessions. Target heart rate (HR) zones were gradually increased from 40–55% to60–75% of HR reserve based on resting and peak HR during cardiorespiratory fitness testing. HR was monitored at the YMCA by conventions chest worn sensor (F4 or FT4, Polar Electro,Inc. Lake Success, NY). Total exercise duration and a rating of perceived exertion (Borg 6–20)were gathered during each session. Exercise trainers supervised all exercise sessions duringWeeks 1–6 and gradually reduced supervised sessions to 1 per week based on perceived abilityto be safe and independent and in consultation with the participant's study partner and studystaff. ● *Duration (weeks)*: 26 ● *Length of follow-up after end of treatment*: None Control ● *Description*: The ST group performed a series of non-aerobic exercises that rotated weekly (core strengthening,resistance bands, modified tai chi, modified yoga). As in several previous studies [42–46]we chose an active control intervention (ST) to account for potential effects of social engagementand physical activity.[47] Participants in the ST group wore HR monitors and were askedto keep their HR below 100 beats per minute. Exercise trainers helped participants adjust exerciseintensity to reduce HR as necessary. Similar to the AEx group, trainers supervised all exercisesessions during Weeks 1–6 and gradually reduced supervised sessions to 1 per week basedon perceived ability to be safe and independent and in consultation with the participant's studypartner and study staff. ● *Duration (weeks)*: 26 ● *Length of follow-up after end of treatment*:

Outcomes	*Kognition_MMSE_change_mean SD* ● **Outcome type**: ContinuousOutcome *Depression_CSDD_change mean SD* ● **Outcome type**: ContinuousOutcome *ADL_DAD, higher=better_change_mean SD* ● **Outcome type**: ContinuousOutcome *Dropouts in absolute numbers* ● **Outcome type**: DichotomousOutcome
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Participants were block randomized, stratified by age (split at 75) and sex, to balance treatment arms."
Allocation concealment (selection bias)	Low risk	Quote: "found in our published protocol.[25] One investigator (JDM) constructed the allocation schedule using SAS, placing index cards in 320 sequentially numbered, sealed envelopes grouped by age and sex strata. Envelopes were opened after baseline testing by staff not involved with primary out- come measure testing. Psychometric and cardiorespiratory exercise testers were"
Blinding of participants and personnel (performance bias)	High risk	Quote: "adverse events at every contact. Severity and relationship of adverse events to intervention was deter- mined by an un-blinded clinician investigator. An independent safety committee reviewed adverse" Judgement Comment: Cardiorespiratory exercise testers were blinded at all times, however it appears as the participants are not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Quote: "Psychometric and cardiorespiratory exercise testers were blinded to the participant’s intervention arm at all times." Judgement Comment: participants are outcome assessors and not blinded

Incomplete outcome data (attrition bias)	Low risk	Judgement Comment: In the intervention group 2 out of 39 did not complete the study and in the control group 3 out of 37 withdrew.There are no intention-to-treat analysis.
Selective reporting (reporting bias)	Low risk	Quote: "important in driving brain benefits. Trial registration ClinicalTrials.gov NCT01128361 Introduction An estimated 5.3 million" Judgement Comment: The trial appears to be free of selective outcome reporting
Other bias	Low risk	Judgement Comment: The study appears to be free of other sources of bias.

Ohman 2017

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention ● *Age, y (SD)*: 77.9(5.2) ● *MMSE (mean)*: 18.9(6.5) Control ● *Age, y (SD)*: 78.1(5.3) ● *MMSE (mean)*: 17.8(6.0) Intervention 2 ● *Age, y (SD)*: 77.4(5.3) ● *MMSE (mean)*: 18.6(6.2) **Included criteria:** Patients over 65 years of age living with a spouse in the Helsinki area and who were listed on the AD drug reimbursement register of the Social Insurance Institution of Finland were invited to participate in this trial. Patients in this register are diagnosed with AD according to the NINCD-ADRDA criteria evaluated by a geriatrician/neurologist. Individuals showing an interest in participating were assessed for additional inclusion criteria: ability to walk independently with or without a mobility aid, no terminal illness, and at least one sign of frailty (one or more falls during the last year, decreased walking speed, or unintentional weight loss).

Interventions	**Intervention Characteristics** Intervention ● *Description*: Both intervention groups exercised under supervision of aphysiotherapist for 60 minutes twice a week for 12 months. Theexercise sessions consisted of aerobic exercise, strength training,balance training, and dual-tasking. Fifteen minutes was allocatedto each exercise domain. The intensity of the training wasgradually increased, and the balance and dual-task exercises weremade more demanding during the intervention phase [25]. The GE group exercised in groups of 10 supervised by twophysiotherapists in day care centres. The visits to day care centreslasted 4 hours and included door-to-door taxi service, lunch, andcoffee breaks. Actual training time was 60 minutes and consistedof components similar to those described for the HE group. Thestrength training was, however, assisted with gym equipment. ● *Duration (weeks)*: 52 ● *Length of follow-up after end of treatment*: None Control ● *Description*: The control group continued in usual care, but was entitled tophysiotherapy provided by the communal health care system ifneeded. All participants and care givers were also given oral andwritten information on exercise and nutrition. ● *Duration (weeks)*: 52 ● *Length of follow-up after end of treatment*: None Intervention 2 ● *Description*: Both intervention groups exercised under supervision of aphysiotherapist for 60 minutes twice a week for 12 months. Theexercise sessions consisted of aerobic exercise, strength training,balance training, and dual-tasking. Fifteen minutes was allocatedto each exercise domain. The intensity of the training wasgradually increased, and the balance and dual-task exercises weremade more demanding during the intervention phase [25].In the HE group, the training was individually tailored to meetthe needs of the participant and the sessions took place at theparticipant’s home. Aerobic exercises included Nordic walking andtraining with a restorator bike. Wrist and ankle weights were usedto assist the strength training. Balance exercises consisted of stairclimbing, picking up items from the floor, and getting up from thefloor. Talking while walking, singing while training, and performingtwo different functions with the left and right hands whilecounting numbers forward or backward are examples of the dualtaskexercises. ● *Duration (weeks)*: 52 ● *Length of follow-up after end of treatment*: None

Outcomes	*BPSD_NPI, proxy_change_mean CI* ● **Outcome type**: ContinuousOutcome *Depression_CSDD_change mean CI* ● **Outcome type**: ContinuousOutcome
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: The participants were randomized after the baseline visit. A separate randomization centre was used to assign the patient- spouse dyads (n = 210) into three groups of equal size (n = 70):
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Insufficient information on allocation concealment
Blinding of participants and personnel (performance bias)	High risk	Judgement Comment: No blinding
Blinding of outcome assessment (detection bias)	High risk	Judgement Comment: Particpants are outcome assessors and not blinded
Incomplete outcome data (attrition bias)	Unclear risk	Quote: The NPI was administered at baseline and 6 months. Of the 210 participants, 179 had complete NPI data from baseline and 6 months, and thus, were included in the analyses. Judment comment: Insufficient information on missing data
Selective reporting (reporting bias)	High risk	Judgement Comment: Even though the trial has been registered, the authors choose to report some of the outcomes at 6 months from baseline only, but not at 12 months (end of treatment), i.e. NPI. For significant outcomes, such as CSDD, where only the 12 month assessment is reported. The study appears to be free of selective outcome reporting
Other bias	Low risk	Judgement Comment: The study appears to be free of other sources of bias

Rolland 2007

Methods	
Participants	
Interventions	
Outcomes	
Notes	Data obtained from: Forbes D, Forbes SC, Blake CM, Thiessen EJ, Forbes S. Exercise programs for people with dementia. Cochrane Database of Systematic Reviews 2015, Issue 4. Art. No.: CD006489. DOI: 10.1002/14651858.CD006489.pub4. www.cochranelibrary.com and Barreto, Philipe de Souto; Demougeot, Laurent; Pillard, Fabien; Lapeyre-Mestre, Maryse; Rolland, Yves Exercise training for managing behavioral and psychological symptoms in people with dementia: A systematic review and meta-analysisAgeing Research Reviews 2015;24(Pt B):274-285.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Reference: Forbes et al., 2015
Allocation concealment (selection bias)	Low risk	Reference: Forbes et al., 2015
Blinding of participants and personnel (performance bias)	High risk	Reference: Forbes et al., 2015
Blinding of outcome assessment (detection bias)	Low risk	Reference: Forbes et al., 2015
Incomplete outcome data (attrition bias)	Low risk	Reference: Forbes et al., 2015
Selective reporting (reporting bias)	Low risk	Reference: Forbes et al., 2015
Other bias	Low risk	Reference: Forbes et al., 2015

