Cochrane Library

Cochrane Database of Systematic Reviews

Exercise programs for people with dementia (Review)

Forbes D, Forbes SC, Blake CM, Thiessen EJ, Forbes S

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

WILEY

TABLE OF CONTENTS

[Intervention Review]

Exercise programs for people with dementia

Dorothy Forbes[1], Scott C Forbes[2], Catherine M Blake[3], Emily J Thiessen[1], Sean Forbes[4]

[1]Faculty of Nursing, University of Alberta, Edmonton, Canada. [2]Biology, Human Kinetics, Okanagan College, Penticton, Canada. [3]School of Nursing, Health Sciences Addition H022, University of Western Ontario, London, Canada. [4]Department of Physical Therapy, University of Florida, Gainesville, FL, USA

Contact: Catherine M Blake, School of Nursing, Health Sciences Addition H022, University of Western Ontario, 1151 Richmond Street, London, ON, N6A 3K7, Canada. cmblake@uwo.ca.

Editorial group: Cochrane Dementia and Cognitive Improvement Group.
Publication status and date: New search for studies and content updated (conclusions changed), published in Issue 4, 2015.

Citation: 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.

ABSTRACT

Background

This is an update of our previous 2013 review. Several recent trials and systematic reviews of the impact of exercise on people with dementia are reporting promising findings.

Objectives

Primary objective

Do exercise programs for older people with dementia improve their cognition, activities of daily living (ADLs), neuropsychiatric symptoms, depression, and mortality?

Secondary objectives

Do exercise programs for older people with dementia have an indirect impact on family caregivers' burden, quality of life, and mortality?

Do exercise programs for older people with dementia reduce the use of healthcare services (e.g. visits to the emergency department) by participants and their family caregivers?

Search methods

We identified trials for inclusion in the review by searching ALOIS (www.medicine.ox.ac.uk/alois), the Cochrane Dementia and Cognitive Improvement Group's Specialised Register, on 4 September 2011, on 13 August 2012, and again on 3 October 2013.

Selection criteria

In this review, we included randomized controlled trials in which older people, diagnosed with dementia, were allocated either to exercise programs or to control groups (usual care or social contact/activities) with the aim of improving cognition, ADLs, neuropsychiatric symptoms, depression, and mortality. Secondary outcomes related to the family caregiver(s) and included caregiver burden, quality of life, mortality, and use of healthcare services.

Data collection and analysis

Independently, at least two authors assessed the retrieved articles for inclusion, assessed methodological quality, and extracted data. We analysed data for summary effects. We calculated mean differences or standardized mean difference (SMD) for continuous data, and synthesized data for each outcome using a fixed-effect model, unless there was substantial heterogeneity between studies, when we used a

random-effects model. We planned to explore heterogeneity in relation to severity and type of dementia, and type, frequency, and duration of exercise program. We also evaluated adverse events.

Main results

Seventeen trials with 1067 participants met the inclusion criteria. However, the required data from three included trials and some of the data from a fourth trial were not published and not made available. The included trials were highly heterogeneous in terms of subtype and severity of participants' dementia, and type, duration, and frequency of exercise. Only two trials included participants living at home.

Our meta-analysis revealed that there was no clear evidence of benefit from exercise on cognitive functioning. The estimated standardized mean difference between exercise and control groups was 0.43 (95% CI -0.05 to 0.92, P value 0.08; 9 studies, 409 participants). There was very substantial heterogeneity in this analysis (I^2 value 80%), most of which we were unable to explain, and we rated the quality of this evidence as very low. We found a benefit of exercise programs on the ability of people with dementia to perform ADLs in six trials with 289 participants. The estimated standardized mean difference between exercise and control groups was 0.68 (95% CI 0.08 to 1.27, P value 0.02). However, again we observed considerable unexplained heterogeneity (I^2 value 77%) in this meta-analysis, and we rated the quality of this evidence as very low. This means that there is a need for caution in interpreting these findings.

In further analyses, in one trial we found that the burden experienced by informal caregivers providing care in the home may be reduced when they supervise the participation of the family member with dementia in an exercise program. The mean difference between exercise and control groups was -15.30 (95% CI -24.73 to -5.87; 1 trial, 40 participants; P value 0.001). There was no apparent risk of bias in this study. In addition, there was no clear evidence of benefit from exercise on neuropsychiatric symptoms (MD -0.60, 95% CI -4.22 to 3.02; 1 trial, 110 participants; P value .0.75), or depression (SMD 0.14, 95% CI -0.07 to 0.36; 5 trials, 341 participants; P value 0.16). We could not examine the remaining outcomes, quality of life, mortality, and healthcare costs, as either the appropriate data were not reported, or we did not retrieve trials that examined these outcomes.

Authors' conclusions

There is promising evidence that exercise programs may improve the ability to perform ADLs in people with dementia, although some caution is advised in interpreting these findings. The review revealed no evidence of benefit from exercise on cognition, neuropsychiatric symptoms, or depression. There was little or no evidence regarding the remaining outcomes of interest (i.e., mortality, caregiver burden, caregiver quality of life, caregiver mortality, and use of healthcare services).

PLAIN LANGUAGE SUMMARY

Exercise programs for people with dementia

Background

In future, as the population ages, the number of people in our communities suffering with dementia will rise dramatically. This will not only affect the quality of life of people with dementia but also increase the burden on family caregivers, community care, and residential care services. Exercise is one lifestyle factor that has been identified as a potential means of reducing or delaying progression of the symptoms of dementia.

Study characteristics

This review evaluated the results of 17 trials (search dates August 2012 and October 2013), including 1,067 participants, that tested whether exercise programs could improve cognition (which includes such things as memory, reasoning ability and spatial awareness), activities of daily living, behaviour and psychological symptoms (such as depression, anxiety and agitation) in older people with dementia. We also looked for effects on mortality, quality of life, caregivers' experience and use of healthcare services, and for any adverse effects of exercise.

Key findings

There was some evidence that exercise programs can improve the ability of people with dementia to perform daily activities, but there was a lot of variation among trial results that we were not able to explain. The studies showed no evidence of benefit from exercise on cognition, psychological symptoms, and depression. There was little or no evidence regarding the other outcomes listed above. There was no evidence that exercise was harmful for the participants. We judged the overall quality of evidence behind most of the results to be very low.

Conclusion

Additional well-designed trials would allow us to enhance the quality of the review by investigating the best type of exercise program for people with different types and severity of dementia and by addressing all of the outcomes.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. Exercise programs for people with dementia

Exercise programs for people with dementia

Patient or population: people with dementia
Settings: long term care, community programs, home
Intervention: exercise program compared to usual care or a social group activity

Outcomes	Illustrative comparative risks* (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
Cognition, SD units Investigators measured cognition using different instruments. Higher scores represent better cognitive function Follow-up: 6-36 weeks	The mean score for cognition in the intervention groups was **0.43 standard deviations units higher** (0.05 lower to 0.92 higher)	409 (9 studies)	⊕⊖⊖⊖ **very low** [a]	As a rough guide, a difference of 0.2 SD represents a small, 0.6 a moderate and 0.8 a large treatment effect
Activities of daily living, SD units Investigators measured ADLs using different instruments. Higher scores represent better performance Follow-up: 7-52 weeks	The mean score activities of daily living in the intervention groups was **0.68 standard deviations higher** (0.08 to 1.27 higher)	289 (6 studies)	⊕⊖⊖⊖ **low** [b]	
Depression, SD units Investigators measured depression using a variety of scales. Lower scores represent improvement Follow-up: 6-52 weeks	The mean score for depression in the intervention groups was **0.14 lower** (0.36 lower to 0.07 higher)	341 (5 studies)	⊕⊕⊕⊖ **moderate** [c]	
Neuropsychiatric symptoms Measured using NPI. Severity of symptoms is measured on a scale of 0-144. A higher score indicates worse symptoms Follow-up: 12 months	The mean NPI score in the intervention group was 0.60 points lower (4.22 lower to 3.02 higher).	110 (1 study)	**very low** [d]	A minimum difference of 8 points in the NPI scale has been considered to be clinically important

GRADE Working Group grades of evidence
High quality: further research is very unlikely to change our confidence in the estimate of effect
Moderate quality: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low quality: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very low quality: we are very uncertain about the estimate

[a] rated down for serious inconsistency between studies (I^2 80%), imprecision and publication bias (12 studies measured cognitive outcomes but data were only available from 9)
[b] rated down for serious inconsistency between studies (I^2 77%) and imprecision
[c] rated down for imprecision
[d] rated down because data came from a single study, for imprecision and for publication bias (5 studies measured neuropsychiatric outcomes but only one provided usable data)

BACKGROUND

Description of the condition

In 2012, the World Health Organization declared dementia to be a public health priority (World Health Organization 2012), citing the high global prevalence and economic impact on families, communities, and health service providers. In the coming decades, with the aging of the population, the number of people living with dementia in our communities will rise dramatically. This will increase the burden on family caregivers, community care, and residential care services (Alzheimer Society of Canada 2010; World Alzheimer Report 2011). People diagnosed with dementia often have unique needs, as they tend to be older and present with acquired impairment in memory, associated with other disturbances of higher cortical function, or personality changes (APA 1995; McKhann 1984). As a first approach, best practice guidelines currently recommend the exploration of behavioural and psychological interventions before initiating pharmacological interventions, due to the limited benefit of pharmacological treatments in reducing functional decline and their potential side effects (Forbes 2008a; Hogan 2008). Exercise is among the potential protective lifestyle factors identified as a strategy for treating the symptoms of dementia or delaying its progression (Lautenschlager 2010).

Description of the intervention

Exercise programs with older adults have been shown to improve cognitive function (Angevaren 2008; Erickson 2011; Tseng 2011), and depression (Chen 2009). Many of these studies used a 60-minute exercise regimen scheduled three times per week that continued for 24 weeks (Tseng 2011). Hamer 2009 conducted a systematic review that included 16 prospective studies (163,797 participants without dementia at baseline with 3219 with dementia at follow-up). The relative risk (RR) of dementia in the highest exercise category compared with the lowest was 0.72 (95% CI 0.60 to 0.86, P value < 0.001) and for Alzheimer's disease (AD) the RR was 0.55 (95% CI 0.36 to 0.84, P value 0.006). The authors concluded that exercise is inversely associated with risk of dementia (i.e. reduces the likelihood of dementia). Others, for example Chang 2010, have also revealed that mid-life exercise may contribute to maintenance of cognitive function and may reduce or delay the risk of late-life dementia. Intlekofer 2012 suggests that evidence is starting to emerge that exercise supports brain health, even when initiated after the appearance of AD pathology. Clearly, further investigation is needed in this area.

How the intervention might work

Physical activity refers to "body movement that is produced by the contraction of skeletal muscles and that increases energy expenditure" (Chodzko-Zajko 2009). Exercise refers to "planned, structured, and repetitive movement to improve or maintain one or more components of physical fitness" (Chodzko-Zajko 2009). A detailed examination of the potential mechanism(s) of physical activity and exercise is beyond the scope of this review. For further information the reader is directed to two recent reviews, Erickson 2012 and Davenport 2012. Briefly, exercise improves vascular health by reducing blood pressure (Fleg 2012), arterial stiffness (Fleg 2012), oxidative stress (Covas 2002), systemic inflammation (Lavie 2011), and enhances endothelial function (Ghisi 2010), all of which are associated in the maintenance of cerebral perfusion (Churchill 2002; Davenport 2012; Rogers 1990). Recent evidence has shown a strong association between cerebral perfusion (i.e. balance between the supply and demand of nutrients to the brain), cognitive function, and fitness in older healthy adults (Brown 2010). Furthermore, insulin resistance or glucose intolerance is linked with amyloid β plaque formation (Farris 2003; Wareham 2000; Watson 2003), which is a feature of AD. Exercise is known to enhance insulin sensitivity and glucose control (Ryan 2000). Exercise may also preserve neuronal structure and promote neurogenesis, synaptogenesis, and capillarization (formation of nerve cells, the gaps between them, and blood vessels, respectively; Colcombe 2003), which may be associated with exercise-induced elevation in brain-derived neurotrophic factor (BDNF; Vaynman 2004), and insulin-like growth factors (Cotman 2007). Animal and human studies investigating the role of BDNF have provided evidence that BDNF supports the health and growth of neurons and may regulate neuroplasticity (adaptability of the brain) as we age (Cheng 2003; Vaynman 2004). Intlekofer 2012 recently reported that exercise reinstates hippocampal function (i.e. memory) by enhancing the expression of BDNF and other growth factors that promote neurogenesis, angiogenesis (formation of blood vessels), and synaptic plasticity. Taken together, animal and human studies indicate that exercise provides a powerful stimulus that can counteract the molecular changes that underlie the progressive loss of hippocampal function in advanced age and AD (Erickson 2012).

Why it is important to do this review

There was tremendous response to our 2013 review from both the media and researchers. Due to the suspected increase in research activity in this area, we feel it is important to keep our review updated and relatively current.

OBJECTIVES

Primary objective

- Do exercise programs for older people with dementia improve their cognition, activities of daily living (ADLs), neuropsychiatric symptoms, depression, and mortality?

Secondary objectives

- Do exercise programs for older people with dementia have an indirect impact on family caregivers' burden, quality of life, and mortality?
- Do exercise programs for older people with dementia reduce the use of healthcare services (e.g. visits to the emergency department) by participants and their family caregivers?

METHODS

Criteria for considering studies for this review

Types of studies

In this review, we included randomized controlled trials (RCTs) in which older people diagnosed with dementia were allocated to either an exercise program or a control group (usual care or social contact/activities). Although we preferred parallel group trials, cross-over trials were eligible, but we only considered data from the first treatment phase (prior to the cross-over). We included non-blinded trials, as it was unrealistic to expect blinding of the

participants and those who conducted the exercise programs. We expected outcome assessors to be blinded to treatment allocation, however, we did not exclude studies if blinding of outcome assessors was not incorporated in the study. We rated studies for blinding in the 'Risk of bias' tables.

Types of participants

The majority of participants in the trials had to be older people (over 65 years of age) and diagnosed as having dementia using accepted criteria such as the Diagnostic and Statistical Manual of Mental Disorders (APA 1987; APA 1995; DSM-IV 1994), the National Institute of Neurological and Communicative Disorders and Stroke, and the Alzheimer's Disease and Related Disorders Association (McKhann 1984), ICD-10 (World Health Organization 1992), or CERAD-K (Hwang 2010).

Types of interventions

Interventions included exercise programs offered over any length of time with the aim of improving cognition, activities of daily living (ADLs), neuropsychiatric symptoms, depression, and mortality in older people with dementia or improving the family caregiver's burden, health, quality of life, or to decrease caregiver mortality, or use of healthcare services, or a combination of these. We included trials where the only difference between groups was the exercise intervention, and the types, frequencies, intensities, duration, and settings of the exercise programs were described. The exercise could be any combination of aerobic-, strength-, or balance-training. The comparison groups received either usual care, or social contact/activities, to ensure that the participants received a similar amount of attention.

Types of outcome measures

Primary outcomes

The primary outcomes concerned the person with dementia, and included: cognition, ADLs, neuropsychiatric symptoms (e.g. agitation, aggression), depression, and mortality.

Secondary outcomes

The secondary outcomes included the family caregiver's burden of care, quality of life, and mortality, and costs related to the use of healthcare services.

Search methods for identification of studies

Electronic searches

We searched ALOIS (www.medicine.ox.ac.uk/alois) - the Cochrane Dementia and Cognitive Improvement Group's Specialised Register - on 4 September 2011, 14 August 2012, and most recently on 3 October 2013. The search terms used were: physical activity OR exercise OR cycling OR swim* OR gym* OR walk* OR danc* OR yoga OR 'tai chi'.