Savikko 2016

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention ● *Age, y (SD)*: 78.3 (5.1) ● *MMSE (mean)*: 18.5 (6.3) Control ● *Age, y (SD)*: 78.1 (5.3) ● *MMSE (mean)*: 17.7 (6.2) Intervention 2 ● *Age, y (SD)*: 77.7 (5.4) ● *MMSE (mean)*: 17.8 (6.6) **Included criteria:** inclusion criteria (establishedAD diagnosis, spouse living at the same address,aged ≥ 65, no diagnosed terminal disease, ability to walkindependently with or without a mobility aid). Participantsalso had to fulfill at least one of the following signs offrailty: one or more falls during the past year, decrease inwalking speed, or unintentional weight loss.
Interventions	**Intervention Characteristics** Intervention ● *Description*: Physical exercise for the GE group was based on 4-hour sessions in adult daycare centers twice a week for12 months. Door-to-door taxi service and lunches wereprovided. The sessions were organized in groups of 10 participantsand supervised by two physiotherapists with aspecialty in dementia. The predetermined exercise programconsisted of aerobic, endurance, balance, and strength training, and dual tasking to improve executive functioning(Table 1). Peer support was used to aid in training.The average active exercise time per person was approximately 1 hour per day because of lunch and coffee breaksand waiting times for gym equipment.Aerobic training was included in both groups (e.g.,Nordic walking). Strength training was aided with wristand ankle weights in home exercise sessions, whereas thegroup exercise group used gym equipment. The trainingalso included various balance exercises. Dual-task exerciseswere simple, such as talking while walking (Table 1). Bothintervention group participants continued regular exerciseeven in the case of hospitalization or respite care, but if aparticipant was admitted to permanent institutional care,the intervention and further study assessments were

	discontinued. ● *Duration (weeks)*: 52 ● *Length of follow-up after end of treatment*: None Control ● *Description*: CG participants received the usual care that the Finnishhealthcare system provides but the study nurses alsogave them oral and written advice on nutrition and exercisemethods. They also access to physiotherapy providedby the community health system. ● *Duration (weeks)*: 52 ● *Length of follow-up after end of treatment*: None Intervention 2 ● *Description*: The HE group performed physical exercise at homefor 1 hour twice a week for 12 months. A physiotherapistwith a specialty in dementia supervised customizedtraining sessions during the home visits, addressing theindividual's needs and problems with daily functioning.Although the exercises were planned according to theindividual's requirements, they always included elementsof executive function training; dual-task exercises; andstrength, balance, endurance, and aerobic training(Table 1). Aerobic training was included in both groups (e.g.,Nordic walking). Strength training was aided with wristand ankle weights in home exercise sessions, whereas thegroup exercise group used gym equipment. The trainingalso included various balance exercises. Dual-task exerciseswere simple, such as talking while walking (Table 1). Bothintervention group participants continued regular exerciseeven in the case of hospitalization or respite care, but if aparticipant was admitted to permanent institutional care,the intervention and further study assessments were discontinued. ● *Duration (weeks)*: 52 ● *Length of follow-up after end of treatment*: None
Outcomes	*Serious adverse events* ● **Outcome type**: DichotomousOutcome *Dropouts in absolute numbers* ● **Outcome type**: DichotomousOutcome *Kognition_MMSE_change_mean CI* ● **Outcome type**: ContinuousOutcom
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Dyads fulfilling all inclusion criteria (N = 210) were ran- domized after the baseline visit into three equal-sized (n = 70) groups (customized HE, GE, and a CG continu- ing in community care) using computer-generated numbers received by telephone from a randomization center."
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Insufficient information on allocation concealment
Blinding of participants and personnel (performance bias)	High risk	Quote: "The study was not blinded."
Blinding of outcome assessment (detection bias)	High risk	Quote: "The study was not blinded. Physiotherapists"
Incomplete outcome data (attrition bias)	Low risk	Quote: "All participants assessed at baseline and 3 months were included in the data analyses of changes in cognitive func- tion (modified intention to treat). There" Judgement Comment: no concern for incomplee outcome data, 11 participants left the HE, 19 left the GE and 19 left the CG
Selective reporting (reporting bias)	Unclear risk	Quote: "The ethics committee of Helsinki University Central Hospital approved the study protocol." Judgement Comment: no reference to tjhe study protocol, and it is therefore unclear if the reporting are complete
Other bias	Low risk	Quote: "Sponsor’s Role: The sponsors had no role in study design, data analysis, interpretation of results, writing the report, or in the decision to submit for publication. The authors were independent researchers not associated with the sponsors." Quote: "Conflict of Interest: The authors declare they that have no conflict of interest directly relevant to this report." Judgement Comment: The study appears to be free of other sources of bias

Vidoni 2017

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention ● *Age, y (SD)*: 74.1 (6.8) Control ● *Age, y (SD)*: 71.1 (8.8) **Included criteria:** Inclusion criteria included participants with mild cogni-tive impairment or dementia with etiologic diagnosis of probable AD based on clinical and cognitive test results using standard criteria, 26,27 Clinical Dementia Rating (CDR) of 0.5 or 1 (very mild to mild dementia) 28; at least 55 years of age; sedentary or underactive as defi ned by the Telephone Assessment of Physical Activity 29; community dwelling; having an informal caregiver; adequate visual and auditory ability to perform cognitive testing; stable medication dose (30 days); and ability to participate in all scheduled evaluations and the exercise program. **Excluded criteria:** Exclusion criteria included clinically signifi cant psychiatric disorder; systemic illness or infection likely to affect safety; clinically evident stroke; myocardial infarction or coronary artery disease in the last 2 years; uncontrolled hypertension in the last 6 months; cancer in the last 5 years; drug or alcohol abuse in the last 2 years; insulin-dependent diabetes; or signifi cant pain or musculoskeletal symptoms that would prohibit exercise. **Pretreatment:** The intervention groups did not differ statistically by age, sex, educational attainment, or baseline dementia severity as measured by CDR Sum of Boxes (P> .13)
Interventions	**Intervention Characteristics** Intervention ● *Description*: Participants were asked not to alter current physical activi-ties other than those prescribed by the study team. The AEx group began the intervention with a weekly goal of 60 min-utes of aerobic exercise in week 1 and increased their weekly exercise duration by approximately 21 minutes per week until they achieved the current public health-recommended target duration of 150 minutes per week, distributed over to 5 sessions. Target heart rate (HR) zones were gradu-ally increased from 40% to 55% to 60% to 75% of HR reserve based on resting and peak HR during cardiorespira-tory fi tness testing. Exercise trainers supervised all exercise sessions during weeks 1 to 6. Supervised sessions were gradually reduced to 1 per week based on perceived ability to be safe and independent and in consultation with the participant’s study partner and study staff.

	● *Duration (weeks)*: 26 ● *Length of follow-up after end of treatment*: None Control ● *Description*: The ST group performed a series of nonaerobic exer-cises that rotated weekly (core strengthening, resistance bands, modifi ed tai chi, and modifi ed yoga). The active control intervention (ST) accounts for potential effects of social engagement and physical activity. 35 Participants in the ST group wore HR monitors and were asked to keep their HR below 100 beats per minute. Exercise trainers helped participants adjust exercise intensity to reduce HR as necessary. Like the AEx group, trainers supervised all exercise sessions during weeks 1 to 6 and gradually reduced supervised sessions to 1 per week based on perceived abil-ity to be safe and independent and in consultation with the participant's study partner and study staff. ● *Duration (weeks)*: 26 ● *Length of follow-up after end of treatment*: None
Outcomes	*ADL_DAD, higher=better_change_mean SD* ● **Outcome type**: ContinuousOutcome *Dropouts in absolute numbers* ● **Outcome type**: DichotomousOutcome
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Participants were block randomized, stratifi ed by age (split at 75) and sex, to balance treatment arms. Testers" Judgement Comment: The study refers to Vidoni et al (ref 25) and there it is reported that "A block randomization procedure is used, stratified by age (<75 years vs. >=75 years old) and gender to ensure the groups are well-matched across these variables. The randomization sequences were constructed prior to study start by the KU Department of Biostatistics. Randomization is performed immediately upon successful completion of the exercise test."

Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Insufficient information on allocation concealment
Blinding of participants and personnel (performance bias)	Unclear risk	Quote: "Testers were blinded to the participant's intervention arm at all timepoints." Judgement Comment: The psychometrician, clinical evaluator, and staff involved in the exercise testing are blinded to randomization assignment. However the particpants were not blinded.Ref 25, "Participants are asked at the beginning of each visit not to discuss anything regarding their intervention with testing staff. However, maintaining blinding can be a challenge with cognitively impaired participants".
Blinding of outcome assessment (detection bias)	Low risk	Quote: "sex, to balance treatment arms. Testers were blinded to the participant's intervention arm at all timepoints. Outcome Measures Functional disability as measured by"
Incomplete outcome data (attrition bias)	Low risk	Judgement Comment: Reported in Morris et al 2017 (ref 16). 3 particpants withdrew from the control group and 5 from the interventiongroup.
Selective reporting (reporting bias)	Low risk	Judgement Comment: No reference to study protocol, but it appears that the study reports on all relevant outcomes.
Other bias	Low risk	Judgement Comment: The study appears to be free of other sources of bias

Yang 2015

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention ● *Age, y (SD)*: 72.0 (6.69) ● *MMSE (mean)*: 21.33 (2.24) Control ● *Age, y (SD)*: 71.92 (7.28) ● *MMSE (mean)*: 20.0 (3.50) **Included criteria:** Age 65-80 yearsStable condition and ADMMSE = 24 and >=10 **Excluded criteria:** Subjects diagnosed with vascular dementia and cannot be coordinate with cognitive fuction tests.

Interventions	**Intervention Characteristics** Intervention ● *Description*: Cycling traing, moderate intensity (70% max heart rate). Each training lasted for 40 minutes. ● *Duration (weeks)*: 12 ● *Length of follow-up after end of treatment*: None Control ● *Description*: Health education ● *Duration (weeks)*: 12 ● *Length of follow-up after end of treatment*: None
Outcomes	*BPSD_NPI, proxy_final_mean SD* ● **Outcome type**: ContinuousOutcome *Kognition_MMSE_final_mean SD* ● **Outcome type**: ContinuousOutcome
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement Comment: Insufficient information on sequence generation
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Insufficient information on allocation concealment
Blinding of participants and personnel (performance bias)	Unclear risk	Judgement Comment: Insufficient information on blinding of participants and personnel
Blinding of outcome assessment (detection bias)	Unclear risk	Judgement Comment: Insufficient information on blinding of outcome assessors
Incomplete outcome data (attrition bias)	Low risk	Judgement Comment: The study appears free of incomplete outcome data

Selective reporting (reporting bias)	Low risk	Judgement Comment: The study has been approved by the ethical commitee, and appears to be free of selective outcome reporting.
Other bias	Low risk	Judgement Comment: The study appears to be free of other sources of bias.

Footnotes

Characteristics of excluded studies

Alessi 1999

Reason for exclusion	Wrong intervention

Anderson Hanley 2017

Reason for exclusion	Wrong patient population

Ballard 2016

Reason for exclusion	Wrong intervention

Barnes 2013

Reason for exclusion	Wrong patient population

Berchtold 2017

Reason for exclusion	Wrong intervention

Bostrom 2016

Reason for exclusion	Wrong intervention

Canbaz 2017

Reason for exclusion	I,C,O culd not be assessed (Abstract)

Christofoletti 2008

Reason for exclusion	Wrong intervention

Conradsson 2010

Reason for exclusion	Wrong patient population

Conradsson 2015

Reason for exclusion	Wrong outcomes

Cott 2002

Reason for exclusion	Wrong intervention

deAndrade 2013

Reason for exclusion	Wrong intervention

Eggermont 2009

Reason for exclusion	Wrong intervention

Eggermont 2009a

Reason for exclusion	Wrong intervention

Francese 1997

Reason for exclusion	Wrong intervention

Henwood 2017

Reason for exclusion	Wrong patient population

Hernandez 2010

Reason for exclusion	Wrong study design

Hirsch 2013

Reason for exclusion	"I" could not be assessed (Abstract)

Hoffmann 2014

Reason for exclusion	I,C,O culd not be assessed (Abstract)

Hokkanen 2008

Reason for exclusion	Wrong intervention

Holliman 2001

Reason for exclusion	Wrong intervention

Holthoff 2015

Reason for exclusion	Wrong intervention

Holthoff 2015a

Reason for exclusion	Wrong intervention

Hwang 2010

Reason for exclusion	No full-text or abstract

Kemoun 2010

Reason for exclusion	No full-text or abstract

Kwak 2008

Reason for exclusion	Wrong intervention

Lautenschlager 2015

Reason for exclusion	Wrong intervention

Liu Ambrose 2016

Reason for exclusion	Wrong patient population

Lowery 2014

Reason for exclusion	Wrong intervention

Lowery 2014a

Reason for exclusion	Wrong intervention

Nakatsuka 2015

Reason for exclusion	Wrong patient population

Obisesan 2015

Reason for exclusion	Wrong patient population

Santana Sosa 2008

Reason for exclusion	Wrong intervention

Sobol 2016

Reason for exclusion	Wrong study design

Sobol 2016a

Reason for exclusion	Duplicate

Steinberg 2009

Reason for exclusion	Wrong intervention

Stevens 2006

Reason for exclusion	Wrong intervention

Suttanon 2013

Reason for exclusion	Wrong intervention

Telenius 2015

Reason for exclusion	Wrong intervention

Toots 2014

Reason for exclusion	Duplicate

Toots 2015

Reason for exclusion	Duplicate

Toots 2016

Reason for exclusion	Wrong intervention

Toots 2017

Reason for exclusion	Wrong intervention

VandeWinckel 2004

Reason for exclusion	Wrong intervention

Venturelli 2011

Reason for exclusion	Wrong intervention

Volkers 2012

Reason for exclusion	Wrong intervention

Vreugdenhil 2012

Reason for exclusion	Wrong intervention

Waldemar 2015

Reason for exclusion	Duplicate

Williams 2008

Reason for exclusion	Wrong intervention

Yaguez 2011

Reason for exclusion	Wrong intervention

Yoon 2013

Reason for exclusion	Wrong intervention

Yu 2013

Reason for exclusion	Wrong study design

Yu 2015

Reason for exclusion	Wrong study design

Zamfirescu 2015

Reason for exclusion	Wrong intervention

Zieschang 2013

Reason for exclusion	Wrong intervention

Footnotes

Characteristics of studies awaiting classification

Footnotes

Characteristics of ongoing studies

Footnotes

References to studies

Included studies

Aguiar 2014

Aguiar, Paula; Monteiro, Larissa; Feres, Ana; Gomes, Irenio; Melo, Ailton. Rivastigmine transdermal patch and physical exercises for Alzheimer's disease: a randomized clinical trial.. Current Alzheimer Research 2014;11(6):532-537. [DOI:]

Arcoverde 2014

Arcoverde, Cynthia; Deslandes, Andrea; Moraes, Helena; Almeida, Cloyra; Araujo, Narahyana Bom de; Vasques, Paulo Eduardo; Silveira, Heitor; Laks, Jerson. Treadmill training as an augmentation treatment for Alzheimer's disease: a pilot randomized controlled study.. Arquivos de Neuro-Psiquiatria 2014;72(3):190-196. [DOI:]

Bossers 2015

Bossers, Willem J. R.; van der Woude,Lucas H V.; Boersma, Froukje; Hortobagyi, Tibor; Scherder, Erik J. A.; van Heuvelen, Marieke J. G.. A 9-Week Aerobic and Strength Training Program Improves Cognitive and Motor Function in Patients with Dementia: A Randomized, Controlled Trial.. American Journal of Geriatric Psychiatry 2015;23(11):1106-1116. [DOI: https://dx.doi.org/10.1016/j.jagp.2014.12.191]

Bossers 2016

Bossers, Willem J. R.; van der Woude,Lucas H V.; Boersma, Froukje; Hortobagyi, Tibor; Scherder, Erik J. A.; van Heuvelen, Marieke J. G.. Comparison of Effect of Two Exercise Programs on Activities of Daily Living in Individuals with Dementia: A 9-Week Randomized, Controlled Trial.. Journal of the American Geriatrics Society 2016;64(6):1258-1266. [DOI: https://dx.doi.org/10.1111/jgs.14160]

Cancela 2016

Cancela, Jose M.; Ayan, Carlos; Varela, Silvia; Seijo, Manuel. Effects of a long-term aerobic exercise intervention on institutionalized patients with dementia.. Journal of Science & Medicine in Sport 2016;19(4):293-298. [DOI: https://dx.doi.org/10.1016/j.jsams.2015.05.007]

deSoutoBarreto 2017

de Souto Barreto, Philipe; Cesari, Matteo; Denormandie, Philippe; Armaingaud, Didier; Vellas, Bruno; Rolland, Yves. Exercise or Social Intervention for Nursing Home Residents with Dementia: A Pilot Randomized, Controlled Trial.. Journal of the American Geriatrics Society 2017;65(9):E123-E129. [DOI: https://dx.doi.org/10.1111/jgs.14947]

Hoffmann 2016

Hoffmann, Kristine; Sobol, Nanna A.; Frederiksen, Kristian S.; Beyer, Nina; Vogel, Asmus; Vestergaard, Karsten; Braendgaard, Hans; Gottrup, Hanne; Lolk, Annette; Wermuth, Lene; Jacobsen, Soren; Laugesen, Lars P.; Gergelyffy, Robert G.; Hogh, Peter; Bjerregaard, Eva; Andersen, Birgitte B.; Siersma, Volkert; Johannsen, Peter; Cotman, Carl W.; Waldemar, Gunhild; Hasselbalch, Steen G.. Moderate-to-High Intensity Physical Exercise in Patients with Alzheimer's Disease: A Randomized Controlled Trial.. Journal of Alzheimer's Disease 2016;50(2):443-453. [DOI: https://dx.doi.org/10.3233/JAD-150817]

Miu 2008

Miu, DKY; Szeto, SL; Mak, YF. A randomised controlled trial on the effect of exercise on physical: cognitive and affective function in dementia subjects. Asian Journal of Gerontology and Geriatrics3(Journal Article):8-16. [DOI:]

Morris 2017

Morris, Jill K.; Vidoni, Eric D.; Johnson, David K.; Van Sciver, Angela; Mahnken, Jonathan D.; Honea, Robyn A.; Wilkins, Heather M.; Brooks, William M.; Billinger, Sandra A.; Swerdlow, Russell H.; Burns, Jeffrey M.. Aerobic exercise for Alzheimer's disease: A randomized controlled pilot trial.. PLoS ONE [Electronic Resource] 2017;12(2):e0170547. [DOI: https://dx.doi.org/10.1371/journal.pone.0170547]