ALOIS is maintained by the Trials Search Co-ordinator of the Cochrane Dementia and Cognitive Improvement Group and contains studies in the areas of dementia prevention, dementia treatment, and cognitive enhancement in healthy adults. The studies are identified from:

1. monthly searches of a number of major healthcare databases: MEDLINE (Ovid SP), EMBASE (Ovid SP), CINAHL (EBSCOhost), PsycINFO (Ovid SP) and LILACS (BIREME);
2. monthly searches of a number of trial registers: ISRCTN; UMIN (Japan's Trial Register); the World Health Organization portal (which covers ClinicalTrials.gov; ISRCTN; the Chinese Clinical Trials Register; the German Clinical Trials Register; the Iranian Registry of Clinical Trials and the Netherlands National Trials Register, plus others);
3. quarterly search of *The Cochrane Library*'s Central Register of Controlled Trials (CENTRAL);
4. six-monthly searches of a number of grey literature sources: ISI Web of Knowledge Conference Proceedings; Index to Theses; and Australasian Digital Theses.

To view a list of all sources searched for ALOIS see About ALOIS on the ALOIS website.

Details of the search strategies used for the retrieval of reports of trials from the healthcare databases, CENTRAL, and conference proceedings can be viewed in the 'Methods used in reviews' section within the editorial information about the Dementia and Cognitive Improvement Group.

We performed additional searches in many of the sources listed above to cover the timeframe from the last searches performed for ALOIS to ensure that the search for the review was as up-to-date and as comprehensive as possible. There was no restriction on language. The search strategies used can be seen in Appendix 1 and Appendix 2.

We performed another search on 3 October 2013.

Data collection and analysis

Selection of studies

After merging search results and discarding duplicates, at least two authors (DF, SCF, ET) independently examined titles and abstracts of citations. If a title or abstract appeared to represent our inclusion criteria, we retrieved the full article for further assessment. At least two authors, one a content expert (SCF) and the others with expertise in conducting systematic reviews (DF, ET), independently assessed the retrieved articles for inclusion in the review according to the eligibility criteria outlined above. We resolved disagreements by discussion, or if necessary, referred to another author. The excluded articles and reasons for exclusion are listed in the 'Characteristics of excluded studies' table.

Data extraction and management

We extracted information from the published articles including the study setting, inclusion and exclusion criteria, participants' diagnosis and level of activity, description of the exercise programs, the randomization process, blinding, drop-out rates, and outcome data.

The mean change from baseline to final measurements and the standard deviation (SD) of the change were often not reported in the published reports. Accordingly, we extracted the final mean following the intervention period, the SD of this mean, and the number of participants for each group at each assessment. The included trials reported no dichotomous data of interest to this review. One author extracted data from published reports,

or requested it from the original first author when necessary, and at least two authors checked this data entry. We resolved disagreements as noted above.

Assessment of risk of bias in included studies

Criteria for judging risk of bias were based on the *Cochrane Handbook for Systematic Reviews of Interventions*, version 5.1.0, chapter 8 (Higgins 2011). At least two authors with content expertise (SCF, SF), and two with expertise in conducting systematic reviews (DF, ET), independently assessed and rated the trials according to the 'Risk of bias' criteria below. The authors used an assessment tool to determine whether there was a low, high, or unclear risk of bias for each factor (see table 8.5.d, Higgins 2011). The identity of the publication and author information for each trial report was not masked. If the description of a process or outcome was unclear or missing, we contacted the original author of the trial in an attempt to retrieve the required information. Again, we resolved disagreements by discussion, or, if necessary, referred to a third author. We assessed the following criteria:

1. Selection bias - systematic differences between baseline characteristics of the groups being compared, including:
   a. random sequence generation;
   b. allocation concealment.
2. Performance bias - systematic differences between groups in the care that is provided, or in exposure to factors other than the interventions of interest, this includes:
   a. blinding of participants and personnel.
3. Detection bias - systematic differences between groups in how outcomes are determined, this includes:
   a. blinding of outcome assessments.
4. Attrition bias - systematic differences between groups in withdrawals from a study, this includes:
   a. incomplete outcome data.
5. Reporting bias - systematic differences between reported and unreported findings, that is:
   a. outcome reporting bias.
   b. publication bias.
6. Other bias, such as:
   a. bias due to other problems.

Measures of treatment effect

Summary statistics were required for each trial and each outcome. For continuous data, we used the mean difference (MD) when the pooled trials used the same rating scale or test to assess an outcome. We used the standardized mean difference (SMD), which is the absolute mean difference divided by the SD, when the pooled trials used different rating scales or tests. We used the inverse variance method in the meta-analysis. We reported all outcomes using 95% confidence intervals (CI). None of the trials included in the review reported dichotomous data of interest to this review.

Unit of analysis issues

If a cross-over design study had been included in the review, we planned to consider only the results prior to the cross-over for inclusion in our analysis, however, we did not have any cross-over design studies to consider. If a trial included three or more arms, we considered the nature of the intervention and control arms, and combined the data from two treatment arms that were similar and had the same control group, as recommended in the *Cochrane Handbook for Systematic Reviews of Interventions*, section 7.7.3.8 and Table 7.7a (Higgins 2011). For one trial, Williams 2008, we pooled two intervention arms (exercise group and a walking group) that were compared with a control (conversation) group.

Dealing with missing data

Many types of information were found to be missing from the published articles, such as descriptions of the process of randomization, blinding of outcome assessors, attrition and adherence to the exercise program, reasons for withdrawing, and statistical data (i.e. means and SDs). We emailed contact authors on at least three separate occasions over a three-month period and requested them to provide the missing data. Some of this missing data is described in the 'Risk of bias' tables. The potential impact of the missing data on the results depended on the extent of missing data, the pooled estimate of the treatment effect, and the variability of the outcomes. We also considered variation in the degree of missing data as a potential source of heterogeneity. If available, we used intention-to-treat (ITT) data, and, if these were not available, we used only the reported completers' data in the analyses.

Assessment of heterogeneity

We considered only trials that demonstrated clinical homogeneity (that is, trials that tested an exercise program and examined similar outcome measures) to be potentially appropriate for meta-analysis. We explored heterogeneity initially through visual exploration of the forest plots. We then performed a test for statistical heterogeneity (a consequence of clinical or methodological diversity, or both, among trials) using the Chi^2 test (with a P value of < 0.10 indicating significance) and I^2 analysis. The I^2 analysis is a useful statistic for quantifying inconsistency (I^2 = [(Q - df)/Q] x 100%, where Q is the Chi^2 statistic and df is its degrees of freedom; Higgins 2002; Higgins 2003). This describes the percentage of variability in effect estimates that is due to heterogeneity rather than sampling error (chance). Values greater than 50% are considered to represent substantial heterogeneity, and, when these occurred, we attempted to explain this variation. If the value was less than 30%, we presented the overall estimate using a fixed-effect model. If, however, there was evidence of heterogeneity of the population or treatment effect, or both, between trials, then we used a random-effects model, for which the confidence intervals are broader than those of a fixed-effect model (Higgins 2011).

Assessment of reporting biases

We examined funnel plots to look for non-significant study effects that might indicate publication bias. To investigate reporting biases within our included studies, we compared outcomes listed in the methods sections with reported results.

Data synthesis

We conducted the meta-analyses using a fixed-effect model except when we considered that there was significant diversity between studies in participants or interventions, or when the I^2 measure of heterogeneity was greater than 30%. In those cases we used a random-effects model.

We assessed the overall quality of the evidence associated with the result of each meta-analysis using the GRADE (Grading of Recommendations Assessment, Development and Evaluation)

approach, which gives an indication of the confidence that can be placed in the estimate of treatment effect. We summarized the effect estimates and GRADE ratings for our primary outcomes in a 'Summary of findings' table.

Subgroup analysis and investigation of heterogeneity

We decided a priori that, if there were sufficient data, we would conduct the following subgroup analyses to explore possible causes of heterogeneity.

Severity of dementia at baseline:

1. mild (Mini Mental State Examination (MMSE) 17 to 26, or similar scale; Hogan 2007);
2. moderate (MMSE 10 to 17, or similar scale; Hogan 2007);
3. severe (MMSE < 10, or similar scale; Feldman 2005).

Disease type:

1. AD;
2. vascular dementia;
3. mixed dementia;
4. unclassified or other dementia.

Type of exercise program:

1. aerobic;
2. strength;
3. balance.

Frequency of exercise program:

1. up to three times per week;
2. more than three times per week.

Duration of exercise program:

1. up to 12 weeks;
2. more than 12 weeks.

Sensitivity analysis

We also considered sensitivity analyses, a priori, to explore possible causes of methodological heterogeneity, such as including studies that used a variety of measurement tools.

RESULTS

Description of studies

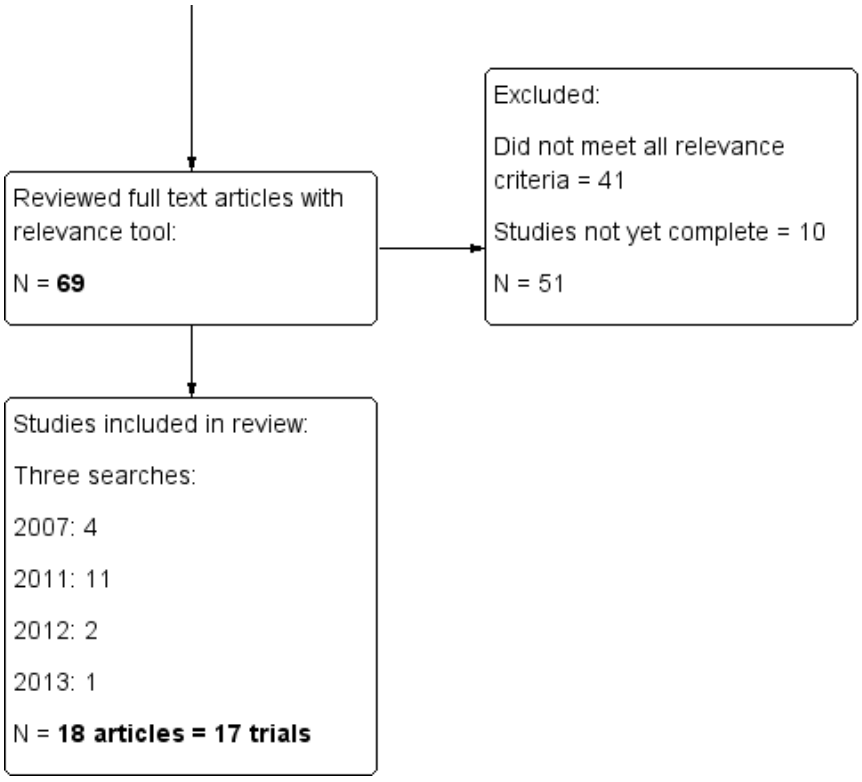
Please see 'Characteristics of included studies', 'Characteristics of excluded studies', and 'Characteristics of ongoing studies' tables.

Results of the search

Database searches located a total of 5241 articles; we screened the abstracts and titles of 542 of these for inclusion. Sixty-nine articles were retrieved and independently rated by two reviewers. Eighteen articles met the inclusion criteria (Christofoletti 2008; Conradsson 2010 (two articles); Eggermont 2009a; Eggermont 2009b; Francese 1997; Hwang 2010; Holliman 2001; Kemoun 2010; Rolland 2007; Santana-Sosa 2008; Steinberg 2009; Stevens 2006; Van de Winckel 2004; Venturelli 2011; Volkers 2012; Vreugdenhil 2012; Williams 2008). Two of these articles reported on different outcomes from the same trial (Conradsson 2010). Thus, 17 trials were included in the review. Only one new trial has been added to our previously published reviwew. See Figure 1 for a flow chart.

Figure 1. Study flow diagram

Figure 1. (Continued)



Included studies

The included articles were published between 1997 and 2012. Four trials were conducted in the USA (Francese 1997; Holliman 2001; Steinberg 2009; Williams 2008), one in Sweden (Conradsson 2010), two in France (Kemoun 2010; Rolland 2007), two in Australia (Stevens 2006; Vreugdenhil 2012), three in the Netherlands (Eggermont 2009a; Eggermont 2009b; Volkers 2012), and one each in Belgium (Van de Winckel 2004), Brazil (Christofoletti 2008), Italy (Venturelli 2011), South Korea (Hwang 2010), and Spain (Santana-Sosa 2008).

Participants

Please see 'Characteristics of included studies' table.

Trial participants had been recruited from nursing homes (Eggermont 2009a; Eggermont 2009b; Francese 1997; Hwang 2010; Kemoun 2010; Rolland 2007; Santana-Sosa 2008; Stevens 2006; Venturelli 2011; Williams 2008), graduated residential care (Conradsson 2010), psychiatric facilities (Christofoletti 2008; Holliman 2001; Van de Winckel 2004), from three different types of institutions (day care centres, homes for the elderly, and nursing homes; Volkers 2012), and their own home settings (Steinberg 2009; Vreugdenhil 2012).

Consent was obtained from the participants in all trials, or from their legal guardian or a family member, or both. Three of the included trials recruited fewer than 20 participants (Francese 1997; Holliman 2001; Santana-Sosa 2008); nine trials recruited between 24 and 66 participants (Christofoletti 2008; Eggermont 2009b; Hwang 2010; Kemoun 2010; Steinberg 2009; Van de Winckel 2004; Venturelli 2011; Vreugdenhil 2012; Williams 2008); and five other trials recruited 100 or more participants (Conradsson 2010; Eggermont 2009a; Rolland 2007; Stevens 2006; Volkers 2012). The total number of participants assessed at baseline was 1067, and 919 of them (86.13%) completed the trials.

All the trials, except one, required a diagnosis of dementia for recruitment. Only 52% of participants (100/191) in the Conradsson 2010 trial had a diagnosed dementia disorder, but separate data were available for these participants.

Conradsson 2010, Venturelli 2011, and Volkers 2012 required participants to be 65 years or older. Eggermont 2009a and Eggermont 2009b required participants to be 70 years or older. Three trials had a length of residency or attendance requirement: participants had to have been living in the nursing home for three weeks (Holliman 2001), two months (Rolland 2007), or four months (Santana-Sosa 2008).

The DSM-IV set of criteria for diagnosis of dementia were the most commonly used in the included studies (Conradsson 2010; Eggermont 2009a; Eggermont 2009b; Kemoun 2010; Vreugdenhil 2012). Other authors used the National Institute of Neurological and Communicative Disorders and Stroke, and the Alzheimer Disease and Related Disorders Association (NINCDS-ADRDA) criteria for probable or possible AD as eligibility for inclusion (Rolland 2007; Santana-Sosa 2008; Steinberg 2009; Van de Winckel 2004; Vreugdenhil 2012; Williams 2008), the International Statistical Classification of Diseases, 10th revision (ICD-10) definition of dementia (Christofoletti 2008), Clinical Dementia Rating (CDR3-CDR4) for late stage AD (Venturelli 2011), Consortium to Establish a Registry for Alzheimer's Disease Assessment Package-Korean (CERAD-K; Hwang 2010), MMSE (Holliman 2001; Volkers 2012), chart review (Francese 1997), and a local Aged Care Assessment Team (Stevens 2006).

The majority of trial participants had AD (Eggermont 2009b; Francese 1997; Kemoun 2010; Rolland 2007; Santana-Sosa 2008; Steinberg 2009; Venturelli 2011; Volkers 2012; Vreugdenhil 2012; Williams 2008). One of the trials had participants with vascular disease and AD (Van de Winckel 2004). In the remaining trials, the participants' type of dementia was not specified (Christofoletti 2008; Conradsson 2010; Eggermont 2009a; Holliman 2001; Hwang 2010; Stevens 2006).

One of the included trials had participants with mild dementia (Santana-Sosa 2008). Six of the trials had participants with mild to moderate dementia (Conradsson 2010; Eggermont 2009a; Eggermont 2009b; Steinberg 2009; Stevens 2006; Vreugdenhil 2012). Only two of the trials had participants with moderate to severe dementia (Venturelli 2011; Williams 2008). Five of the trials had participants with mild to severe dementia (Hwang 2010; Kemoun 2010; Rolland 2007; Van de Winckel 2004; Volkers 2012), and two had participants with severe dementia (Francese 1997; Holliman 2001).

Eleven of the trials specified the participants' level of physical ability: Eggermont 2009a required the ability to walk short distances with no aid; Eggermont 2009b required no apparent disability in hand motor function; Kemoun 2010 required the ability to walk 10 metres without technical assistance; Conradsson 2010 required the ability to stand up from a chair with help from no more than one person; Rolland 2007 required that the residents be able to transfer from a chair and walk six metres without human assistance; Francese 1997 required the residents to need one- to two-person assistance to transfer; Van de Winckel 2004 required the ability to mimic the movements of the therapist and to be able to hear the music; Venturelli 2011 required an absence of mobility limitations; Steinberg 2009 and Volkers 2012 required that participants be ambulatory; and Williams 2008 required that participants be able to walk with assistance, but also that they be dependent in at least one of the following, bed mobility, transfers, gait, or balance. Conradsson 2010 and Venturelli 2011 required participants to be dependent on assistance from a person in one or more personal ADLs. Santana-Sosa 2008 required that participants be free of neurological, vision, muscle or cardio-respiratory disorders, and Christofoletti 2008 required that participants had no other neurological or neuropsychiatric conditions, had no prescriptions of antidepressant medications with central anti-cholinergic or sedative action, and had no drug-related cognitive or balance impairment. Eggermont 2009a and Eggermont 2009b required participants without visual disturbances, hearing difficulties, history of alcoholism, personality disorders, cerebral trauma, or disturbances of consciousness. Volkers 2012 required participants without diagnosis of personality disorders, cerebral traumata, hydrocephalus, neoplasm, disturbances of consciousness or focal brain disorders.

Additional inclusion criteria required participants to have: good general health, a stable medical history and had a caregiver who spent at least 10 hours per week with the participant (Steinberg 2009); a caregiver who either lived with the participant or visited daily (Vreugdenhil 2012); a score of seven or above on the Cornell Scale for Depression in Dementia (CSDD; Williams 2008); a MMSE score lower than 24/30 (Van de Winckel 2004); a MMSE score from 5 to 15 and a minimum score of 23 on the Performance Oriented Mobility Assessment (POMA) index, with a constant oxygen saturation during walking (SpO_2 that exceeded 85%; Venturelli 2011); discharge scheduled after the trial (Holliman 2001); medical fitness (Christofoletti 2008); physical ability to participate (Francese 1997; Hwang 2010; Stevens 2006); ability to respond to most verbal requests (Stevens 2006; Van de Winckel 2004); and the ability to understand English (Francese 1997). Participants in the Holliman 2001 trial were not permitted to be participants in another, simultaneous research trial.

Exercise programs

The administration of the exercise programs ranged from twice a week (Rolland 2007), to three times a week (Christofoletti 2008; Hwang 2010; Kemoun 2010; Santana-Sosa 2008), four times a week (Venturelli 2011), five times a week (Eggermont 2009a; Eggermont 2009b; Volkers 2012; Williams 2008), to daily (Van de Winckel 2004; Vreugdenhil 2012). Conradsson 2010 required participants to complete five sessions every two weeks. Steinberg 2009 required the participants in the exercise group to achieve a number of points that were accrued for performing activities in the aerobic, strength, and balance categories (one point for partially performing a task; two for completing). The goal was to achieve six aerobic points and four each of strength and balance per week. Each session varied in length from 20 minutes (Francese 1997), to 30 minutes (Eggermont 2009a; Eggermont 2009b; Holliman 2001; Stevens 2006; Van de Winckel 2004; Venturelli 2011; Volkers 2012; Vreugdenhil 2012; Williams 2008), 45 minutes (Conradsson 2010), 50 minutes (Hwang 2010), 60 minutes (Christofoletti 2008; Kemoun 2010), up to 75 minutes (Santana-Sosa 2008). The period of time the program was offered varied greatly from two weeks (Holliman 2001), to six weeks (Eggermont 2009a; Eggermont 2009b), seven weeks (Francese 1997), 12 weeks (Santana-Sosa 2008; Stevens 2006; Steinberg 2009; Van de Winckel 2004), 13 weeks (Conradsson 2010); 15 weeks (Kemoun 2010), 16 weeks (Vreugdenhil 2012; Williams 2008), six months (Christofoletti 2008; Venturelli 2011), 12 months (Rolland 2007), and up to 18 months (Volkers 2012).

In three trials the exercises were performed while seated in order to accommodate people in wheelchairs (Francese 1997; Holliman 2001; Stevens 2006). In the Rolland 2007 trial, the first half hour of the session consisted of walking, and the remainder of the program included strength and balance training. Francese 1997 offered an exercise regime that consisted of activities such as catching, throwing, and kicking balls; leg weight exercises; and parachute reaches. Holliman 2001 designed the exercise program to target the training of gross and fine motor skills and movement, and also to be meaningful and appropriate for the residents. This program included several interactive exercises such as passing a bean bag or playing volleyball in order to promote socialization. The program used by Stevens 2006 was based on joint and large muscle group movement with the intention of creating gentle, aerobic exertion. Christofoletti 2008 and Vreugdenhil 2012 used walking and upper and lower limb exercises to stimulate strength, balance, motor co-ordination, agility, flexibility, and aerobic endurance. The Santana-Sosa 2008 training sessions included joint mobility, resistance, and co-ordination exercises. Hwang 2010 conducted an upper body dance therapy program. Van de Winckel 2004 incorporated upper and lower body strengthening as well as balance, trunk movements, and flexibility training, all supported by music. Participants in Conradsson 2010 performed a high-intensity functional weight-bearing exercise program, including strength and balance exercises. Steinberg 2009 focused on walking,

strength training, balance, and flexibility training. Eggermont 2009a, Venturelli 2011, and Volkers 2012 provided a supervised walking program. Participants in Eggermont 2009b performed hand movements only. Williams 2008 compared two experimental interventions: the first combined walking and strength-based exercises focusing on improving strength, balance, and flexibility, while the second consisted of supervised walking.

Control groups

The control groups for eight of the studies received usual care with no additional interventions (Christofoletti 2008; Hwang 2010; Kemoun 2010; Rolland 2007; Santana-Sosa 2008; Stevens 2006; Venturelli 2011; Vreugdenhil 2012). The control group for five studies included social contact (Eggermont 2009a; Steinberg 2009; Van de Winckel 2004; Volkers 2012; Williams 2008). In three studies the control groups consisted of social contact with additional activities such as films, singing, and reading (Conradsson 2010; Eggermont 2009b; Francese 1997). One study did not provide any details about the control group (Holliman 2001).

Primary outcomes

Cognitive functioning

The MMSE test was used frequently in trials to assess cognitive functioning (Christofoletti 2008; Holliman 2001; Steinberg 2009; Van de Winckel 2004; Venturelli 2011; Vreugdenhil 2012). In addition, Hwang 2010 used the Cognitive Memory Performance Scale; Kemoun 2010 used the Rapid Evaluation of Cognition Functions Test; Stevens 2006 measured the progression of dementia with the Clock Drawing Test; while Eggermont 2009a, Eggermont 2009b, and Volkers 2012 used a Delayed Recall score using the Eight Words Test. For all these measuring scales, higher scores indicate less cognitive impairment.

Activities of daily living (ADL)

ADL were assessed using the Barthel ADL index (Conradsson 2010; Santana-Sosa 2008; Venturelli 2011; Vreugdenhil 2012), Katz Index of ADLs (Rolland 2007; Santana-Sosa 2008), and Changes in Advanced Dementia Scale (CADS; Francese 1997). Higher scores in the Barthel ADL Index, Katz Index and the CADS indicate greater ability to perform ADLs.

Neuropsychiatric symptoms

Five trials measured neuropsychiatric symptoms of the participants (Holliman 2001; Rolland 2007; Steinberg 2009; Stevens 2006; Van de Winckel 2004). The Holliman 2001 trial used a subscale of the Psychogeriatric Dependency Rating Scale (PGDRS) to measure behaviours such as wandering, active aggression and restlessness related to dementia. Rolland 2007 and Steinberg 2009 evaluated neuropsychiatric symptoms using the Neuropsychiatric Inventory (NPI). Stevens 2006 used the Revised Elderly Disability Scale, which assesses self-help skills, behaviour, and six other categories that reflect functional ability. Van de Winckel 2004 also evaluated neuropsychiatric symptoms with the abbreviated Stockton Geriatric Rating Scale. Higher scores on these scales indicate worse or dependent behaviours; all measures were appropriate for people with dementia.

Depression

Trialists evaluated depression using the Montgomery-Asberg Depression Rating Scale (Rolland 2007), the Cornell Scale for Depression in Dementia (CSDD; Steinberg 2009; Williams 2008), and the Geriatric Depression Scale (Conradsson 2010; Eggermont 2009a; Eggermont 2009b; Vreugdenhil 2012). All of these measures are valid, reliable and specific to people with dementia; higher scores indicate greater depression.

Mortality

None of the included studies measured mortality.

Secondary outcomes

Caregiver burden

Caregiver burden was assessed using the Screen for Caregiver Burden (Steinberg 2009), and the Zarit Burden Interview Scale (Vreugdenhil 2012). In both cases, higher scores indicate increased burden.

Caregiver quality of life

None of the included studies measured caregiver quality of life.

Caregiver mortality

None of the included studies measured caregiver mortality.

Use of healthcare services

None of the included studies measured use of healthcare services.

Excluded studies

Forty-one trials were excluded for the following reasons:

1. nine were not or were probably not randomized (Aman 2009; Arcoverde 2008; Batman 1999; Christofoletti 2011; de Melo Coelho 2013; Garuffi 2013; Kwak 2008; Litchke 2012; Thurm 2011);
2. 11 did not include people diagnosed with dementia (Anon 1986; Hariprasad 2013; Kerse 2008; Littbrand 2006; Netz 1994; Powell 1974; Rodgers 2002; Scherder 2005; Suzuki 2012; van Uffelen 2005; Viscogliosi 2000);
3. five were complex interventions in which exercise was combined with additional treatments or training so that groups did not differ in exposure to exercise alone (Burgener 2008; Logsdon 2012a; Oswald 2007; Pitkala 2013; Schwenk 2010);
4. one study did not include an exercise program (Onor 2007);
5. ne study did not incorporate a comparison group comprised of people with dementia (Heyn 2008);
6. two studies did not include usual care in the control group (Day 2012; Obisesan 2011); and
7. 12 studies examined outcomes that were not of interest to this review (Abreu 2013; Hauer 2012; Littbrand 2011; McCurry 2011; Netz 2007; Padala 2012; Roach 2011; Rodriguez-Ruiz 2013; Suttanon 2013; Tappen 2000; Williams 2007; Yagüez 2011).

Risk of bias in included studies

(See Characteristics of included studies.)

Allocation

Random sequence generation (selection bias)

In 12 trials the methods used to generate allocation sequence were not described or were unclear (Christofoletti 2008; Conradsson 2010; Eggermont 2009b; Francese 1997; Holliman 2001; Hwang

2010; Kemoun 2010; Santana-Sosa 2008; Steinberg 2009; Venturelli 2011; Volkers 2012; Williams 2008). We judged the remaining trials to be at low risk of bias for this domain, as sufficient information about the way the allocation sequence was generated was available (Eggermont 2009a; Rolland 2007; Stevens 2006; Van de Winckel 2004; Vreugdenhil 2012).

Allocation (selection bias)

In 12 of the trials the methods used to conceal allocation sequence were unclear or not described (Eggermont 2009a; Eggermont 2009b; Francese 1997; Holliman 2001; Hwang 2010; Kemoun 2010; Santana-Sosa 2008; Steinberg 2009; Stevens 2006; Van de Winckel 2004; Volkers 2012; Williams 2008). In the remaining trials, allocation concealment was adequate and, due to this factor, we rated the risk of selection bias as low (Christofoletti 2008; Conradsson 2010; Rolland 2007; Venturelli 2011; Vreugdenhil 2012).

Blinding

Blinding of participants and personnel (performance bias)

All studies were at high risk of performance bias, as blinding of participants and personnel to the intervention was not possible, due to the nature of rehabilitation trials.

Blinding of outcome assessment (detection bias)

Blinding of outcome assessors was not described in Francese 1997, Hwang 2010, and Stevens 2006. Venturelli 2011 stated that the evaluation was completed in a "blinded way" and provided no further explanation, so it was not clear whether outcome assessments had been blinded. Van de Winckel 2004 stated, "The physiotherapist who was conducting both treatments evaluated the patients on cognition. However, the nurses who scored the patients on behaviours were all blind to the group assignment." Therefore, this study was rated as being at high risk for detection bias for cognition outcomes. We judged the remaining trials to be at low risk for detection bias since outcome assessors were blinded (Christofoletti 2008; Conradsson 2010; Eggermont 2009a; Eggermont 2009b; Holliman 2001; Kemoun 2010; Rolland 2007; Santana-Sosa 2008; Steinberg 2009; Volkers 2012; Vreugdenhil 2012; Williams 2008).

Incomplete outcome data

Attrition rates (drop-outs from the trials) varied from 0% to 37% in the included trials. The risk of attrition bias was unclear for Steinberg 2009, since the trial report did not provide data on attrition; we received no response when we requested this information. In Volkers 2012 the risk of attrition bias was also unclear, as the dropout rate for the experimental and control groups at the end of the study was not specified, instead the author provided the actual and expected number of observations made for each outcome measure over the course of the trial. Stevens 2006 was the only author who did not indicate the group (experimental or control) from which the drop-outs occurred. The drop-out rates were higher in the experimental arms for Christofoletti 2008 (29% experimental versus 15% control), Kemoun 2010 (20% experimental versus 17% control), Conradsson 2010 (14% experimental versus 9% control), and Eggermont 2009b (12% experimental versus 3% control). Attrition was higher in the control groups for Francese 1997 (0% experimental versus 17% control), Van de Winckel 2004 (0% experimental versus 10% control), Venturelli 2011 (8% experimental versus 17% control), Rolland 2007 (16% experimental versus 19% control), and Hwang 2010 (29% experimental versus 43% control). Reasons for attrition were provided, and included: death, illness, increased disability, disinterest, physician's disapproval, withdrawal of consent by family, moving to another institution, and refusal to continue to participate.

In summary, we judged the majority of the trials to be at low risk of attrition bias. A high risk of attrition bias was reported for five of the included studies for a variety of reasons that included: failure to report attrition rates for individual groups; a high attrition rate; or an imbalance of attrition between the groups, or failure to provide reasons for attrition, or both (Christofoletti 2008; Holliman 2001; Hwang 2010; Kemoun 2010; Stevens 2006; see Characteristics of included studies). None of these studies used ITT principles of analysis.

Eggermont 2009a, Eggermont 2009b, and Conradsson 2010 did report conducting modified ITT analyses, but did not include all randomized participants. Eggermont 2009a enrolled 103 nursing home residents with dementia in the study, but included only 97 participants in the modified ITT analysis. Similarly Eggermont 2009b enrolled 66 participants, but included only 61 in the ITT analysis. Conradsson 2010 included 91 of the original 100 participants with dementia in the ITT analysis with no explanation. Thus, there was a potential risk of attrition bias in these studies.

Selective reporting

We judged all of the included trials as being at low risk of reporting bias.

Other potential sources of bias

Figure 2 and Figure 3 provide summaries of risk of bias.