Ohman 2017

Ohman H.; Savikko N.R.N.; Strandberg T.E.; Kautiainen H.; Raivio M.M.; Laakkonen M.L.; Tilvis R.; Pitkala K.H.. Effects of frequent and long-term exercise on neuropsychiatric symptoms in patients with Alzheimer's disease - Secondary analyses of a randomized, controlled trial (FINALEX). European Geriatric Medicine 2017;8(2):153-157. [DOI: http://dx.doi.org/10.1016/j.eurger.2017.01.004]

Rolland 2007

[Empty]

Savikko 2016

Savikko, Ohman H.. Effects of exercise on cognition: the Finnish Alzheimer disease exercise trial: a randomized, controlled trial. Journal of the American Geriatrics Society 2016 Apr;64(4):731-738 2016;(Journal Article). [DOI:]

Vidoni 2017

Vidoni, Eric D.; Perales, Jaime; Alshehri, Mohammed; Giles, Abdul-Mannaan; Siengsukon, Catherine F.; Burns, Jeffrey M.. Aerobic Exercise Sustains Performance of Instrumental Activities of Daily Living in Early-Stage Alzheimer Disease.. Journal of Geriatric Physical Therapy 2017;(Journal Article). [DOI: https://dx.doi.org/10.1519/JPT.0000000000000172]

Yang 2015

Yang, Si-Yu; Shan, Chun-Lei; Qing, He; Wang, Wei; Zhu, Yi; Yin, Meng-Mei; Machado, Sergio; Yuan, Ti-Fei; Wu, Ting. The Effects of Aerobic Exercise on Cognitive Function of Alzheimer's Disease Patients.. CNS & Neurological Disorders Drug Targets 2015;14(10):1292-1297. [DOI:]

Excluded studies

Alessi 1999

Alessi, C. A.; Yoon, E. J.; Schnelle, J. F.; Al-Samarrai, N. R.; Cruise, P. A.. A randomized trial of a combined physical activity and environmental intervention in nursing home residents: do sleep and agitation improve? Journal of the American Geriatrics Society 1999;47(7):784-791. [DOI:]

Anderson Hanley 2017

Anderson-Hanley, Cay; Maloney, Molly; Barcelos, Nicole; Striegnitz, Kristina; Kramer, Arthur. Neuropsychological Benefits of Neuro-Exergaming for Older Adults: A Pilot Study of an Interactive Physical and Cognitive Exercise System (iPACES).. Journal of Aging & Physical Activity 2017;25(1):73-83. [DOI: https://dx.doi.org/10.1123/japa.2015-0261]

Ballard 2016

Ballard C.; Fossey J.. Wheld: An RCT of an optimized nonpharmacological intervention to improve agitation and quality of life in 1006 people with dementia living in nursing homes. Alzheimer's and Dementia 2016;12(7):P599. [DOI:]

Barnes 2013

Barnes, Deborah E.; Santos-Modesitt, Wendy; Poelke, Gina; Kramer, Arthur F.; Castro, Cynthia; Middleton, Laura E.; Yaffe, Kristine. The Mental Activity and eXercise (MAX) trial: a randomized controlled trial to enhance cognitive function in older adults.. JAMA Internal Medicine 2013;173(9):797-804. [DOI: https://dx.doi.org/10.1001/jamainternmed.2013.189]

Berchtold 2017

Berchtold, Burge E.. Does physical exercise improve ADL capacities in people over 65 years with moderate or severe dementia hospitalized in an acute psychiatric setting? A multisite randomized clinical trial. International Psychogeriatrics 2017 Feb;29(2):323-332 2017;(Journal Article). [DOI:]

Bostrom 2016

Bostrom, Gustaf; Conradsson, Mia; Hornsten, Carl; Rosendahl, Erik; Lindelof, Nina; Holmberg, Henrik; Nordstrom, Peter; Gustafson, Yngve; Littbrand, Hakan. Effects of a high-intensity functional exercise program on depressive symptoms among people with dementia in residential care: a randomized controlled trial.. International journal of geriatric psychiatry 2016;31(8):868-878. [DOI: https://dx.doi.org/10.1002/gps.4401]

Canbaz 2017

Canbaz M.; Lok N.; Lok S.. Effects of a physical activity program on cognitive function, depression and quality of life in first-stage Alzheimer's patients: A randomized controlled trial. EPMA Journal 2017;8(1):S16-S17. [DOI: http://dx.doi.org/10.1007/s13167-017-0108-4]

Christofoletti 2008

Christofoletti, G.; Oliani, M. M.; Gobbi, S.; Stella, F.; Bucken Gobbi, L. T.; Renato Canineu, P.. A controlled clinical trial on the effects of motor intervention on balance and cognition in institutionalized elderly patients with dementia. Clinical rehabilitation 2008;22(7):618-626. [DOI: 10.1177/0269215507086239 [doi]]

Conradsson 2010

Conradsson, M.; Littbrand, H.; Lindelof, N.; Gustafson, Y.; Rosendahl, E.. Effects of a high-intensity functional exercise programme on depressive symptoms and psychological well-being among older people living in residential care facilities: A cluster-randomized controlled trial. Aging & mental health 2010;14(5):565-576. [DOI: 10.1080/13607860903483078 [doi]]

Conradsson 2015

Conradsson M.; Gustafson Y.; Holmberg H.; Lindelof N.; Littbrand H.; Nordstrom P.; Rosendahl E.. Effects of a high-intensity exercise program on well-being among older people with dementia living in care facilities: A cluster-randomized trial. Physiotherapy (United Kingdom) 2015;101(Journal Article):eS263-eS264. [DOI: http://dx.doi.org/10.1016/j.physio.2015.03.448]

Cott 2002

Cott, C. A.; Dawson, P.; Sidani, S.; Wells, D.. The effects of a walking/talking program on communication, ambulation, and functional status in residents with Alzheimer disease. Alzheimer Disease and Associated Disorders 2002;16(2):81-87. [DOI:]

deAndrade 2013

de Andrade, L. P.; Gobbi, L. T.; Coelho, F. G.; Christofoletti, G.; Costa, J. L.; Stella, F.. Benefits of multimodal exercise intervention for postural control and frontal cognitive functions in individuals with Alzheimer's disease: a controlled trial. Journal of the American Geriatrics Society 2013;61(11):1919-1926. [DOI: 10.1111/jgs.12531 [doi]]

Eggermont 2009

Eggermont, L. H.; Swaab, D. F.; Hol, E. M.; Scherder, E. J.. Walking the line: a randomised trial on the effects of a short term walking programme on cognition in dementia. Journal of neurology, neurosurgery, and psychiatry 2009;80(7):802-804. [DOI: 10.1136/jnnp.2008.158444 [doi]]

Eggermont 2009a

Eggermont, L. H.; Knol, D. L.; Hol, E. M.; Swaab, D. F.; Scherder, E. J.. Hand motor activity, cognition, mood, and the rest-activity rhythm in dementia: a clustered RCT. Behavioural brain research 2009;196(2):271-278. [DOI: 10.1016/j.bbr.2008.09.012 [doi]]

Francese 1997

Francese, Theresa; Sorrell, Jeanne; Butler, Frieda R.. The effects of regular exercise on muscle strength and functional abilities of late stage Alzheimer's residents. American Journal of Alzheimer's Disease 1997;12(3):122-127. [DOI: 10.1177/153331759701200305]

Henwood 2017

Henwood T.; Neville C.; Baguley C.; Beattie E.. Aquatic exercise for residential aged care adults with dementia: Benefits and barriers to participation. International Psychogeriatrics 2017;29(9):1439-1449. [DOI: http://dx.doi.org/10.1017/S104161021700028X]

Hernandez 2010

Hernandez SS; Coelho FG; Gobbi S; et al.. Effects of physical activity on cognitive functions, balance and risk of falls in elderly patients with Alzheimer's dementia. Braz J Phys Ther 2010;14(1):68-74. [DOI:]

Hirsch 2013

Hirsch, Calvin. A 12-month, in-home exercise program delayed functional deterioration in Alzheimer disease. ACP Journal Club 2013;159(4):1-1. [DOI:]

Hoffmann 2014

Hoffmann K.; Frederiksen K.S.; Sobol N.A.; Beyer N.; Vogel A.; Andersen B.B.; Lolk A.; Gottrupp H.; Waldemar G.; Hasselbalch S.G.. Impact of physical activity and cognition onactivities of daily living in home-dwelling patients with mild to moderate Alzheimer's disease. Alzheimer's and Dementia 2014;10(Journal Article):P761-P762. [DOI:]

Hokkanen 2008

Hokkanen, L.; Rantala, L.; Remes, A. M.; Harkonen, B.; Viramo, P.; Winblad, I.. Dance and movement therapeutic methods in management of dementia: a randomized, controlled study. Journal of the American Geriatrics Society 2008;56(4):771-772. [DOI: 10.1111/j.1532-5415.2008.01611.x [doi]]

Holliman 2001

Holliman, Diane C.; Orgassa, Ute C.; Forney, Jennie Pillion. Developing an Interactive Physical Activity Group in a Geriatric Psychiatry Facility. Activities, Adaptation & Aging 2001;26(1):57-69. [DOI: 10.1300/J016v26n01_04]

Holthoff 2015

Holthoff, V. A.; Marschner, K.; Scharf, M.; Steding, J.; Meyer, S.; Koch, R.; Donix, M.. Effects of physical activity training in patients with Alzheimer's dementia: results of a pilot RCT study. PloS one 2015;10(4):e0121478. [DOI: 10.1371/journal.pone.0121478 [doi]]

Holthoff 2015a

Holthoff, Vjera A.; Marschner, Kira; Scharf, Maria; Steding, Julius; Meyer, Shirin; Koch, Rainer; Donix, Markus. Effects of physical activity training in patients with Alzheimer's dementia: results of a pilot RCT study.. PLoS ONE [Electronic Resource] 2015;10(4):e0121478. [DOI: https://dx.doi.org/10.1371/journal.pone.0121478]

Hwang 2010

Hwang HH; Choi YJ. The effects of the dance therapy program through rhythmic exercise on cognitive memory performance of the elderly with dementia. Proceedings of the 21st Pan-Asian Congress of Sports and Physical Education 2010;(4):12-17. [DOI:]

Kemoun 2010

Kemoun, G.; Thibaud, M.; Roumagne, N.; Carette, P.; Albinet, C.; Toussaint, L.; Paccalin, M.; Dugue, B.. Effects of a physical training programme on cognitive function and walking efficiency in elderly persons with dementia. Dementia and geriatric cognitive disorders 2010;29(2):109-114. [DOI: 10.1159/000272435 [doi]]

Kwak 2008

Kwak, Y. S.; Um, S. Y.; Son, T. G.; Kim, D. J.. Effect of regular exercise on senile dementia patients. International Journal of Sports Medicine 2008;29(6):471-474. [DOI: 10.1055/s-2007-964853 [doi]]

Lautenschlager 2015

Lautenschlager N.T.; Cox K.L.; Flicker L.; Cyarto E.; Ames D.; Logiudice D.; Hill K.; Etherton-Beer C.; Byrne G.; Appadurai K.; Almeida O.P.. A randomized controlled trial evaluating the effects of physical activity in people with Alzheimer's disease: the fitness for the ageing brain study ii (fabs II). Alzheimer's and Dementia 2015;11(7):P280-P281. [DOI:]

Liu Ambrose 2016

Liu-Ambrose, Teresa; Best, John R.; Davis, Jennifer C.; Eng, Janice J.; Lee, Philip E.; Jacova, Claudia; Boyd, Lara A.; Brasher, Penelope M.; Munkacsy, Michelle; Cheung, Winnie; Hsiung, Ging-Yuek R.. Aerobic exercise and vascular cognitive impairment: A randomized controlled trial.. Neurology 2016;87(20):2082-2090. [DOI:]

Lowery 2014

Lowery, David; Cerga-Pashoja, Arlinda; Iliffe, Steve; Thune-Boyle, Ingela; Griffin, Mark; Lee, James; Bailey, Alex; Bhattacharya, Rahul; Warner, James. The effect of exercise on behavioural and psychological symptoms of dementia: the EVIDEM-E randomised controlled clinical trial.. International journal of geriatric psychiatry 2014;29(8):819-827. [DOI: https://dx.doi.org/10.1002/gps.4062]

Lowery 2014a

Lowery, David; Cerga-Pashoja, Arlinda; Iliffe, Steve; Thune-Boyle, Ingela; Griffin, Mark; Lee, James; Bailey, Alex; Bhattacharya, Rahul; Warner, James. The effect of exercise on behavioural and psychological symptoms of dementia: the EVIDEM-E randomised controlled clinical trial.. International journal of geriatric psychiatry 2014;29(8):819-827. [DOI: https://dx.doi.org/10.1002/gps.4062]

Nakatsuka 2015

Nakatsuka, Masahiro; Nakamura, Kei; Hamanosono, Ryo; Takahashi, Yumi; Kasai, Mari; Sato, Yuko; Suto, Teiko; Nagatomi, Ryoichi; Meguro, Kenichi. A Cluster Randomized Controlled Trial of Nonpharmacological Interventions for Old-Old Subjects with a Clinical Dementia Rating of 0.5: The Kurihara Project.. Dementia and Geriatric Cognitive Disorders Extra 2015;5(2):221-232. [DOI: https://dx.doi.org/10.1159/000380816]

Obisesan 2015

Obisesan T.O.. Gene, exercise, and memory study (gems): A randomized controlled clinicaltrial to evaluate the effects of standardized aerobic exercise on cognition and neurodegeneration in African Americans with mild Alzheimer's disease. Alzheimer's and Dementia 2015;11(7):P834. [DOI:]

Santana Sosa 2008

Santana-Sosa, E.; Barriopedro, M. I.; Lopez-Mojares, L. M.; Perez, M.; Lucia, A.. Exercise training is beneficial for Alzheimer's patients. International Journal of Sports Medicine 2008;29(10):845-850. [DOI: 10.1055/s-2008-1038432 [doi]]

Sobol 2016

Sobol, Nanna Aue; Hoffmann, Kristine; Vogel, Asmus; Lolk, Annette; Gottrup, Hanne; Hogh, Peter; Hasselbalch, Steen G.; Beyer, Nina. Associations between physical function, dual-task performance and cognition in patients with mild Alzheimer's disease.. Aging & Mental Health 2016;20(11):1139-1146. [DOI:]

Sobol 2016a

Sobol N.; Hasselbalch S.G.; Dall C.H.; Hogh P.; Hoffmann K.; Frederiksen K.S.; Vogel A.; Siersma V.; Waldemar G.; Beyer N.. Improved fitness after aerobic exercise in patients with mild Alzheimer's disease. European Journal of Neurology 2016;23(Journal Article):347-348. [DOI: http://dx.doi.org/10.1111/ene.13093]

Steinberg 2009

Steinberg, M.; Leoutsakos, J. M.; Podewils, L. J.; Lyketsos, C. G.. Evaluation of a home-based exercise program in the treatment of Alzheimer's disease: the Maximizing Independence in Dementia (MIND) study. International journal of geriatric psychiatry 2009;24(7):680-685. [DOI: 10.1002/gps.2175 [doi]]

Stevens 2006

Stevens, J.; Killeen, M.. A randomised controlled trial testing the impact of exercise on cognitive symptoms and disability of residents with dementia. Contemporary nurse 2006;21(1):32-40. [DOI: 10.5555/conu.2006.21.1.32 [doi]]

Suttanon 2013

Suttanon, Plaiwan; Hill, Keith D.; Said, Catherine M.; Williams, Susan B.; Byrne, Karin N.; LoGiudice, Dina; Lautenschlager, Nicola T.; Dodd, Karen J.. Feasibility, safety and preliminary evidence of the effectiveness of a home-based exercise programme for older people with Alzheimer's disease: a pilot randomized controlled trial.. Clinical rehabilitation 2013;27(5):427-438. [DOI: https://dx.doi.org/10.1177/0269215512460877]

Telenius 2015

Telenius, Elisabeth Wiken; Engedal, Knut; Bergland, Astrid. Long-term effects of a 12 weeks high-intensity functional exercise program on physical function and mental health in nursing home residents with dementia: a single blinded randomized controlled trial.. BMC Geriatrics 2015;15(Journal Article):158. [DOI: https://dx.doi.org/10.1186/s12877-015-0151-8]

Toots 2014

Toots A.; Littbrand H.; Lindelof N.; Wiklund R.; Holmberg H.; Nordstrom P.; Lundin-Olsson L.; Gustafson Y.; Rosendahl E.. Effects of a high-intensity functional exercise program on activities of daily living in people with dementia living in residential facilities: A clusterrandomised controlled trial. Alzheimer's and Dementia 2014;10(Journal Article):P163. [DOI:]

Toots 2015

Toots A.; Littbrand H.; Lindelof N.; Wiklund R.; Holmberg H.; Nordstrom P.; Lundin-Olsson L.; Gustafson Y.; Rosendahl E.. Effects of a high-intensity functional exercise program on adls and balance in people with dementia: A cluster randomised controlled trial. Physiotherapy (United Kingdom) 2015;101(Journal Article):eS1526-eS1527. [DOI: http://dx.doi.org/org/10.1016/j.physio.2015.03.1514]

Toots 2016

Toots, Annika; Littbrand, Hakan; Lindelof, Nina; Wiklund, Robert; Holmberg, Henrik; Nordstrom, Peter; Lundin-Olsson, Lillemor; Gustafson, Yngve; Rosendahl, Erik. Effects of a High-Intensity Functional Exercise Program on Dependence in Activities of Daily Living and Balance in Older Adults with Dementia.. Journal of the American Geriatrics Society 2016;64(1):55-64. [DOI: https://dx.doi.org/10.1111/jgs.13880]

Toots 2017

Toots, Annika; Littbrand, Hakan; Bostrom, Gustaf; Hornsten, Carl; Holmberg, Henrik; Lundin-Olsson, Lillemor; Lindelof, Nina; Nordstrom, Peter; Gustafson, Yngve; Rosendahl, Erik. Effects of Exercise on Cognitive Function in Older People with Dementia: A Randomized Controlled Trial.. Journal of Alzheimer's Disease 2017;60(1):323-332. [DOI: https://dx.doi.org/10.3233/JAD-170014]

VandeWinckel 2004

Van de Winckel, A.; Feys, H.; De Weerdt, W.; Dom, R.. Cognitive and behavioural effects of music-based exercises in patients with dementia. Clinical rehabilitation 2004;18(3):253-260. [DOI: 10.1191/0269215504cr750oa [doi]]