Figure 2. Risk of bias graph: review authors' judgments about each risk of bias item presented as percentages across all included trials

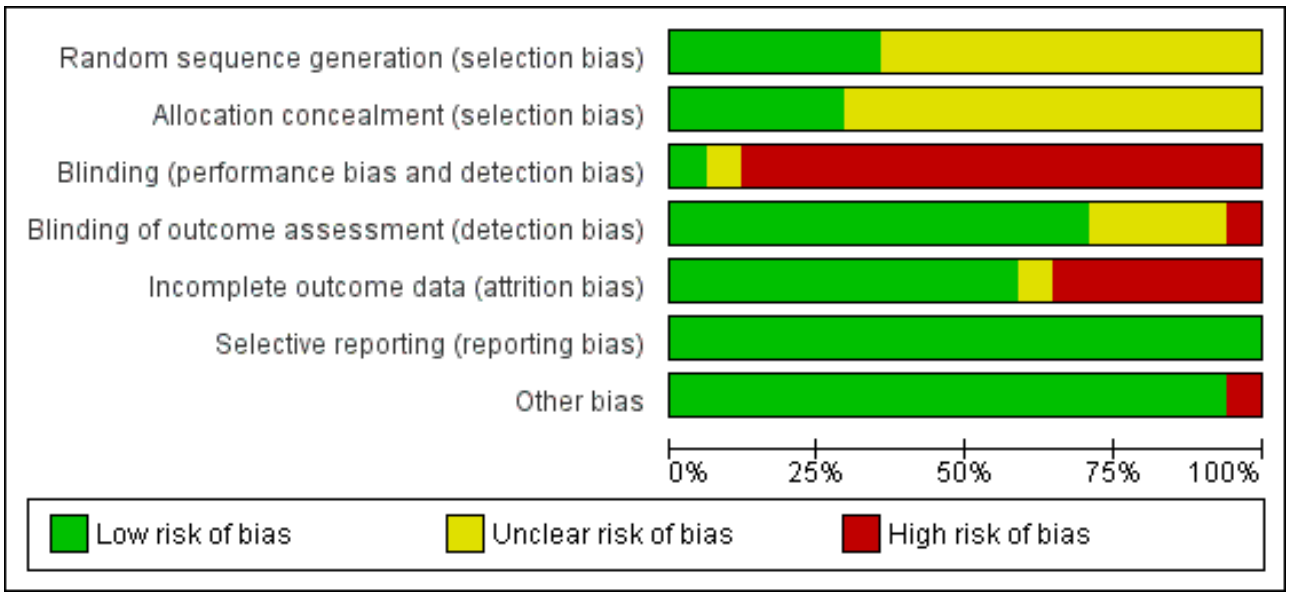
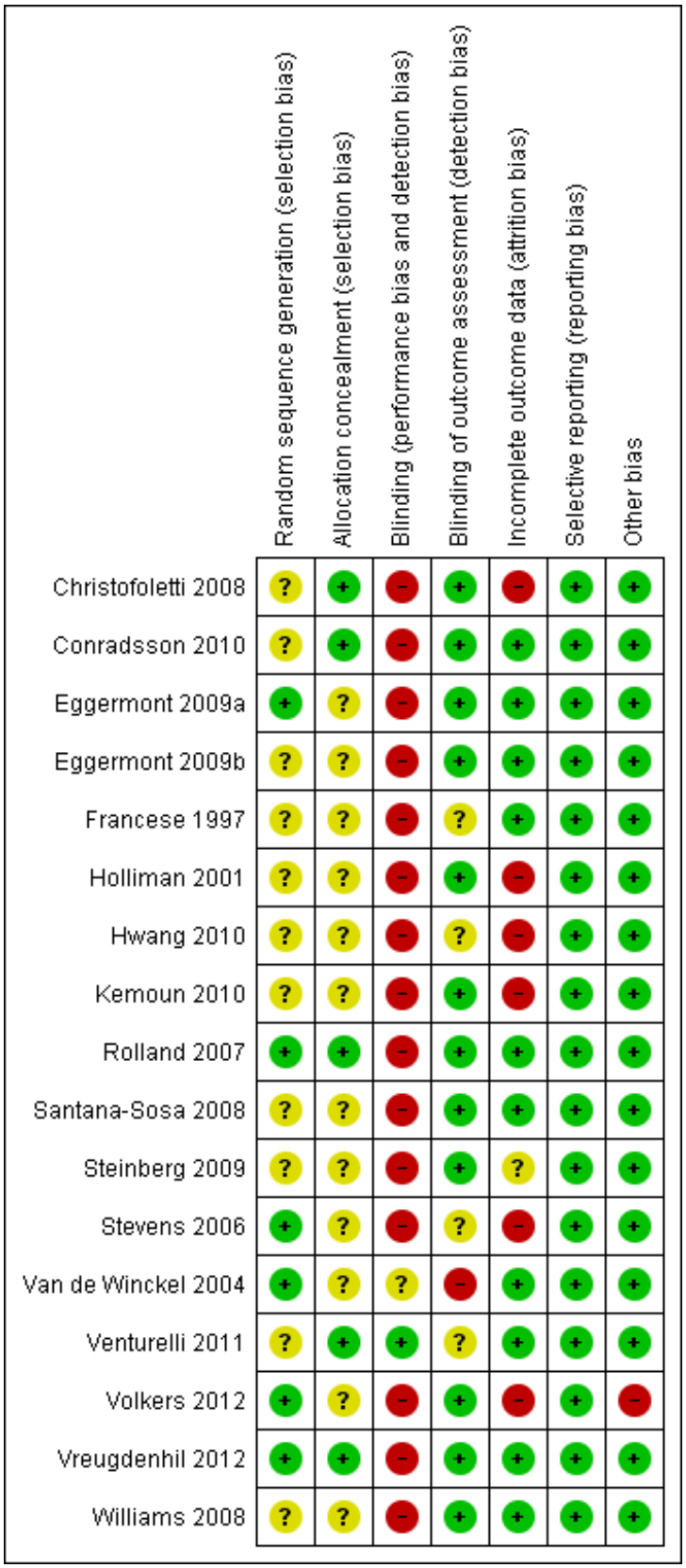


Figure 3. Risk of bias summary: review authors' judgments about each risk of bias item for each included trial



Effects of interventions

See: **Summary of findings for the main comparison** Exercise programs for people with dementia

Primary outcomes

Cognition (nine trials; 409 participants)

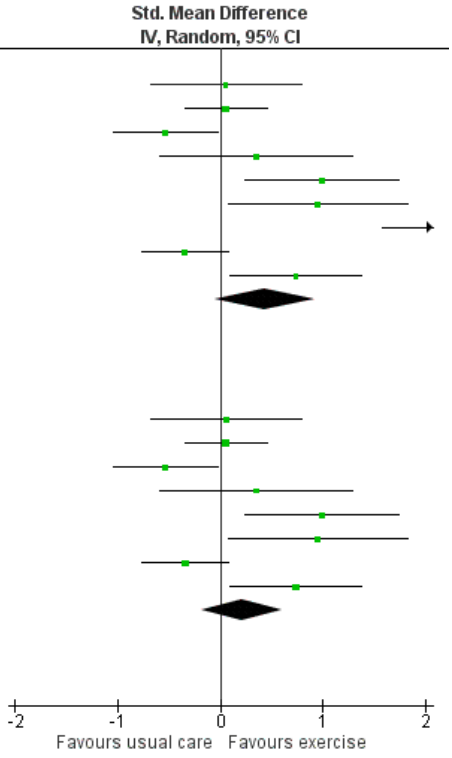
Twelve of the included studies measured cognitive outcomes, but we were only able to obtain data from nine to include in the meta-analysis of the effect of exercise on cognition (Christofoletti 2008; Eggermont 2009a; Eggermont 2009b; Hwang 2010; Kemoun 2010; Van de Winckel 2004; Venturelli 2011; Volkers 2012; Vreugdenhil 2012). We included post-intervention measures following six weeks to six months of exercise intervention.

As a result of the clinical diversity among studies (participants; type, intensity and duration of exercise programs), we used a random-effects model. The estimated standardized mean difference (SMD) between exercise and control groups was 0.43 (95% CI -0.05 to 0.92, P value 0.08; Analysis 1.1; Figure 4a), with nine studies and 409 participants. No clear conclusion can be drawn from this result because of the imprecision; it is compatible with both minimal harm or substantial benefit from the intervention. There was very substantial heterogeneity in this analysis (I^2 value 80%). We rated the quality of this evidence as very low because of the imprecision, inconsistency between studies, risk of bias and publication bias (see Summary of findings for the main comparison).

We explored potential reasons for the high heterogeneity by conducting meta-analyses that included only trials: 1) with people diagnosed with AD; 2) that ran the exercise programs for: more than 12 weeks; more than three times per week; or less than three times per week; 3) that included only aerobic exercise; or only strength exercise. None of these meta-analyses reduced the heterogeneity. However, when we removed the Venturelli 2011 trial - since it was the only trial that included only participants with moderate to severe dementia - the heterogeneity was reduced (Chi^2 value 23.15; I^2 value 70%). However the result of this meta-analysis was still inconclusive (SMD 0.21, 95% CI -0.18 to 0.61, P value 0.28; 8 trials; 388 participants; very low quality evidence; Analysis 1.1; Figure 4b).

Figure 4. Forest plot of comparison 1: Physical activity vs usual care: cognition

Study or Subgroup	Exercise Mean	SD	Total	Usual care Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.1.1 Cognition: all trials								
Christofoletti 2008	14.9	2.2	12	14.8	1.3	17	11.0%	0.06 [-0.68, 0.80]
Eggermont 2009a	0.24	0.78	51	0.2	0.63	46	13.5%	0.06 [-0.34, 0.45]
Eggermont 2009b	0.07	0.37	30	0.47	0.97	31	12.7%	-0.53 [-1.05, -0.02]
Hwang 2010	28.9	11.86	10	24	14.68	8	9.5%	0.35 [-0.58, 1.29]
Kemoun 2010	30.38	7.66	16	22.23	8.37	15	10.9%	0.99 [0.24, 1.74]
Van de Winckel 2004	15.33	4.44	15	11	4.3	9	10.0%	0.95 [0.08, 1.83]
Venturelli 2011	12	2	11	6	2	10	7.2%	2.88 [1.59, 4.17]
Volkers 2012	0.14	0.5	50	0.38	0.89	38	13.3%	-0.34 [-0.77, 0.08]
Vreugdenhil 2012	23.9	5	20	19	7.7	20	11.8%	0.74 [0.10, 1.38]
Subtotal (95% CI)			**215**			**194**	**100.0%**	**0.43 [-0.05, 0.92]**
Heterogeneity: Tau² = 0.42; Chi² = 40.90, df = 8 (P < 0.00001); I² = 80%								
Test for overall effect: Z = 1.75 (P = 0.08)								
1.1.2 Cognition: excluded moderate-severe dementia								
Christofoletti 2008	14.9	2.2	12	14.8	1.3	17	11.4%	0.06 [-0.68, 0.80]
Eggermont 2009a	0.24	0.78	51	0.2	0.63	46	15.9%	0.06 [-0.34, 0.45]
Eggermont 2009b	0.07	0.37	30	0.47	0.97	31	14.4%	-0.53 [-1.05, -0.02]
Hwang 2010	28.9	11.86	10	24	14.68	8	9.1%	0.35 [-0.58, 1.29]
Kemoun 2010	30.38	7.66	16	22.23	8.37	15	11.2%	0.99 [0.24, 1.74]
Van de Winckel 2004	15.33	4.44	15	11	4.3	9	9.8%	0.95 [0.08, 1.83]
Volkers 2012	0.14	0.5	50	0.38	0.89	38	15.6%	-0.34 [-0.77, 0.08]
Vreugdenhil 2012	23.9	5	20	19	7.7	20	12.6%	0.74 [0.10, 1.38]
Subtotal (95% CI)			**204**			**184**	**100.0%**	**0.21 [-0.18, 0.61]**
Heterogeneity: Tau² = 0.21; Chi² = 23.15, df = 7 (P = 0.002); I² = 70%								
Test for overall effect: Z = 1.07 (P = 0.28)								



Volkers 2012 was the only study that reported cognitive outcomes in which the intervention lasted longer than six months. Results from participants who remained in the study were also reported after 12 and 18 months of the exercise program. The estimated effect at both time-points was imprecise and compatible with either benefit or harm from the exercise intervention (after 12 months: SMD 0.02, 95% CI -0.42 to 0.46, P value 0.93; 1 study, 62 participants; and after 18 months: SMD -0.08, 95% CI -0.61 to 0.45, P value 0.77; 1 study, 52 participants). We considered this to be very low quality evidence because of the imprecision and risk of bias. The level of compliance with the walking program in this study was low. The quantitative findings of this study have not been published in a peer-reviewed journal.

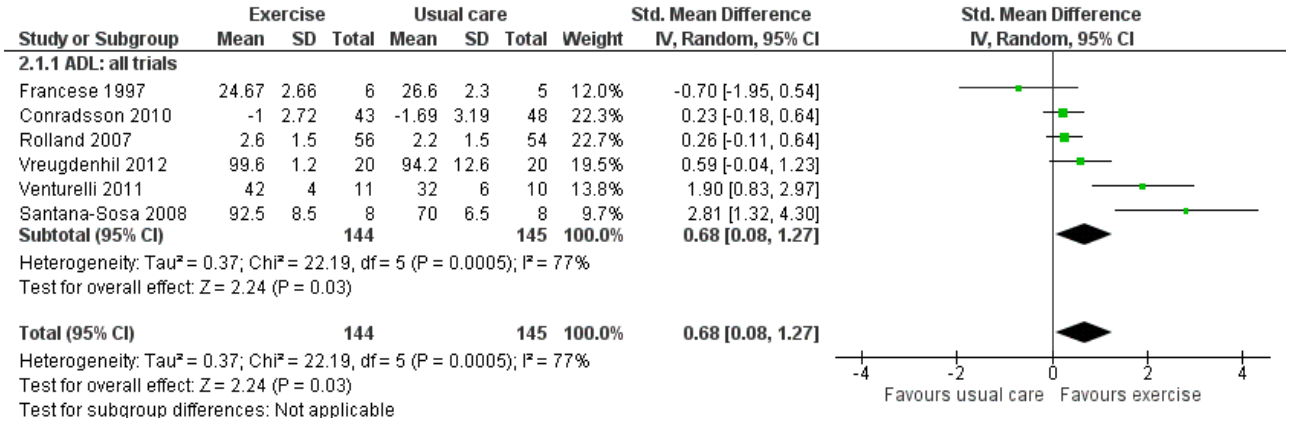
Although three additional trials also examined cognition (Holliman 2001; Steinberg 2009; Stevens 2006), they could not be included in the analyses as the necessary data were not reported, and the authors did not provide them upon request. The conclusions of these studies were mixed: Holliman 2001 and Steinberg 2009 reported finding no benefit of exercise on cognition, whereas Stevens 2006 reported that participants in the exercise program showed cognitive benefits relative to the control group.

Activities of daily living (ADLs) (six trials; 289 participants)

Six studies measured the effect of exercise on ADLs (Conradsson 2010; Francese 1997; Rolland 2007; Santana-Sosa 2008; Venturelli 2011; Vreugdenhil 2012). The exercise programs ranged from seven to 52 weeks in length. We included end point measures of means, standard deviations (SDs), and number of participants in each group in the meta-analysis. As a result of the clinical diversity among studies (types and severity of dementia and type, intensity and duration of exercise programs), we used a random-effects model.

The meta-analysis yielded an estimated SMD between exercise and control groups of 0.68 favouring the exercise group (95% CI 0.08 to 1.27, P value 0.03; six trials, 289 participants; Analysis 2.1; Figure 5). There was considerable heterogeneity in this analysis (I^2 value 77%). We rated the quality of this evidence as low because of the inconsistency and imprecision (results compatible with both minimal and moderate effect size; see Summary of findings for the main comparison).

Figure 5. Forest plot of comparison 2: Physical activity vs usual care: Activities of daily living (ADLs)



We explored potential reasons for the high heterogeneity by conducting meta-analyses that included only trials: 1) with participants diagnosed with AD; 2) that ran the exercise programs for more than 12 weeks; less than 12 weeks; more than three times per week; less than three times per week; 3) with a combination of aerobic and strength exercises; and 4) removing the trial that included only persons with moderate to severe dementia (Venturelli 2011). None of these meta-analyses reduced the heterogeneity.