Venturelli 2011

Venturelli, M.; Scarsini, R.; Schena, F.. Six-month walking program changes cognitive and ADL performance in patients with Alzheimer. American Journal of Alzheimer's Disease and Other Dementias 2011;26(5):381-388. [DOI: 10.1177/1533317511418956 [doi]]

Volkers 2012

Volkers KM. Chapter 7: The effect of regular walks on cognition in older people with mild to severe cognitive impairment: a long-term randomized controlled trial. Physical (in)activity an cognition in cognitively impaired older people 2012;(Book, Section):87-99. [DOI:]

Vreugdenhil 2012

Vreugdenhil, A.; Cannell, J.; Davies, A.; Razay, G.. A community-based exercise programme to improve functional ability in people with Alzheimer's disease: a randomized controlled trial. Scandinavian Journal of Caring Sciences 2012;26(1):12-19. [DOI: 10.1111/j.1471-6712.2011.00895.x [doi]]

Waldemar 2015

Waldemar G.; Hoffmann K.; Sobol N.; Frederiksen K.; Beyer N.; Vogel A.; Vestergaard K.; Braendgaard H.; Gottrup H.; Lolk A.; Wermuth L.; Jacobsen S.; Laugesen L.; Gergeleffly L.; Hogh P.; Bjerregaard E.; Andersen B.; Johannsen P.; Hasselbalch S.. Effect of moderate-to-high intensity endurance exercise in elderly community-dwelling persons with mild-moderate Alzheimer's disease. European Journal of Neurology 2015;22(Journal Article):95. [DOI: http://dx.doi.org/10.1111/ene.12805]

Williams 2008

Williams, C. L.; Tappen, R. M.. Exercise training for depressed older adults with Alzheimer's disease. Aging & mental health 2008;12(1):72-80. [DOI: 10.1080/13607860701529932 [doi]]

Yaguez 2011

Yaguez, L.; Shaw, K. N.; Morris, R.; Matthews, D.. The effects on cognitive functions of a movement-based intervention in patients with Alzheimer's type dementia: a pilot study. International journal of geriatric psychiatry 2011;26(2):173-181. [DOI: 10.1002/gps.2510 [doi]]

Yoon 2013

Yoon, Jung Eun; Lee, Suk Min; Lim, Hee Sung; Kim, Tae Hoon; Jeon, Ji Kyeng; Mun, Mee Hyang. The effects of cognitive activity combined with active extremity exercise on balance, walking activity, memory level and quality of life of an older adult sample with dementia.. Journal of Physical Therapy Science 2013;25(12):1601-1604. [DOI: https://dx.doi.org/10.1589/jpts.25.1601]

Yu 2013

Yu, Fang; Nelson, Nathaniel W.; Savik, Kay; Wyman, Jean F.; Dysken, Maurice; Bronas, Ulf G.. Affecting cognition and quality of life via aerobic exercise in Alzheimer's disease.. Western journal of nursing research 2013;35(1):24-38. [DOI: https://dx.doi.org/10.1177/0193945911420174]

Yu 2015

Yu, Fang; Thomas, William; Nelson, Nathaniel W.; Bronas, Ulf G.; Dysken, Maurice; Wyman, Jean F.. Impact of 6-month aerobic exercise on Alzheimer's symptoms.. Journal of Applied Gerontology 2015;34(4):484-500. [DOI: https://dx.doi.org/10.1177/0733464813512895]

Zamfirescu 2015

Zamfirescu A.; Mirsu-Paun A.; Capisizu A.A.; Aurelian S.M.; Slavila M.; Omer I.; Nica A.S.; Capisizu A.. Effectiveness of physical exercise training in elderly with mild to moderate dementia. European Journal of Neurology 2015;22(Journal Article):173. [DOI: http://dx.doi.org/10.1111/ene.12807]

Zieschang 2013

Zieschang T.; Schwenk M.; Oster P.; Hauer K.. Long-term effect of a standardized motor training on cognition in patients with dementia: Results of a RCT. European Geriatric Medicine 2013;4(Journal Article):S211. [DOI: http://dx.doi.org/10.1016/j.eurger.2013.07.704]

Data and analyses

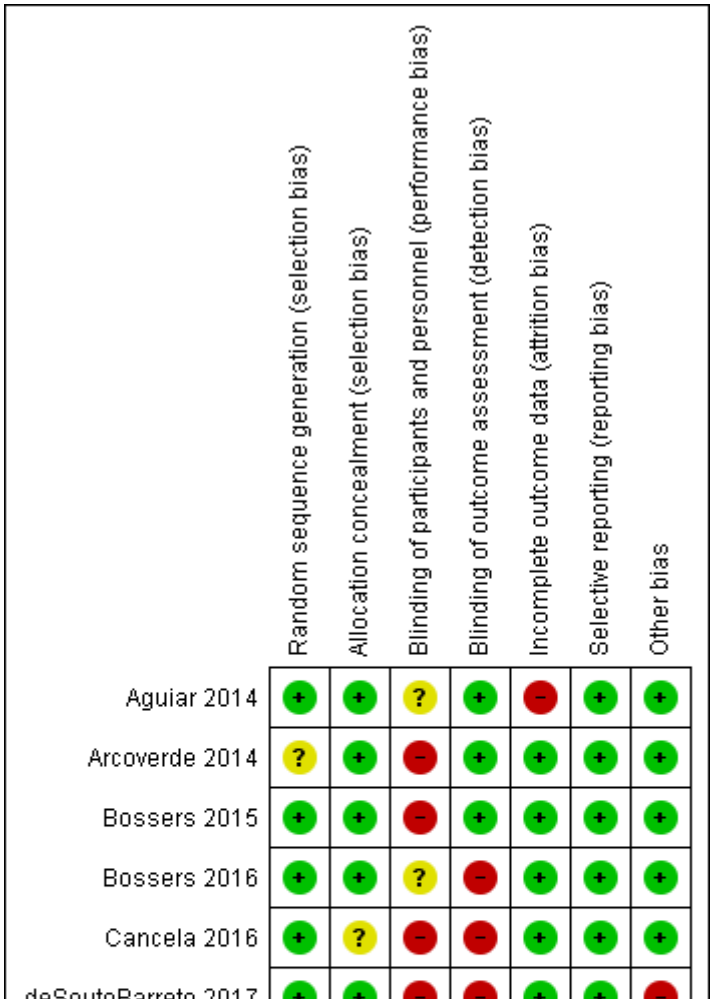
1 Aerobic exercise vs no aerob exercise

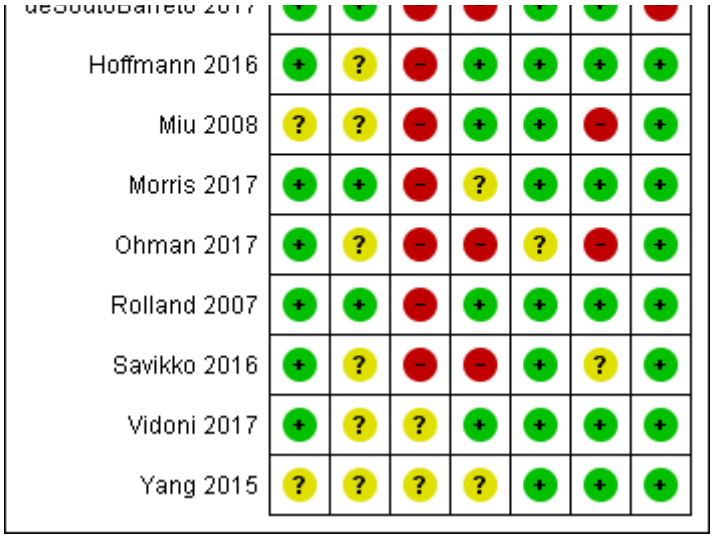
Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 Serious adverse events_EoT	6	748	Risk Ratio (IV, Random, 95% CI)	0.57 [0.24, 1.36]
1.2 Dropouts in absolute numbers_EoT	10	1130	Risk Ratio (IV, Random, 95% CI)	0.81 [0.62, 1.04]
1.3 Global BPSD score_NPI_EoT	5	718	Mean Difference (IV, Random, 95% CI)	-2.03 [-4.42, 0.36]
1.4 Global BPSD score_NPI_FU between 1 to 6 months after EoT	0	0	Std. Mean Difference (IV, Random, 95% CI)	Not estimable
1.5 Usage of antipsychotic medication_FU max 3 months after EoT	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable
1.6 Institutionalization_FU between 3 to 6 months after EoT	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable
1.8 Cognition_EoT_SMD	10	968	Std. Mean Difference (IV, Random, 95% CI)	0.20 [-0.07, 0.47]

1.9 Depression_EoT	5	744	Std. Mean Difference (IV, Random, 95% CI)	0.12 [-0.15, 0.39]
1.12 ADL_EoT	8	825	Std. Mean Difference (IV, Random, 95% CI)	-0.21 [-0.39, -0.03]

Figures

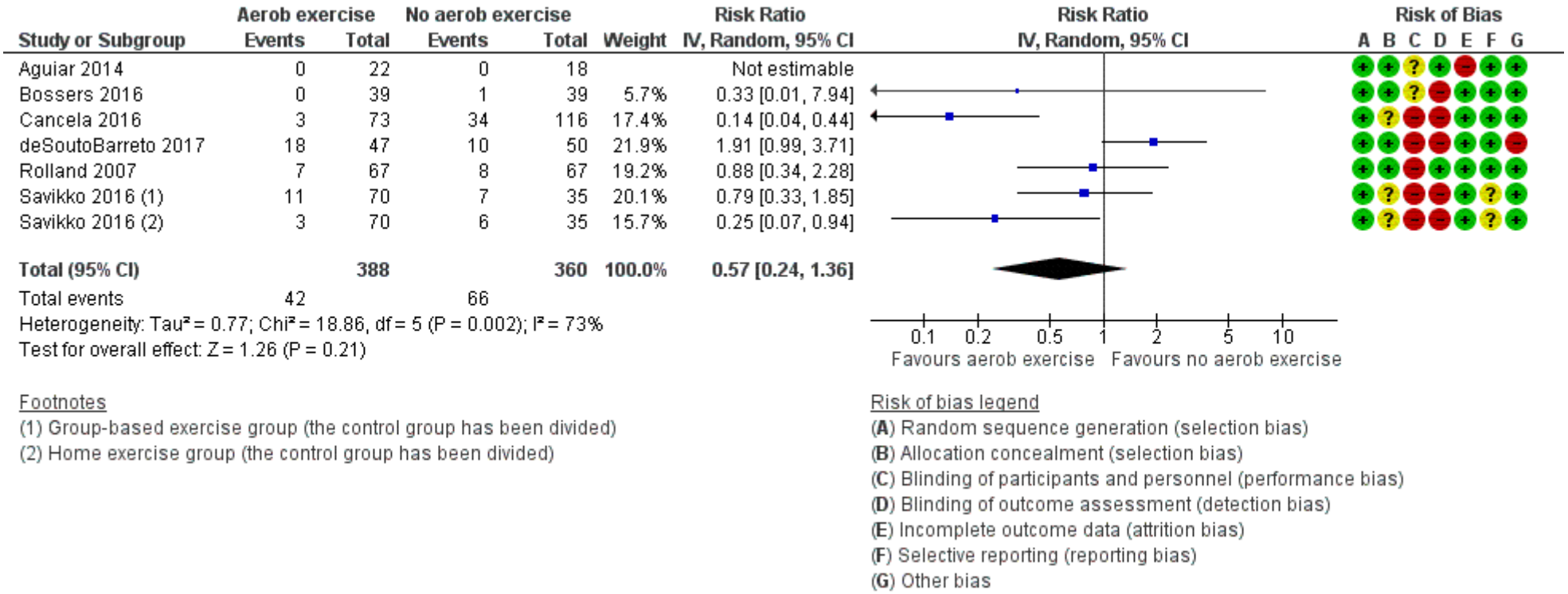
Figure 1





Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

Figure 2 (Analysis 1.1)

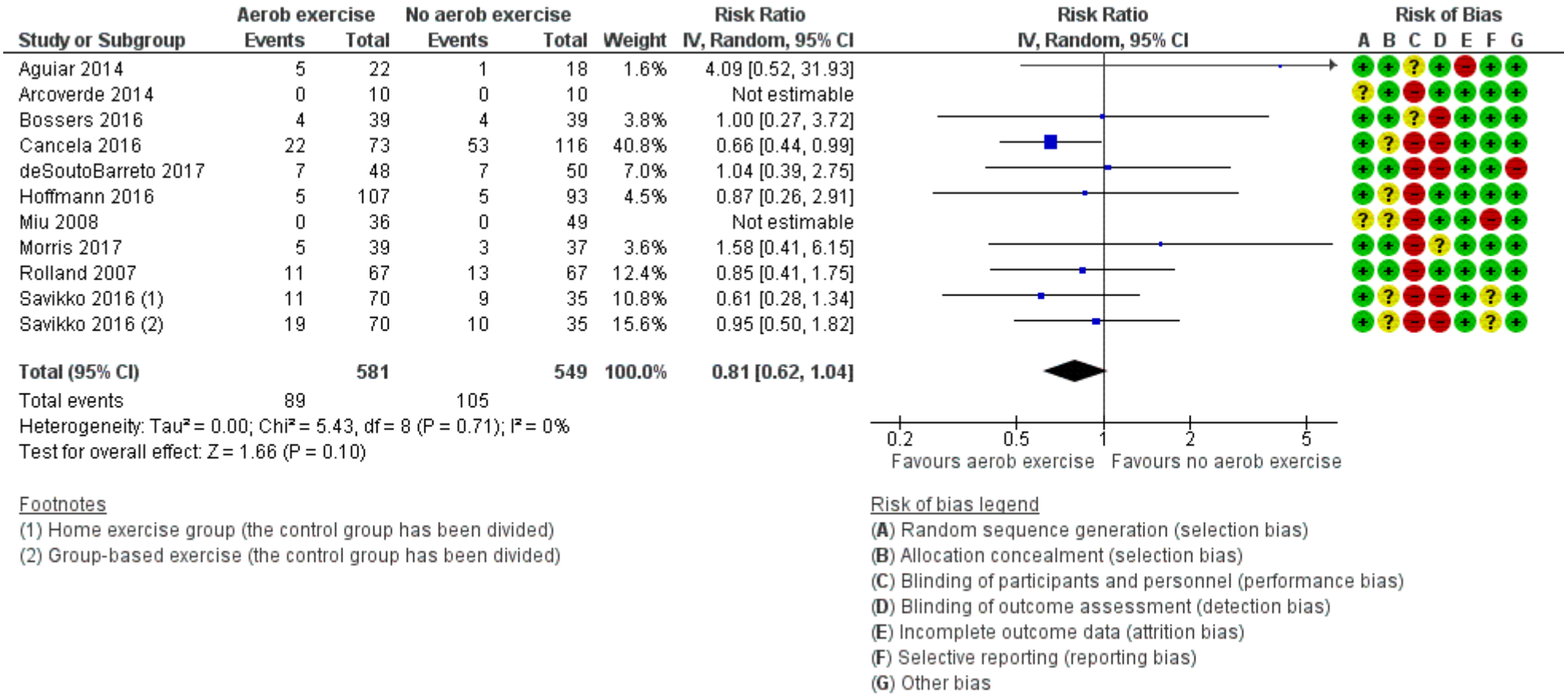


Footnotes
(1) Group-based exercise group (the control group has been divided)
(2) Home exercise group (the control group has been divided)

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 1 Aerobic exercise vs no aerob exercise, outcome: 1.1 Serious adverse events_EoT.

Figure 3 (Analysis 1.2)



Footnotes
(1) Home exercise group (the control group has been divided)
(2) Group-based exercise (the control group has been divided)

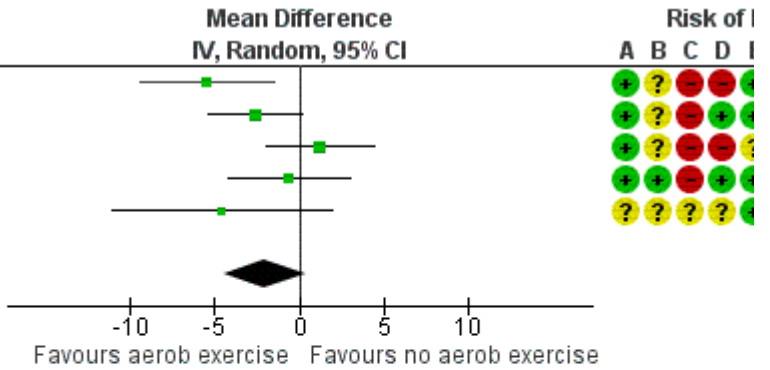
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 1 Aerobic exercise vs no aerob exercise, outcome: 1.2 Dropouts in absolute numbers_EoT.

Figure 4 (Analysis 1.3)

Study or Subgroup	Aerob exercise Mean	SD	Total	No aerob exercise Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Cancela 2016	-0.84	12.72882191	73	4.6	14.50697458	116	19.3%	-5.44 [-9.38, -1.50]
Hoffmann 2016	8.8	8.5	102	11.4	11	88	25.9%	-2.60 [-5.43, 0.23]
Ohman 2017 (1)	1.8513	8.0278	120	0.64	11.1494	59	23.6%	1.21 [-1.98, 4.40]
Rolland 2007	8.3	8.9	56	8.9	10.4	54	21.0%	-0.60 [-4.22, 3.02]
Yang 2015	7.96	8.15	25	12.54	14.4	25	10.2%	-4.58 [-11.07, 1.91]
Total (95% CI)			**376**			**342**	**100.0%**	**-2.03 [-4.42, 0.36]**

Heterogeneity: Tau² = 3.65; Chi² = 8.15, df = 4 (P = 0.09); I² = 51%
Test for overall effect: Z = 1.67 (P = 0.10)



Footnotes
(1) Group-based exercise and Home exercise have been pooled

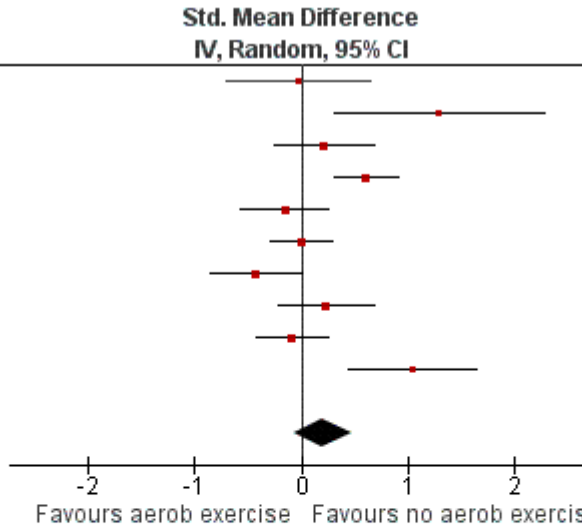
Risk of bias legend
(**A**) Random sequence generation (selection bias)
(**B**) Allocation concealment (selection bias)
(**C**) Blinding of participants and personnel (performance bias)
(**D**) Blinding of outcome assessment (detection bias)
(**E**) Incomplete outcome data (attrition bias)
(**F**) Selective reporting (reporting bias)
(**G**) Other bias

Forest plot of comparison: 1 Aerobic exercise vs no aerob exercise, outcome: 1.3 Global BPSD score_NPI_EoT.