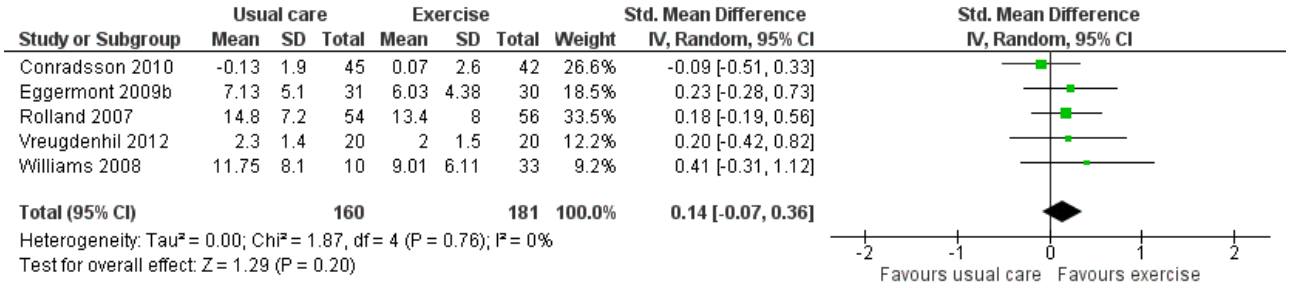
Neuropsychiatric symptoms (one trial; 110 participants)

Holliman 2001, Rolland 2007, Steinberg 2009, Stevens 2006, and Van de Winckel 2004 examined the effect of exercise on neuropsychiatric symptoms. Holliman 2001 did not provide the SDs when using the PGDRS behaviour scale, but did report that participants showed improved behaviour only during group sessions, and not outside the group. Steinberg 2009 and Stevens 2006 did not provide useable data. Stevens 2006 reported that the participants in the exercise program showed improvement in behaviour, while Steinberg 2009 reported increased neuropsychiatric symptoms. Van de Winckel 2004 also did not provide useable data and reported no significant behavioural effects. At 12 months, the Rolland 2007 study revealed no clear effect of exercise on neuropsychiatric symptoms (MD -0.60, 95% CI -4.22 to 3.02, P value 0.75; 1 trial, 110 participants). We considered this to be very low quality evidence (an imprecise result from a single study, publication bias; see Summary of findings for the main comparison).

Depression (five studies; 341 participants)

Six studies examined the effect of exercise on depression (Conradsson 2010; Eggermont 2009b; Rolland 2007; Steinberg 2009; Vreugdenhil 2012; Williams 2008). Steinberg 2009 did not report the data needed for the analysis, or respond to requests for this data, so could not be included in the meta-analysis. Williams 2008 included two experimental groups: a supervised individual walking group and a comprehensive individual exercise group. For this trial, we combined the data from the two experimental groups. Our meta-analysis revealed no clear effect of exercise (SMD -0.14, 95% CI -0.36 to 0.07, P value 0.20; 5 trials, 341 participants). Heterogeneity in this analysis was low (I^2 value 0%; Analysis 3.1; Figure 6). We rated the quality of this evidence as moderate because of the imprecision. In addition, publication bias was suspected due to the missing Steinberg 2009 data (see Summary of findings for the main comparison).

Figure 6. Forest plot of comparison 3: Physical activity vs usual care: depression



Mortality

No trials reported on mortality in people with dementia.

Secondary outcomes

Caregiver burden (one trial; 40 participants)

Two trials examined caregiver burden (Steinberg 2009; Vreugdenhil 2012). Steinberg 2009 did not report the data needed for the analysis, and the trial authors did not respond to requests for this data. The community-based exercise program in Vreugdenhil 2012 was associated with a reduction in caregiver burden. The fixed-effect model meta-analysis yielded a mean difference between exercise and control groups of -15.30 (95% CI -24.73 to -5.87, P value 0.001; 1 trial, 40 participants). We rated this as low quality evidence (a single study, publication bias).

Caregiver quality of life

No studies reported on caregivers' quality of life.

Caregiver mortality

No studies reported on caregivers' mortality.

Use of healthcare services

No studies reported on use of healthcare services.

Adverse events (five trials)

Five studies addressed potential adverse events of exercise programs for people with dementia (Conradsson 2010; Rolland 2007; Santana-Sosa 2008; Steinberg 2009; Venturelli 2011). None of these trials reported any serious adverse events that could be attributed to the exercise intervention. One trial, Christofoletti 2008, indirectly addressed adverse events by stating there were no drop-outs related to the treatment.

DISCUSSION

Summary of main results

This review included 17 trials (18 articles) with a total of 1067 participants. Most participants were older people with AD. The exercise programs varied greatly; the length of time that they ran ranged from two weeks to 18 months, and activities varied (e.g. hand movements, sitting, walking, and upper and lower limb exercises). The review suggests that exercise programs may improve people with dementia's ability to perform ADLs, though there was considerable unexplained statistical heterogeneity observed in the ADL analyses, which suggests the need for caution in interpreting these results. In addition, one trial revealed that the burden experienced by informal caregivers providing care in the home may be reduced if they supervise their family member with dementia during participation in an exercise program. This review found no clear evidence of benefit from exercise on cognitive functioning, neuropsychiatric symptoms, and depression. Nevertheless, these are encouraging results, as dementia is a debilitating disease that results in progressive decline in ability to perform ADLs, as well as other symptoms. A slowing of the development of dependence in ADLs is critical for enhancing the quality of life for people with dementia, and will have an impact on the family caregivers' ability to sustain their caregiving role.

Overall completeness and applicability of evidence

The number of included trials was sufficient to address the first three objectives relating to the effect of exercise on cognition, ADLs, and depression. However, only one trial was included in the analyses of the effect on neuropsychiatric symptoms and caregiver burden, and no analyses were completed for the following outcomes: mortality in people with dementia, caregiver quality of life, caregiver mortality, and use of healthcare services. Although several additional included trials investigated cognition (three trials), neuropsychiatric symptoms (three trials), depression (one trial), and caregiver burden (one trial), useable data for inclusion in the meta-analyses were not provided by the authors. It is important to include means and SDs for end point measures, or change from baseline to final measurement scores in published reports, or, alternatively, the trial authors should be willing to provide these data on request. Clearly, additional research is needed that examines these important outcomes and provides the data needed for meta-analysis.

Only two studies were based in the community (Steinberg 2009; Vreugdenhil 2012), all others were conducted largely in institutions. Most people with dementia are cared for at home, and most caregivers wish to keep the family member with dementia at home for as long as possible. Knowing how to support family caregivers and delay the symptoms of dementia will have profound benefits for all involved. In addition, enabling people with dementia to remain in their homes for longer will lead to decreased healthcare costs. Further community-based trials are needed that examine the benefit or harm of exercise on multiple domains of the person with dementia and the impact on their family caregivers.

The participants within the trials were not homogeneous in terms of their diagnosis (e.g. AD, vascular dementia, mixed dementia, other) or severity of dementia (e.g. mild, moderate, severe). This was unfortunate, as dementia should not be viewed as a single

disease entity, and there is some evidence that exercise might affect the risk of these conditions differently (Rockwood 2007). Several observational studies have found that the preventive effects of exercise may be weaker for vascular dementia than for AD or dementia in general (Rockwood 2007). However, a more recent meta-analysis revealed a significant association between exercise and a reduced risk of developing vascular dementia (odds ratio 0.62, 95% CI 0.42 to 0.92; Aarsland 2010).

Also, the exercise programs were not homogeneous in terms of the type (e.g. aerobic, strength, balance), duration (range: two weeks to 18 months), and frequency (range: two times per week to daily) of activities. Therefore, we compared type, duration (less than 12 weeks versus longer than 12 weeks), and frequency (less than three times per week versus more than three times per week) of the exercise programs in further subgroup analyses. However, because of the low number of trials in each category it was not possible to identify any relationship between the type, duration, or frequency of exercise, and the effect on ADL performance or on other outcomes.

Quality of the evidence

One additional trial was included in this updated review. As a result the number of participants increased to 1067 at baseline and 919 (86.13%) completed the trials, compared with 280 participants at baseline and 208 (74%) completing the trials in the original 2008 review. These are encouraging results.

Factors that may influence the quality of the evidence (our confidence in estimates of effect) include inconsistency, imprecision, and indirectness. Inconsistency refers to considering the upper and lower limits of the confidence intervals (CIs). The quality of evidence should be rated down if clinical action would differ if the upper versus the lower boundary of the CI represented the truth. Similarly, the quality of the evidence would be rated down for imprecision if the 95% CI includes appreciable benefit or harm. Indirectness refers to substantial differences that may exist between the population, the intervention or the outcomes measured in studies included in a systematic review. Publication bias was not reported in this review as at least 10 studies should be included in the meta-analysis to adequately test for publication bias (Higgins 2011; section 10.4.3.1).

The three primary outcomes (cognition, ADLs, and depression) were all rated as very low on quality of evidence due to serious risk of bias, inconsistency, indirectness, and imprecision, and potential publication bias in some or all of these outcomes (see GRADE, Summary of findings for the main comparison). Serious risk of bias was a possibility as many of the authors of the trials did not report the random sequence generation and allocation concealment processes adequately. A computer-generated program managed by a third party is a rigorous approach that can be used to generate random allocation to groups, and ensures allocation concealment. Several authors did not report or did not describe adequately the outcome data for each main outcome. Although blinding of the participants and individuals conducting the exercise programs was not possible, it was expected that outcome assessors would be blinded. A few authors failed to report on the blinding of outcome assessors. High attrition rates, an imbalance of attrition between groups, and unknown reasons for attrition and poor adherence (or no description) to the exercise programs were also potential sources of bias in several of the included trials. In addition, some trials with high attrition rates did not conduct ITT analysis (see Figure 2 and Figure 3).

We rated inconsistency as serious for two of the outcomes of interest (cognition and ADLs) and not serious for the depression outcome. We rated indirectness and imprecision as serious for all three outcomes. The funnel plots revealed potential publication bias with the outcome of cognition, no publication bias for the outcome of depression, and suspected publication bias for the depression outcome (see GRADE, Summary of findings for the main comparison).

Potential biases in the review process

This review was conducted as outlined in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011), therefore, the introduction of bias during the review process was minimized. We are fairly confident that all relevant studies were identified, as the literature searches were conducted by Anna Noel-Storr of the Cochrane Dementia and Cognitive Improvement Group and are updated at least every six months. However, not all of the included trials reported data that could be used in the meta-analysis, and some authors did not respond to requests for this data. This meant that the results of four trials could not be included in our meta-analyses. This was unfortunate as the total number of trials that have examined the evidence of the benefit or lack of benefit of exercise programs in improving the symptoms of dementia is limited.

Agreements and disagreements with other studies or reviews

A recent systematic review, that included 13 RCTs with 896 participants (Potter 2011), found similar results to those identified in this review for depression; only one of the four trials identified by Potter 2011 that reported depression as an outcome found a benefit. However, Thune-Boyle 2012 used a critical interpretive approach to synthesize the literature, and concluded that exercise appears to be beneficial in reducing depressed mood. The Potter 2011 review reported on two trials that found an improvement in quality of life; our review did not include any trials that examined quality of life, and only one trial that examined neuropsychiatric symptoms. Bowes 2013 was a scoping review that concluded that a more holistic approach is needed, which examines the benefit of exercise on mental health and well-being in people with dementia living at home and the impact on their family caregivers. So we concur with Thune-Boyle 2012 that the evidence is weak or lacking of the benefit of exercise on neuropsychiatric symptoms, such as repetitive behaviours, and also with Potter 2011 and Bowes 2013 that the evidence of the benefit of exercise on depression and quality of life is limited. We would agree with these authors that further research is needed that examines the benefit of exercise on cognition, ADLs, depression, neuropsychiatric symptoms, and quality of life.

AUTHORS' CONCLUSIONS

Implications for practice

With an increased number of trials now available, there is evidence that suggests that exercise programs may improve people with dementia's ability to perform activities of daily living (ADLs). Healthcare providers who work with people with dementia and their caregivers should feel confident in promoting exercise among

this population, as decreasing the progression of dependence in ADLs will have significant benefits for people with dementia and their family caregivers' quality of life, and possibly delay the need for placement in long-term care settings. No trials reported adverse events related to exercise programs.

One trial that examined the burden experienced by family caregivers who provide care in the home revealed that this burden can be reduced if caregivers supervise the family member with dementia during participation in an exercise program. Therefore, encouraging caregivers to participate in exercise may also have a beneficial impact on their quality of life.

Setting of intervention (home versus institutional) should be considered in the future, if more studies become available. There was an insufficient number of trials to permit subgroup analyses that would determine which type of exercise (aerobic, strength training, balance, or a combination), at what frequency and duration, is most beneficial for specific types and severity of dementia. Clearly further research is needed to be able to develop best practice guidelines that would be helpful to healthcare providers in advising people with dementia living in institutional and community settings.

Implications for research

For older people in general, recent research recommends at least 150 minutes of moderate- to vigorous-intensity aerobic exercise per week, in bouts of 10 minutes or more to achieve better quality of life, improve functional abilities, and reduce risk of disease, death, and loss of independence by up to 60%. In addition, muscle and bone strengthening activities using major muscle groups, at least two times per week is recommended (Chodzko-Zajko 2009; Tremblay 2011). Other research has revealed that aerobic-type exercise has a clear benefit over strength training, and moderate-intensity exercise of at least one hour a day, three to five times or more a week may be more effective in improving cognition (Kramer 2007; Middleton 2007).

However, these recommendations may not be appropriate for people with dementia. Further research is necessary to identify the optimal exercise modalities particularly in terms of frequency, intensity, and duration for people with different types and severity of dementia and to identify barriers and facilitators to improving adherence. Attempting to match the exercise programs with the needs, capabilities, and preferences of people with dementia, and ensuring adequate funding to provide regular, appropriate programs, over extended periods, by qualified instructors may increase adherence (Forbes 2007). Additional well designed trials that are conducted in the community setting, which is where most people with dementia live, and that examine outcomes of relevance to people with dementia (e.g. cognition, ADLs, depression, neuropsychiatric symptoms, quality of life and mortality), family caregiver outcomes (e.g. caregiver burden, quality of life, and mortality) and economic analysis of visits to emergency departments, acute care settings, and cost of residential care are also needed.

No serious adverse events were attributed to participation in the trials. Recent research suggests that high-intensity weight-bearing exercise does not seem to have a negative effect on functional balance (Conradsson 2010). However, further research is needed about potential adverse events from aerobic exercise programs to determine whether this population is similar to older adults in general who are less likely to fall and less likely to injure themselves from falls if they are physically active (Kannus 2005; Sherrington 2004), or if the risk of falling and of cardiovascular events is higher in people with dementia during aerobic exercise.

Clinical researchers should make a practice of ensuring that their trials are of high methodological quality and provide information on the randomization process (sequence generation and allocation concealment), blinding of outcome assessors, attrition rates and reasons for drop-outs from both treatment and control groups, rate of adherence to the exercise programs and reasons for withdrawal, and adverse events to the exercise programs in published articles, or be willing to share this information with reviewers when contacted. Providing statistically appropriate data (e.g. end point means and standard deviations) would also ensure that the trial results can be incorporated into meta-analysis.

ACKNOWLEDGEMENTS

We wish to thank Anna Noel-Storr, Cochrane Dementia and Cognitive Improvement Group, for conducting the literature searches, and Sue Marcus, Cochrane Dementia and Cognitive Improvement Group, for her assistance throughout the review. We also wish to thank the following authors who contributed to previous reviews: Debra Morgan, Maureen Markle-Reid, Jennifer Wood, and Ivan Culum.

REFERENCES

References to studies included in this review

Christofoletti 2008 *{published data only}*

Christofoletti G, Oliani MM, Gobbi S, Stella F, Bucken-Gobbi LT, 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):618-26.

Conradsson 2010 *{published data only}*

* 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):565-76.

Littbrand H, Lundin-Olsson L, Gustafson Y, Rosendahl E. The effect of a high-intensity functional exercise program on activities of daily living: a randomized controlled trial in residential care facilities. *Journal of the American Geriatrics Society* 2009;**57**(10):1741-9.

Eggermont 2009a *{published data only}*

Eggermont LH, Swaab DF, Hol EM, Scherder EJ. Walking the line: a randomised trial on the effects of a short term walking programme on cognition in dementia. *Journal of Neurology, Neurosurgery & Psychiatry* 2009;**80**(7):802-4.

Eggermont 2009b *{published data only}*

Eggermont LH, Knol, DL, Hol EM, Swaab DF, Scherder EJ. Hand motor activity, cognition, mood, and the rest-activity rhythm in dementia: a clustered RCT. *Behavioural Brain Research* 2009;**196**:271-8.

Francese 1997 *{published data only}*

Frances T, Sorrell J, Butler FR. 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):122-7.

Holliman 2001 *{published data only}*

Holliman DC, Orgassa UC, Forney JP. Developing an interactive physical activity group in a geriatric psychiatry facility. *Activities, Adaptation and Aging* 2001;**26**(1):57-69.

Hwang 2010 *{published data only}*

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**:12-7.

Kemoun 2010 *{published data only}*

Kemoun G, Thibaud M, Roumagne N, Carette P, Albinet C, Toussaint L, et al. 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):109-14.

Rolland 2007 *{published data only}*

Rolland Y, Pillard F, Klapouszczak A, Reynish E, Thomas D, Andrieu S, et al. Exercise program for nursing home residents with Alzheimer's Disease: a one-year randomized, controlled trial. Journal of the American Geriatric Society 2007; Vol. 55, issue 2:158-65.

Santana-Sosa 2008 *{published data only}*

Santana-Sosa E, Barriopedro MI, López-Mojares LM, Pérez M, Lucia A. Exercise training is beneficial for Alzheimer's patients. *International Journal of Sports Medicine* 2008;**29**(10):845-50.

Steinberg 2009 *{published data only}*

Steinberg M, Leoutsakos JM, Podewils LJ, Lyketsos CG. 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):680-5.

Stevens 2006 *{published data only}*

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.

Van de Winckel 2004 *{published data only}*

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):253-60.

Venturelli 2011 *{published data only}*

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 & Other Dementias* 2011;**26**(5):381-8.

Volkers 2012 *{published data only}*

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. PhD Dissertation: Physical (in)activity an cognition in cognitively impaired older people. Amsterdam: Vrije University, 2012:87-99.

Vreugdenhil 2012 *{published data only}*

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**:12-9.

Williams 2008 *{published data only}*

Williams CL, Tappen RM. Exercise training for depressed older adults with Alzheimer's disease. *Aging & Mental Health* 2008;**12**(1):72-80.

References to studies excluded from this review

Abreu 2013 *{published data only}*

Abreu M, Hartley G. The effects of salsa dance on balance, gait, and fall risk in a sedentary patient with Alzheimer's dementia,

multiple comorbidities, and recurrent falls. *Journal of Geriatric Physical Therapy* 2013;**36**(2):100-8.

Aman 2009 *{published data only}*

Aman E, Thomas DR. Supervised exercise to reduce agitation in severely cognitively impaired persons. *Journal of the American Medical Directors Association* 2009;**10**(4):271-6.

Anon 1986 *{published data only}*

Anon. Study links exercise, improved mental ability. *Geriatrics* 1986;**41**(3):24.

Arcoverde 2008 *{published data only}*

Arcoverde C, Deslandes A, Rangel A, Rangel A, Pavao R, Nigri F, et al. Role of physical activity on the maintenance of cognition and activities of daily living in elderly with Alzheimer's Disease. *Arquivos De Neuro-Psiquiatria* 2008;**66**(2B):323-7.

Batman 1999 *{published data only}*

Batman MW. The effects of therapeutic aquatic exercise on patients with Alzheimer's Disease. *Dissertation Abstracts International Section B The Sciences and Engineering* 1999;**60**(6):2933.

Burgener 2008 *{published data only}*

Burgener SC, Yang Y, Gilbert R, Marsh-Yant S. The effects of a multimodal intervention on outcomes of persons with early-stage dementia. *American Journal of Alzheimer's Disease & Other Dementias* 2008;**23**(4):382-94.

Christofoletti 2011 *{published data only}*

Christofoletti G, Oliani MM, Bucken-Gobbi LT, Gobbi S, Beinotti F, Stella F. Physical activity attenuates neuropsychiatric disturbances and caregiver burden in patients with dementia. *Clinics* 2011;**66**(4):613-8.

Day 2012 *{published data only}*

Day L, Hill KD, Jolley D, Cicuttini F, Flicker L, Segal L. Impact of tai chi on impairment, functional limitation, and disability among preclinically disabled older people: A randomized controlled trial. *Archives of Physical Medicine and Rehabilitation* 2012;**93**(8):1400-7.

de Melo Coelho 2013 *{published data only}*

de Melo Coelho FG, Andrade LP, Pedroso RV, Santos-Galduroz RF, Gobbi S, Costa JLR, et al. Multimodal exercise intervention improves frontal cognitive functions and gait in Alzheimer's disease: a controlled trial. *Geriatrics & Gerontology International* 2013;**13**(1):198-203.

Garuffi 2013 *{published data only}*

Garuffi M, Riani Costa JL, Soleman HSS, Vital TM, Stein AM, Dos Santos JG, et al. Effects of resistance training on the performance of activities of daily living in patients with Alzheimer's disease. *Geriatrics & Gerontology International* 2013;**13**(2):322-8.

Hariprasad 2013 *{published data only}*

Hariprasad VR, Koparde V, Sivakumar PT, Varambally S, Thirthalli J, Varghese M, et al. Randomized clinical trial of yoga-based intervention in residents from elderly homes: effects on cognitive function. *Indian Journal of Psychiatry* 2013;**55**(Suppl 3):S357-63.

Hauer 2012 *{published data only}*

Hauer K, Schwenk M, Zieschang T, Essig M, Becker C, Oster P. Physical training improves motor performance in people with dementia: a randomized controlled trial. *Journal of the American Geriatrics Society* 2012;**60**(1):8-15.

Heyn 2008 *{published data only}*

Heyn PC, Johnson KE, Kramer AF. Endurance and strength training outcomes on cognitively impaired and cognitively intact older adults: a meta-analysis. *Journal of Nutrition, Health & Aging* 2008;**12**(6):401-9.

Kerse 2008 *{published data only}*

Kerse N, Peri K, Robinson E, Wilkinson T, von Randow M, Kiata L, et al. Does a functional activity programme improve function, quality of life, and falls for residents in long term care? Cluster randomised controlled trial. *BMJ (Clinical research ed.)* 2008;**Oct 9**:337.

Kwak 2008 *{published data only}*

Kwak YS, Um SY, Son TG, Kim DJ. Effect of regular exercise on senile dementia patients. *International Journal of Sports Medicine* 2008;**29**(4):471-4.

Litchke 2012 *{published data only}*

Litchke LG, Hodges JS, Reardon RF. Benefits of chair yoga for persons with mild to severe Alzheimer's Disease. *Activities, Adaptation & Aging* 2012;**36**(4):317-28.

Littbrand 2006 *{published data only}*

Littbrand H, Rosendahl E, Lindelof N, Lundin Olsson L, Gustafson Y, Nyberg L. 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. *Physical Therapy* 2006;**86**(4):489-98.

Littbrand 2011 *{published data only}*

Littbrand H, Carlsson M, Lundin-Olsson L, Lindelof N, Haglin L, Gustafson Y, et al. Effect of a high-intensity functional exercise program on functional balance: preplanned subgroup analyses of a randomized controlled trial in residential care facilities. *Journal of the American Geriatrics Society* 2011;**59**(7):1274-82.

Logsdon 2012b *{published data only}*

Logsdon RG, Teri L, McCurry SM. A randomized trial of social support and physical activity interventions for early stage dementia. *Gerontologist* 2012;**52**:244.

McCurry 2011 *{published data only}*

McCurry SM, Pike KC, Vitiello MV, Logsdon RG, Larson EB, Teri L. Increasing walking and bright light exposure to improve sleep in community-dwelling persons with Alzheimer's disease: results of a randomized, controlled trial. *Journal of the American Geriatrics Society* 2011;**59**(8):1393-402.

Netz 1994 *{published data only}*

Netz Y, Yaretzki A, Salganik I, Jacob T, Finkeltov B, Argov E. The effect of supervised physical activity on cognitive and affective state of geriatric and psychogeriatric in-patients. *Clinical Gerontologist* 1994;**15**(1):47-56.

Netz 2007 *{published data only}*

Netz Y, Axelrad S, Argov E. Group physical activity for demented older adults - feasibility and effectiveness. *Clinical Rehabilitation* 2007;**21**(11):977-86.

Obisesan 2011 *{published data only}*

Obisesan T, Gillum R, Umar N, Bond V, Williams D. Gene, exercise and memory study (GEMS): a randomized controlled clinical trial to evaluate the effects of standardized aerobic exercise on neurocognition and neurodegeneration in African Americans with mild Alzheimer's Disease. Alzheimer's and Dementia Conference: Alzheimer's Association International Conference, AAIC 11 Paris France. Conference Start: 20110716 Conference End: 20110721. 2011; Vol. 7 (4 suppl 1):S615-6.

Onor 2007 *{published data only}*

Onor ML, Trevisiol M, Negro C, Alessandra S, Saina M, Aguglia E. Impact of a multimodal rehabilitative intervention on demented patients and their caregivers. *American Journal of Alzheimer's Disease & Other Dementias* 2007;**22**(4):261-72.

Oswald 2007 *{published data only}*

Oswald WD, Gunzelmann T, Ackermann A. Effects of a multimodal activation program (SimA-P) in residents of nursing homes. *European Review of Aging and Physical Activity* 2007;**4**(2):91-102.

Padala 2012 *{published data only}*

Padala KP, Padala PR, Malloy TR, Geske J, Dubbert PM, Dennis R, et al. Wii-fit for improving gait and balance in an assisted living facility: a pilot study. *Journal of Aging Research* 2012:1-6. [Article ID 597573]

Pitkala 2013 *{published data only}*

Pitkala KH, Poysti MM, Laakkonen ML, Tilvis RS, Savikko N, Kautiainen H, et al. Effects of the Finnish Alzheimer Disease Exercise Trial (FINALEX): a randomized controlled trial. *JAMA Internal Medicine* 2013;**173**(10):894-901.

Powell 1974 *{published data only}*

Powell RR. Psychological effects of exercise therapy upon institutionalized geriatric mental patients. *Journals of Gerontology* 1974;**29**(2):157-61.

Roach 2011 *{published data only}*

Roach KE, Tappen RM, Kirk-Sanchez N, Williams CL, Loewenstein D. A randomized controlled trial of an activity specific exercise program for individuals with Alzheimer disease in long-term care settings. *Journal of Geriatric Physical Therapy (2001)* 2011;**34**(2):50-6.

Rodgers 2002 *{published data only}*

Rodgers ME. Effects of a structured low-level exercise program on age-related cognitive decline in veteran patients. *Dissertation Abstracts International: Section B: The Sciences and Engineering* 2002;**63**(6-B):2810.

Rodriguez-Ruiz 2013 *{published data only}*

Rodriguez-Ruiz D, Sarmiento S, Rodriguez-Matoso D, Henriquez Del Pino Y, Alvarez-Pinera L, Garcia-Manso JM. Changes in response of vastus lateralis and biceps femoris after a physical activity program in subjects diagnosed with Alzheimer's disease. *British Journal of Sports Medicine* 2013;**47**(10):e3.

Scherder 2005 *{published data only}*

Scherder EJ, Van Paasschen J, Deijen JB, Van Der Knokke S, Orlebeke JF, Burgers I, et al. Physical activity and executive functions in the elderly with mild cognitive impairment. *Aging and Mental Health* 2005;**9**(3):272-80.

Schwenk 2010 *{published data only}*

Schwenk M, Zieschang T, Oster P, Hauer K. Dual-task performances can be improved in patients with dementia. *Neurology* 2010;**74**:1961-8.

Suttanon 2013 *{published data only}*

Suttanon P, Hill KD, Said CM, Williams SB, Byrne KN, LoGiudice D, et al. 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):427-38.

Suzuki 2012 *{published data only}*

Suzuki T, Shimada H, Makizako H, Doi T, Yoshida D, Tsutsumimoto K, et al. Effects of multicomponent exercise on cognitive function in older adults with amnestic mild cognitive impairment: a randomized controlled trial. *BMC Neurology* 2012;**12**(128):1-9.

Tappen 2000 *{published data only}*

Tappen RM, Roach KE, Touhy TA. Effect of a comprehensive exercise program on function in nursing home residents with Alzheimer's disease. Proceedings of the World Alzheimer Congress; 2000 July 9-13, Washington, DC. 2000.

Thurm 2011 *{published data only}*

Thurm F, Scharpf A, Liebermann N, Kolassa S, Elbert T, Luchtenberg D, et al. Improvement of cognitive function after physical movement training in institutionalized very frail older adults with dementia. *GeroPsych: The Journal of Gerontopsychology and Geriatric Psychiatry* 2011;**24**(4):197-208.

van Uffelen 2005 *{published data only}*

van Uffelen JG, Hopman-Rock M, Chin A Paw MJ, van Mechelen W. Protocol for Project FACT: a randomised controlled trial on the effect of a walking program and vitamin B supplementation on the rate of cognitive decline and psychosocial wellbeing in older adults with mild cognitive impairment [ISRCTN19227688]. *BMC Geriatrics* 2005;**5**:18.

Viscogliosi 2000 *{published data only}*

Viscogliosi C, Desrosiers J, Gauthier P, Beauchemin R. Effect of a multi-strategic group program on performance of the activities of daily living for elderly people with mild cognitive deficits.

Canadian Journal of Occupational Therapy; Revue Canadienne d'Ergotherapie 2000;**67**(5):314-23.

Williams 2007 *{published data only}*

Williams CL, Tappen RM. Effect of exercise on mood in nursing home residents with Alzheimer's disease. *American Journal of Alzheimer's Disease and Other Dementias* 2007;**22**(5):389-97.

Yagüez 2011 *{published data only}*

Yagüez L, Shaw KN, 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):173-81.

References to ongoing studies

Cerga-Pashoja 2010 *{published data only}*

Cerga-Pashoja A, Lowery D, Bhattacharya R, Griffin M, Iliffe S, Lee J, et al. Evaluation of exercise on individuals with dementia and their carers: a randomised controlled trial. *Trials* 2010;**11**(53). [PUBMED: 20465799]

Cyarto 2010 *{published data only}*

Cyarto EV, Cox KL, Almeida OP, Flicker L, Ames D, Byrne G, et al. The fitness for the Ageing Brain Study II (FABS II): protocol for a randomized controlled clinical trial evaluating the effect of physical activity on cognitive function in patients with Alzheimer's disease. *Trials* 2010;**11**(120). [PUBMED: 21143943]

Gennep van 2011 *{published data only}*

Gennep van, M. Effects of a program combining walking and cognitive training on memory and behavior of older persons with dementia. *www.trialregister.nl/trialreg/admin/rctview.asp?TC=3121* 2011.

Hasselbalch 2012 *{published data only}*

Hasselbalch SG, Hoffmann K, Frederiksen KS, Sobol NA, Beyer N, Vogel A, et al. A multicentre randomized clinical trial of physical exercise in Alzheimer's disease (AD): rationale and design of the ADEX study. European Journal of Neurology 2012 Conference: 16th Congress of the European Federation of Neurological Societies, EFNS; 2012 September 8-11; Stockholm Sweden. 2012, accessed August 1, 2013; Vol. clinicaltrials.gov/ct2/show/NCT01681602?term=NCT01681602&rank=1:65.

Laks 2012 *{published data only}*

Laks, J. Physical exercise as an additional treatment for Alzheimer disease. *http://clinicaltrials.gov/ct2/show/NCT01515982* 2012.

Lamb 2011 *{published data only}*

Lamb S. Physical activity programmes for community dwelling people with mild to moderate dementia (DAPA - Dementia and Physical Activity) date accessed April 9, 2013. ISRCTN32612072.

Logsdon 2012a *{published data only}*

Logsdon RG. Two interventions for early stage dementia: a comparative efficacy trial. *http://clinicaltrials.gov/ct2/show/NCT01550718* 2012.

Potemkowski 2011 *{published data only}*

Potemkowski A, Kolenda J, Ratajczak A, Ratajczak M. Influence of physical activity on cognitive dysfunction in patients with mild and moderate Alzheimer dementia. Neurodegenerative Diseases. 10th International Conference AD/PD - Alzheimer's and Parkinson's Diseases: Advances, Concepts and New Challenges Barcelona Spain. Conference Start: 20110309 Conference End: 20110313. 2011.

Rosendahl 2012 *{published data only}*

Rosendahl, E. A high-intensity functional exercise program for older people with dementia and living in residential care facilities (The Umeå Dementia and Exercise Study). *ISRCTN: http://isrctn.org/ISRCTN31767087,* 2012.

Tartaglia 2013 *{published data only}*

Tartaglia C. Benefits of Exercise in Alzheimer's Disease. clinicaltrials.gov/ct2/show/NCT01935024 23 August 2013.

Additional references

Aarsland 2010

Aarsland D, Sardahaee FS, Anderssen S, Ballard C, Alzheimer's Society Systematic Review group. Is physical activity a potential preventive factor for vascular dementia? A systematic review. *Aging & Mental Health* 2010;**14**(4):386-95.