Figure 5 (Analysis 1.8)

Study or Subgroup	Std. Mean Difference	SE	Aerob exercise Total	No aerob exercise Total	Weight	Std. Mean Difference IV, Random, 95% CI
Aguiar 2014 (1)	-0.021	0.343	17	17	7.7%	-0.02 [-0.69, 0.65]
Arcoverde 2014 (2)	1.285	0.5014	10	10	5.0%	1.28 [0.30, 2.27]
Bossers 2015 (3)	0.21	0.2364	36	36	10.2%	0.21 [-0.25, 0.67]
Cancela 2016 (4)	0.6045	0.1527	73	116	12.3%	0.60 [0.31, 0.90]
deSoutoBarreto 2017 (5)	-0.1503	0.2101	44	47	10.9%	-0.15 [-0.56, 0.26]
Hoffmann 2016 (6)	0	0.1455	102	88	12.5%	0.00 [-0.29, 0.29]
Miu 2008 (7)	-0.4247	0.222	36	49	10.6%	-0.42 [-0.86, 0.01]
Morris 2017 (8)	0.2329	0.2303	39	37	10.4%	0.23 [-0.22, 0.68]
Savikko 2016 (9)	-0.0838	0.1695	110	51	11.9%	-0.08 [-0.42, 0.25]
Yang 2015 (10)	1.0417	0.303	25	25	8.6%	1.04 [0.45, 1.64]
Total (95% CI)			**492**	**476**	**100.0%**	**0.20 [-0.07, 0.47]**

Heterogeneity: Tau² = 0.13; Chi² = 34.79, df = 9 (P < 0.0001); I² = 74%
Test for overall effect: Z = 1.45 (P = 0.15)



Footnotes
(1) MMSE
(2) MMSE
(3) MMSE
(4) MMSE (anført som MEC)
(5) MMSE
(6) MMSE
(7) MMSE
(8) Memomry composit
(9) MMSE
(10) MMSE

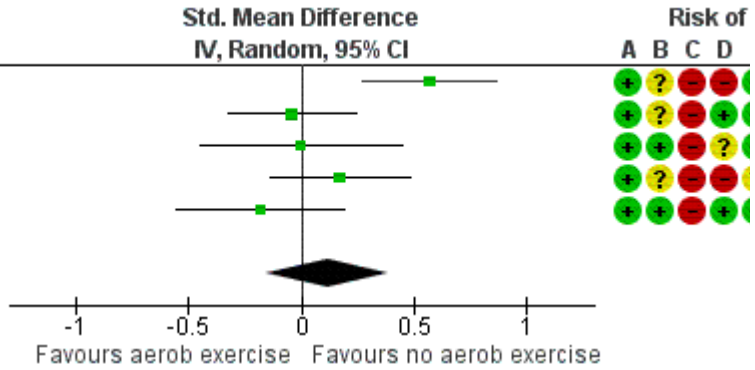
Risk of bias legend
(**A**) Random sequence generation (selection bias)
(**B**) Allocation concealment (selection bias)
(**C**) Blinding of participants and personnel (performai
(**D**) Blinding of outcome assessment (detection bias)
(**E**) Incomplete outcome data (attrition bias)
(**F**) Selective reporting (reporting bias)
(**G**) Other bias

Forest plot of comparison: 1 Aerobic exercise vs no aerob exercise, outcome: 1.8 Cognition_EoT_SMD.

Figure 6 (Analysis 1.9)

Study or Subgroup	aerob exercise Mean	SD	Total	no aerob exercise Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Cancela 2016 (1)	1.84	11.50824994	73	-2.71	4.42352823	116	21.7%	0.57 [0.27, 0.87]
Hoffmann 2016 (2)	1.7	2.5	102	1.8	2.3	88	22.2%	-0.04 [-0.33, 0.24]
Morris 2017 (3)	7.8	5.2	39	7.8	4.4	37	16.2%	0.00 [-0.45, 0.45]
Ohman 2017 (4)	0.9038	4.6582	120	0.04	5.8	59	21.1%	0.17 [-0.14, 0.48]
Rolland 2007 (5)	-14.8	7.2	54	-13.4	8	56	18.8%	-0.18 [-0.56, 0.19]
Total (95% CI)			**388**			**356**	**100.0%**	**0.12 [-0.15, 0.39]**

Heterogeneity: Tau² = 0.06; Chi² = 12.81, df = 4 (P = 0.01); I² = 69%
Test for overall effect: Z = 0.85 (P = 0.40)



Footnotes
(1) CSDD
(2) Hamilton Depression Rating Scale
(3) CSDD
(4) Home exercise and group-based exercise have been pooled
(5) MADRS

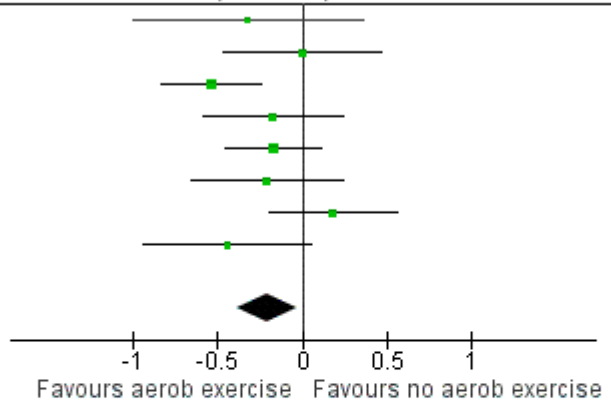
Risk of bias legend
(**A**) Random sequence generation (selection bias)
(**B**) Allocation concealment (selection bias)
(**C**) Blinding of participants and personnel (performance bias)
(**D**) Blinding of outcome assessment (detection bias)
(**E**) Incomplete outcome data (attrition bias)
(**F**) Selective reporting (reporting bias)
(**G**) Other bias

Forest plot of comparison: 1 Aerobic exercise vs no aerob exercise, outcome: 1.9 Depression_EoT.

Figure 7 (Analysis 1.12)

Study or Subgroup	aerob exercise Mean	SD	Total	no aerob exercise Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Aguiar 2014 (1)	-38.8	20.4	17	-32.9	15.5	17	5.8%	-0.32 [-1.00, 0.36]
Bossers 2016 (2)	-11.1	2.9	35	-11.1	3.1	35	10.3%	0.00 [-0.47, 0.47]
Cancela 2016 (3)	-0.22	1.17698011	73	0.25	0.60445727	116	18.2%	-0.54 [-0.84, -0.24]
deSoutoBarreto 2017 (4)	-1.7	3.3166	44	-1.1	3.4278	47	12.3%	-0.18 [-0.59, 0.24]
Hoffmann 2016 (5)	-64.4	9.4	102	-62.7	10.4	88	19.0%	-0.17 [-0.46, 0.11]
Morris 2017 (6)	-89.5	13.7	39	-86.7	13.3	37	10.9%	-0.21 [-0.66, 0.25]
Rolland 2007 (7)	-13.4	8	56	-14.8	7.2	54	14.0%	0.18 [-0.19, 0.56]
Vidoni 2017 (8)	0	9	33	4	9	32	9.6%	-0.44 [-0.93, 0.05]
Total (95% CI)			**399**			**426**	**100.0%**	**-0.21 [-0.39, -0.03]**

Heterogeneity: Tau² = 0.02; Chi² = 10.65, df = 7 (P = 0.15); I² = 34%
Test for overall effect: Z = 2.32 (P = 0.02)



Footnotes
(1) ADL-Q
(2) Katz-ADL
(3) Katz-ADL
(4) ADCS-ADL
(5) ADCS-ADL
(6) total DAD
(7) Katz-ADL
(8) total DAD

Risk of bias legend
(**A**) Random sequence generation (selection bias)
(**B**) Allocation concealment (selection bias)
(**C**) Blinding of participants and personnel (performance bias)
(**D**) Blinding of outcome assessment (detection bias)
(**E**) Incomplete outcome data (attrition bias)
(**F**) Selective reporting (reporting bias)
(**G**) Other bias

Forest plot of comparison: 1 Aerobic exercise vs no aerob exercise, outcome: 1.12 ADL_EoT.