Alzheimer Society of Canada 2010

Alzheimer Society of Canada. Rising Tide: The Impact of Dementia on Canadian Society. www.alzheimer.ca/~/media/Files/national/Advocacy/ASC_Rising_Tide_Full_Report_e.ashx Date accessed 6 November 2013 2010:65.

Angevaren 2008

Angevaren M, Aufdemkampe G, Verhaar HJJ, Aleman A, Vanhees L. Physical activity and enhanced fitness to improve cognitive function in older people without known cognitive impairment (Review). *Cochrane Database of Systematic Reviews* 2008, Issue 2. [DOI: 10.1002/14651858.CD005381.pub2]

APA 1987

American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 3rd Edition. Washington, DC: Author, 1987.

APA 1995

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 4th Edition. Washington, DC: American Psychiatric Association, 1995.

Bowes 2013

Bowes A, Dawson A, Jepson R, McCabe L. Physical activity for people with dementia: a scoping study. *BMC Geriatrics* 2013;**13**(129). [DOI: 10.1186/1471-2318-13-129]

Brown 2010

Brown AD, McMorris CA, Longman RS, Leigh R, Hill MD, Friedenreich CM, et al. Effects of cardiorespiratory fitness and cerebral blood flow on cognitive outcomes in older women. *Neurobiology of Aging* 2010;**31**(12):2047-57.

Chang 2010

Chang M, Jonsso PV, Snaedal J, Bjornsson S, Saczynski JS, Aspelund T, et al. The effect of midlife physical activity on cognitive function among older adults: AGES--Reykjavik Study. *Journals of Gerontology Series A-Biological Sciences & Medical Sciences* 2010;**65**(12):1369-74.

Chen 2009

Chen KM, Chen MH, Chao HC, Hung HM, Lin HS, Li CH. Sleep quality, depression state, and health status of older adults after silver yoga exercises: cluster randomized trial. *International Journal of Nursing Studies* 2009;**46**(2):154-63.

Cheng 2003

Cheng A, Wang S, Cai J, Rao MS, Mattson MP. Nitric oxide acts in a positive feedback loop with BDNF to regulate neural progenitor cell proliferation and differentiation in the mammalian brain. *Developmental Biology* 2003;**258**(2):319-33.

Chodzko-Zajko 2009

Chodzko-Zajko W, Proctor D, Fiatarone Singh M, Minson C, Nigg C, Salem G, et al. American College of Sports Medicine position stand. Exercise and physical activity for older adults. *Medicine and Science in Sports and Exercise* 2009;**41**(7):1510-30.

Churchill 2002

Churchill JD, Galvez R, Colcombe S, Swain RA, Kramer AF, Greenough WT. Exercise, experience and the aging brain. *Neurobiology of Aging* 2002;**23**:941-55.

Colcombe 2003

Colcombe S, Kramer AF. Fitness effects on the cognitive function of older adults: a meta-analytic study. *Psychological Science* 2003;**14**(2):125-30.

Cotman 2007

Cotman CW, Berchtold NC, Christie LA. Exercise builds brain health: key roles of growth factor cascades and inflammation. *Trends in Neurosciences* 2007;**30**(9):464-72.

Covas 2002

Covas MI, Elosua R, Fito M, Alcantara M, Coca L, Marrugat J. Relationship between physical activity and oxidative stress biomarkers in women. *Medicine and Science in Sports and Excercise* 2002;**34**(5):814-9.

Cummings 1994

Cummings JL, Mega M, Gray K, Rosenberg-Thompson S, Carusi DA, Gornbein J. The Neuropsychiatric Inventory: comprehensive assessment of psychopathology in dementia. *Neurology* 1994;**44**(12):2308-14.

Cummings 1997

Cummings JL. The Neuropsychiatric Inventory: assessing psychopathology in dementia patients. *Neurology* 1997;**48**(S):10-6.

Davenport 2012

Davenport MH, Hogan DB, Eskes GA, Longman RS, Poulin MJ. Cerebrovascular reserve: the link between fitness and cognitive function?. *Exercise and Sport Sciences Reviews* 2012;**40**(3):153-8.

DSM-III-R 1987

American Psychiatric Association. Diagnostic and statistical manual of mental disorders. Diagnostic and statistical manual of mental disorders. 3rd Edition. Washington, DC: Authors, 1987.

DSM-IV 1994

American Psychiatric Association. Diagnostic and statistical manual of mental disorders: DSM-IV. 4th Edition. Washington, DC: American Psychiatric Association, 1994.

Erickson 2011

Erickson KI, Voss MW, Prakash RS, Basak C, Szabo A, Chaddock L, et al. Exercise training increases size of hippocampus and improves memory. *Proceedings of the National Academy of Sciences of the United States of America* 2011;**108**(7):3017-22.

Erickson 2012

Erickson KI, Weinstein AM, Lopez OL. Physical activity, brain plasticity, and Alzheimer's disease. *Archives of Medical Research* 2012;**43**(8):615-21.

Farris 2003

Farris W, Mansourian S, Chang Y, Lindsley L, Eckman EA, Frosch MP, et al. Insulin-degrading enzyme regulates the levels of insulin, amyloid β-protein, and the β-amyloid precursor protein intracellular domain in vivo. *Proceedings of the National Academy of Sciences* 2003;**100**(7):4162-7.

Feldman 2005

Feldman HH, Woodward M. The staging and assessment of moderate to severe Alzheimer disease. *Neurology* 2005;**65**(suppl 3):S10-S17.

Fleg 2012

Fleg JL. Aerobic exercise in the elderly: a key to successful aging. *Discovery Medicine* 2012;**13**(70):223-8.

Forbes 2007

Forbes D. An exercise programme led to a slower decline in activities of daily living in nursing home patients with Alzheimer's disease. *Evidence Based Nursing* 2007;**10**(3):89.

Forbes 2008a

Forbes D, Gibson M, Hogan D. The CCCDTD3 dementia recommendations: caring for a family member with dementia. *The Canadian Review of Alzheimer's Disease and Other Dementias* 2008;**11**(12):20-5.

Ghisi 2010

Ghisi GL, Durieux A, Pinho R, Benetti M. Physical exercise and endothelial dysfunction. *Arquivos Brasileiros de Cardiologia* 2010;**95**(5):30-7.

Hamer 2009

Hamer M, Chida Y. Physical activity and risk of neurodegenerative disease: a systematic review of prospective evidence. *Psychological Medicine* 2009;**39**(1):3-11.

Higgins 2002

Higgins JPT, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Statistics in Medicine* 2002;**21**:1539-58.

Higgins 2003

Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003;**327**:557-60.

Higgins 2011

Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Hogan 2007

Hogan DB, Bailey P, Carswell A, Clarke B, Cohen C, Forbes D, et al. Management of mild to moderate Alzheimer's disease and dementia. *Alzheimer's & Dementia: Journal of the Alzheimer's Association* 2007;**3**(4):355-84.

Hogan 2008

Hogan DB, Bailey P, Black S, Carswell A, Chertkow H, Clarke B, et al. Diagnosis and treatment of dementia: non-pharmacologic and pharmacologic therapy for mild to moderate dementia: Recommendations from the Third Canadian Consensus Conference on Diagnosis and Treatment of Dementia. *Canadian Medical Association Journal* 2008;**179**(10):1019-26.

Intlekofer 2012

Intlekofer KA, Cotman CW. Exercise counteracts declining hippocampal function in aging and Alzheimer's disease. *Neurobiology of Disease* 2012;**in press**:9. [DOI: 10.1016/j.nbd.2012.06.011]

Kannus 2005

Kannus P, Uusi-Rasi K, Palvanen M, Parkkari J. Non-pharmacological means to prevent fractures among older adults. *Annals of Medicine* 2005;**37**(4):303-10.

Kramer 2007

Kramer AF, Erickson KI. Effects of physical activity on cognition, well-being, and brain: human interventions. *Alzheimer's & Dementia* 2007;**3**:S45-S51.

Lautenschlager 2010

Lautenschlager NT, Cox K, Kurz AF. Physical activity and mild cognitive impairment and Alzheimer's disease. *Current Neurology and Neuroscience Reports* 2010;**10**(5):352-8.

Lavie 2011

Lavie CJ, Church TS, Milani RV, Earnest CP. Impact of physical activity, cardiorespiratory fitness, and exercise training on markers of inflammation. *Journal of Cardiopulmonary Rehabilitation and Prevention* 2011;**31**(3):137-45.

McKhann 1984

McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: Report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services task force on Alzheimer's disease. *Neurology* 1984;**34**:939-44.

Middleton 2007

Middleton L, Rockwood K. Exercise and the prevention of dementia. *The Canadian Review of Alzheimer's Disease and Other Dementias* 2007;**September**:13-7.

Potter 2011

Potter R, Ellard D, Rees K, Thorogood M. A systematic review of the effects of physical activity on physical functioning, quality of life and depression in older people with dementia. *International Journal of Geriatric Psychiatry* 2011;**26**(10):1000-11.

Rockwood 2007

Rockwood K, Middleton L. Physical activity and the maintenance of cognitive function. *Alzheimer's & Dementia* 2007;**3**:S38-S44.

Rogers 1990

Rogers RL, Meyer JS, Mortel KF. After reaching retirement age physical activity sustains cerebral perfusion and cognition. *Journal of the American Geriatrics Society* 1990;**38**(2):123-8.

Ryan 2000

Ryan AS. Insulin resistance with aging: effects of diet and exercise. *Sports Medicine* 2000;**30**(5):327-46.

Sherrington 2004

Sherrington C, Lord SR, Finch CF. Physical activity interventions to prevent falls among older people: update of the evidence. *Journal of Science of Medical Sport* 2004;**7**(1 Suppl):43-51.

Thune-Boyle 2012

Thune-Boyle ICV, Iliffe S, Cerga-Pashoja A, Lowery D, Warner J. The effect of exercise on behavioral and psychological symptoms of dementia: towards a research agenda. *International Psychogeriatrics* 2012;**24**(7):1046-57.

Tremblay 2011

Tremblay MS, Warburton DE, Janssen I, Paterson DH, Latimer AE, Rhodes RE, et al. New Canadian physical activity guidelines. *Applied Physiology, Nutrition, and Metabolism* 2011;**36**(1):36-46.

Tseng 2011

Tseng CN, Gau BS, Lou MF. The effectiveness of exercise on improving cognitive function in older people: a systematic review. *The Journal of Nursing Research* 2011;**19**(2):119-31.

Vaynman 2004

Vaynman S, Ying Z, Gomez-Pinilla F. Hippocampal BDNF mediates the efficacy of exercise on synaptic plasticity and cognition. *The European Journal of Neuroscience* 2004;**20**(10):2580-90.

Wareham 2000

Wareham NJ, Wong M-Y, Day NE. Glucose intolerance and physical inactivity: the relative importance of low habitual activity energy expenditure and cardiorespiratory fitness. *American Journal of Epidemiology* 2000;**152**(2):132-9.

Watson 2003

Watson GS, Peskind ER, Asthana S, Purganan K, Wait C, Chapman D, et al. Insulin increases CSF Abeta42 levels in normal older adults. *Neurology* 2003;**60**(12):1899-903.

World Alzheimer Report 2011

Alzheimer Disease International. World Alzheimer Report 2011: The benefits of early diagnosis and intervention. www.alz.co.uk/research/world-report-2011, Date accessed 6 November 2013 September 2011.

World Health Organization 1992

World Health Organization. The ICD-10 Classification of Mental and Behavioural Disorders: Clinical Descriptions and Diagnostic Guidelines. Geneva: World Health Organisation, Division of Mental Health, 1992.

World Health Organization 2012

World Health Organization (WHO) and Alzheimer Disease International. Dementia: A Public Health Priority. www.who.int/mental_health/publications/dementia_report_2012/en/ , Date accessed 6 November 2013 2012.

References to other published versions of this review

Forbes 2008b

Forbes DA, Forbes SC, Markle-Reid M, Morgan D, Wood J, Culum I. Physical activity programs and dementia. (Review). *Cochrane Database of Systematic Reviews* 2008;**3**. [DOI: 10.1002/14651858; CD006489]

* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Christofoletti 2008

Methods	6-month RCT
Participants	Country: Brazil Centre: long-term psychiatric institution Diagnosis: moderate stage mixed dementia Participants: 54 at baseline, and 41 completed Baseline: 54 (37 women and 17 men), mean age (SD) = 74.3 years (1.4), mean years of education (SD) = 4.8 (0.7) Group 1 (n = 17) was an interdisciplinary program Group 2 (n = 17) was physiotherapy Group 3 (n = 20) was the control Of the two experimental groups, only Group 2 was included in this review Experimental Group: n = 17, mean MMSE (SD) = 12.7 (2.1) Control Group: n = 20, mean MMSE (SD) = 14.6 (1.2) Inclusion criteria: "primary diagnosis of dementia" using ICD-10 criteria and confirmed by MMSE and Katz ADL score, medically fit for participation in intervention, resident of psychiatric institution Exclusion criteria: cognitive impairment associated with other neuropsychiatric conditions or neurological diagnosis; antidepressant prescriptions with sedative or anticholinergic actions; impairment of cognition or balance related to drugs
Interventions	Experimental Group: physiotherapy kinesiotherapeutic exercises (strength, balance, memory, and recognition exercise using balls, elastic ribbons, and proprioceptive plates), provided by physiotherapist Type of physical activity: strength, balance Frequency: 3 times a week, exercise duration = 1 hour Time period: 6 months

Christofoletti 2008 *(Continued)*

	Control Group: received usual care Time period: 6 months
Outcomes	Cognition outcomes 1. MMSE 2. Brief Cognitive Screening Battery
Notes	The participants' medications were kept the same throughout the study. If a change in medication was required the participant was removed from the study

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Unclear process of randomization: (quote) "A sealed envelope with an identification number was assigned to each subject, each one filled with a slip giving the group. When a patient was registered and given a number, the appropriate envelope was opened"
Allocation concealment (selection bias)	Low risk	Sealed envelope used, but did not specify whether envelopes were opaque or non-opaque
Blinding (performance bias and detection bias) All outcomes	High risk	Not possible to blind participants and the personnel to the intervention allocated: (quote) "As a common bias presented on most rehabilitation trials, it was not possible to 'blind' the subjects regarding the treatments"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	Study attrition rate was 24.1% Attrition rate for each group: Experimental Group: 29.4% = 5 participants Control Group: 15.0% = 3 participants Reasons for attrition given, however, not specified according to group
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Attendance and adherence not stated

Conradsson 2010

Methods	6-month cluster-RCT
Participants	Country: Sweden Multicentre: 9 residential facilities Diagnosis: 100 of a total of 191 participants diagnosed with mild to moderate dementia (type of dementia unspecified)

Conradsson 2010 *(Continued)*

	Participants: 191 (139 women and 52 men), mean age (SD) = 84.7 years (6.5), mean MMSE (SD) = 17.8 (5.1) Baseline age, education, and MMSE, not reported for dementia subgroup (n = 100) Of the 100 participants with dementia, 91 completed Experimental Group: n = 47; Control Group: n = 53 Inclusion criteria: 65 years or older, MMSE score ≥ 10, dependent for assistance with at least 1 ADL as per Katz index, able to stand from arm chair with help from no more than 1 person, resident physician approval Exclusion criteria: none stated
Interventions	Experimental Group: the high-intensity group exercise (3-9 participants per exercise group) focused on weight bearing and progressively increased in difficulty. Activity consisted of strength and balance exercises including walking, squats and trunk exercises Type of physical activity: strength, balance, aerobic Frequency: 5 sessions every 2 weeks, exercise duration = 45 minutes Time period: 13 weeks Control Group: social contact plus seated activities provided by occupational therapists, e.g. watching films, singing, reading, conversation Frequency: 5 sessions every 2 weeks, activity duration = 45 minutes Time period: 13 weeks
Outcomes	Depression outcome (Conradsson 2010): Geriatric Depression Scale 15-item Psychological well-being outcome (Conradsson 2010): Philadelphia Geriatric Centre Morale Scale Activity of Daily Living outcome (Littbrand 2009): Barthel ADL Index
Notes	Note: Conradsson 2010 and Littbrand 2009 articles report on the same trial. Conradsson 2010 reports on depression and Littbrand 2009 reports on ADL We used only data specific to people with dementia in the analysis. Adherence of participants in the intervention was 72%.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Process of random selection not described
Allocation concealment (selection bias)	Low risk	Quote: "Researchers not involved in this study performed the randomization using lots in sealed non-transparent envelopes" (Conradsson 2010)
Blinding (performance bias and detection bias) All outcomes	High risk	Not possible to blind participants and the personnel to the intervention allocated
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "The assessors of the outcome measures were blinded to group allocation and previous test results" (Conradsson 2010)

Conradsson 2010 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	The attrition rate for the Experimental Group was 14.3%, and that of the Control Group 9.0%. Trial authors specified reasons for attrition in each group. ITT principles used in analyses. However, only 91 of the original 100 participants were included in the ITT analysis
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	None apparent

Eggermont 2009a

Methods	12-week RCT
Participants	Country: the Netherlands Multicentre: 23 nursing homes Diagnosis: mild to moderate dementia (type of dementia not specified) Participants: 103* (79 women and 18 men), mean age (SD) = 85.4 years, mean MMSE (SD) = 17.7. Information about level of education not provided * 6 did not complete study protocol so number who actually took part in the study = 97 Experimental Group: n = 51; Control Group: n = 46 Inclusion criteria: age > 70 years; diagnosis of dementia; able to walk for short distances with or without a walking aid; written consent from participants and relatives Exclusion criteria: MMSE score of < 10 or > 24; visual disturbances; hearing difficulties; history of alcoholism; personality disorders; cerebral trauma; hydrocephalus; neoplasm; or disturbances of consciousness
Interventions	Experimental Group: walking group, walks occurred on unit wards and in public places Frequency: 5 days a week, exercise duration = 30 minutes Type of physical activity: aerobic Time period: 6 weeks Control Group: social contact Frequency: 5 days a week, social visit duration = 30 minutes Time period: 6 weeks
Outcomes	Executive function, memory and cognitive domains outcomes 1. Rivermead Behavioural Memory Test 2. Wechsler Memory Scale-revised
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

Eggermont 2009a *(Continued)*

Random sequence generation (selection bias)	Low risk	Quote: "By tossing a coin subjects were randomly allocated to either an experimental or control group."
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	High risk	Not possible to blind participants and the personnel to the intervention allocated
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome measures were evaluated by a trained psychology student blinded to the participants' intervention
Incomplete outcome data (attrition bias) All outcomes	Low risk	Study attrition rate 5.8%. Trial authors did not report group attrition rates, or reasons for attrition. Modified ITT used in analysis, however 103 participants were enrolled in the study but only 97 participants were included in the modified ITT analysis.
Selective reporting (reporting bias)	Low risk	Used 2 rating scales to measure executive function, memory, and cognitive domains. Components of both scales were reported elsewhere: (quote) "The following tests were administered (details are published elsewhere)"
Other bias	Low risk	Attendance and adherence not stated

Eggermont 2009b

Methods	6-week clustered-RCT
Participants	Country: the Netherlands Multicentre: 10 nursing homes Diagnosis: mild to moderate dementia (subtype unknown), diagnosed with dementia using the DSM-IV criteria Participants: 66 at baseline, and 61 completed; mean age = 84.6 years Experimental Group: n = 30, mean MMSE (SD) = 15.8 (5.0); Control Group: n = 31, mean MMSE (SD): 84.2 (4.6)
Interventions	Experimental Group: hand movement activity group performing activities such as "finger movement, pinching a soft ball, or handling a rubber ring" Type of physical activity: hand movement Frequency: 5 days a week, duration = 30 minutes Time period: 6 weeks Control Group; social contact plus read out loud program Frequency: 5 days a week, duration = 30 minutes Time period: 6 weeks
Outcomes	Cognition: MMSE (at baseline)

Eggermont 2009b *(Continued)*

	Memory: examined using the face recognition test from the Rivermead Behavioural Memory Test and the Eight Word Test Executive function: tested using the stop signal task, attention network test, and the digit span subset from the Weschsler Memory Scale-Revised Mood: examined using the Geriatric Depression Scale (a Dutch version) Actigraphy data: rest and activity domain All outcomes were measured at baseline, after 6 weeks and 12 weeks
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Unclear process of randomization
Allocation concealment (selection bias)	Unclear risk	Unclear process of allocation concealment
Blinding (performance bias and detection bias) All outcomes	High risk	Not possible to blind participants or personnel to the intervention allocated
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Reasons for attrition provided Used ITT analysis, however, 66 participants were enrolled in the study and only 61 were included in the ITT analysis Per-protocol analysis included participants that attended 80% of the sessions
Selective reporting (reporting bias)	Low risk	Reported all outcomes measured
Other bias	Low risk	None apparent

Francese 1997

Methods	7-week RCT
Participants	Country: USA Centre: long-term care facility Diagnosis: severe AD Participants: 12 participants at baseline, and 11 completed Completed: 11 (gender not specified), age, years of education, and baseline MMSE not provided Experimental Group: n = 6; Control Group: n = 5

Francese 1997 *(Continued)*

	Inclusion criteria: documentation in chart of late stage Alzheimer-type dementia, could understand English, considered medically fit, required assistance from 1 or 2 care providers to transfer, informed consent obtained by family member or legal guardian Exclusion criteria: none stated
Interventions	Experimental Group: exercises targeting strength and function that included the use of music, various types of exercise balls and parachute leg weights; participants provided with snack Type of physical activity: strength, balance Frequency: 3 times a week, duration = 20 minutes Time period: 7 weeks Control Group: social contact plus sing-along group that watched music videos; participants provided with snack. Frequency: 3 times a week, duration of social activity = 20 minutes Time period: 7 weeks
Outcomes	Function (particularly ADL) outcomes Changes in Advanced Dementia Scale
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Methods of randomization not described
Allocation concealment (selection bias)	Unclear risk	Methods used to conceal allocation not described
Blinding (performance bias and detection bias) All outcomes	High risk	Not possible to blind participants and the personnel to the intervention allocated
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding of the outcome assessors not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	Study attrition was 8%, one participant dropped out of Control Group as (quote) "had a major CVA and was confined to bed"
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Attendance and adherence not stated

Holliman 2001

Methods	2-week, quasi-experimental design

Holliman 2001 *(Continued)*

Participants	Country: USA Centre: geriatric psychiatric facility Diagnosis: dementia Participants: 14 at baseline, and 12 completed 14 (12 women and 2 men); age range: 65-89 years; education: 1-16 years; mean MMSE (SD) = 4.57 (4.88) Number of participants in Experimental and Control Groups not specified Inclusion criteria: primary diagnosis of dementia, living with in psychiatric facility for at least 3 weeks, not scheduled to be discharged until after study completed Exclusion criteria: participating in another research trial at same time All participants were pronounced to be a danger to themselves or others
Interventions	Experimental Group: activity targeted gross and fine motor skills, and movement in a way that was meaningful and appropriate for participants. Snack provided Type of physical activity: aerobic and balance Frequency: 3 times per week, duration = 30 minutes Time period: 2 weeks Control Group: activities not described
Outcomes	Behaviour outcomes 1. Psychogeriatric Dependency Rating Scale 2. Patient Behaviour Rating Sheet (PBRS - used in the Experimental Group only)
Notes	The following statement was made In the published article, "the sample was not fully randomly assigned due to patient availability, informed consent matters, and institutional procedures". Email messages clarified the process of randomization. "Randomly assigned eligible residents a number. In order to assign each resident to either the control or treatment group, copies of these numbers were made and put into an envelope and the numbers were then drawn from the envelope" (personal communication on 5 June 2007 and 5 July 2007) All exercises completed while sitting in chair, as majority of the participants in wheelchairs The necessary data were not reported on cognition and the authors did not provide them upon request

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Numbers used, but review authors unaware of from where they originated
Allocation concealment (selection bias)	Unclear risk	Used envelopes
Blinding (performance bias and detection bias) All outcomes	High risk	Not possible to blind participants and the personnel to the intervention allocated
Blinding of outcome assessment (detection bias)	Low risk	Outcome assessors were blinded to group allocation

Holliman 2001 *(Continued)*

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	High risk	Attrition rate was 14.29% and (quote) "all participants were active almost all the time". Reason for attrition provided, but unclear in which group the attrition occurred
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Attendance and adherence not stated Control group activity not described

Hwang 2010

Methods	8-week trial with random assignment to groups
Participants	Country: Korea Centre: nursing home Diagnosis: mild-severe dementia (type of dementia unspecified) Participants: 28 at baseline, and 18 completed Baseline: 28 (all women) Experimental Group: n = 14; mean age (SD) = 81.30 years (5.4); mean education years (SD) = 3.3 (0.95); mean MMSE-KC (SD) = 11.6 (3.47) Control Group: n = 14, mean age (SD) = 81.75 years (8.86), mean education years (SD) = 3.0 (1.07), mean MMSE-KC (SD) = 13.88 (5.06) Inclusion criteria: aged 65 or older, from nursing home residence; agreement of family; recommended by head of facility; dementia confirmed by MMSE-KC score, based on age, years of schooling, and gender; and capable of taking part in intervention activity Exclusion criteria: none stated
Interventions	Experimental Group: a dance program consisting mainly of upper body exercises, with a 10-minute warm-up and warm-down Type of physical activity: strength, balance Frequency: 3 times a week, duration = 50 minutes Time period: 8 weeks Control Group: usual care
Outcomes	Cognitive outcome: Cognitive Memory Performance Measuring Tool in the Korean version (CERAD-K)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

Hwang 2010 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Randomization process not described. Emailed 13 March 2012, 10 April 2012 and 9 May 2012 to clarify randomization, no response received
Allocation concealment (selection bias)	Unclear risk	No description of methods used to conceal allocation
Blinding (performance bias and detection bias) All outcomes	High risk	Not possible to blind participants and the personnel to the intervention allocated
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding of outcome assessors not described
Incomplete outcome data (attrition bias) All outcomes	High risk	Attrition rate: study = 35.7%: Experimental Group = 28.6%; Control Group = 42.9% Reason for attrition: (quote) "10 subjects quit due to personal affairs and health issues, and the materials that were used for the final analysis were those of 18 subjects in total". Contacted by email for details 10 April 2012 and 9 May 2012, but no response received
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Attendance and adherence not stated. The Control Group activity was not described, and participants were recommended by head of facility

Kemoun 2010

Methods	19-week RCT
Participants	Country: France Centre: nursing home Diagnosis: mild to severe AD Participants: 38 at baseline, and 31 completed (23 women and 8 men) Experimental Group: n = 20, mean age (SD) = 82.0 years (5.8), mean MMSE (SD) = 12.6 (range = 7-20) Control Group: n = 18, mean age (SD) = 81.7 years (5.1), mean MMSE = 12.9 Information about education level of participants not provided Inclusion criteria: diagnosis of Alzheimer dementia using DSM-IV criteria, MMSE < 23, able to walk 10 m without technical assistance Exclusion criteria: none stated
Interventions	Experimental Group: the exercise program included three different sessions each week, i.e. 1) walking, 2) stamina exercise and 3) a combination of walking, stamina, and balance exercises. For the first 2 weeks of the program participants prepared for the routine program with specific muscles and joint exercises Type of physical exercise: aerobic, balance Frequency: 3 times a week, duration = 1 hour

Kemoun 2010 *(Continued)*

	Time period: 15 weeks Control Group: usual care
Outcomes	Cognition outcome: Rapid Evaluation of Cognitive Functions test (ERFC, French Version)
Notes	Adherence of participants in the intervention was 90%

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomization process not described. Email correspondence, Kemoun, 13 May 2012, description was as follows "The process of randomization was conducted by the randomization manager of the clinical investigation centre of the university hospital of Poitiers. Each randomization number was given for each patient after he had been included in the study by the principal investigator."
Allocation concealment (selection bias)	Unclear risk	Quote: "Subjects were randomized into two groups using a permutation table". Methods used to conceal allocation not described
Blinding (performance bias and detection bias) All outcomes	High risk	Not possible to blind participants and the personnel to the intervention allocated
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessor blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	Attrition rate was 18.4%: 4 participants lost from Experimental Group and 3 from Control Group. Reasons for attrition provided
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	None apparent

Rolland 2007

Methods	12-month RCT, 2-week enrolment, single-blinded
Participants	Country: France Multicentre: 5 nursing homes Diagnosis: mild to severe AD Participants: 134 at baseline, and 110 completed Baseline: 134 (101 women and 33 men), mean age (SD) = 83 years (7.4); mean ADL = 3.1 (1.3); mean MMSE (SD) = 8.8 (6.6) Experimental Group: n = 67; mean age (SD) = 82.8 years (7.8); mean ADL = 3.2 (1.3); mean MMSE (SD) = 9.7 (6.8)

Rolland 2007 *(Continued)*

	Control Group: n = 67; mean age (SD) = 83.1 years (7.0); mean ADL (SD) = 3.1 (1.3); mean MMSE (SD) = 7.9 (6.4) Inclusion criteria: diagnosis in chart of AD or MMSE < 25, diagnosis of AD confirmed by trained geriatrician, met criteria for Alzheimer Disease of National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association, had resided in nursing home for at least 2 months, could transfer from chair and walk 6 m without assistance from people Exclusion criteria: evidence of Parkinson's disease or vascular dementia, life expectancy < 6 months due to terminal illness, cardiac condition that could worsen with exercise, planned transfer from nursing home for surgery within the next year
Interventions	Experimental Group: aerobic (walking), strength (lower extremity), flexibility and balance training, gradually increased in intensity, (2-7 participants per group). Music with sessions Type of physical activity: aerobic, strength, balance Frequency: 2 times per week, duration = 1 hour Time period: 1 year Control Group: usual care
Outcomes	ADL outcome: Katz Index of ADLs Behaviour disturbance outcome: Neuropsychiatric Inventory Depression outcome: Montgomery-Asberg Depression Rating Scale
Notes	Adherence of participants was 33% (SD 25.5) of the 88 sessions offered, although 100% were included in the ITT analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Used lottery draw
Allocation concealment (selection bias)	Low risk	Published in Forbes 2007
Blinding (performance bias and detection bias) All outcomes	High risk	Not possible to blind participants and the personnel to the intervention allocated
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Geriatrician outcome assessor was blinded to group allocation, data analysts also blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Attrition rate of 18%, reasons for attrition provided. ITT analysis used
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	None apparent

Santana-Sosa 2008

Methods	12-week randomized, block-controlled design
Participants	Country: Spain Centre: nursing home Diagnosis: mild AD Participants: 16 at baseline (10 women and 6 men), all of whom completed Information about mean education level not provided Experimental Group: n = 8; mean age (SD) = 76 years (4); mean MMSE (SD) = 20.1 (2.3) Control Group: n = 8; mean age (SD) = 73 years (4); mean MMSE (SD) = 19.9 (1.7) Inclusion criteria: consent of closest relative and geriatrician; diagnosis of AD by geriatrician; MMSE between 18-23 in Spanish validated MMSE; resided in nursing home for at least 4 months Exclusion criteria: vision, muscle, cardio-respiratory, or neurological disorder (other than AD)
Interventions	Experimental Group: individualized exercise with walking, stretching, joint mobility, resistance and coordination exercises (with music) Type of physical activity: aerobic, strength Frequency: 3 times a week, duration = 75 minutes Time period: 12 weeks Control Group: usual care
Outcomes	ADL outcome: Katz ADL score, Barthel ADL index
Notes	Adherence of participants in the intervention was 98.9% for five subjects and 97% for three subjects.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomly assigned with a block design according to gender. Email correspondence 10 May 2012 with Alejandro Lucia: "Participants were randomly assigned to either the control or training group with a block on gender based on a randomization sequence."
Allocation concealment (selection bias)	Unclear risk	Methods used to conceal allocation not described
Blinding (performance bias and detection bias) All outcomes	High risk	Not possible to blind participants and the personnel to the intervention allocated
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome measure assessors blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	100% of participants completed the trial. Adherence to trained program averaged at 98.8%

Santana-Sosa 2008 *(Continued)*

Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	None apparent

Steinberg 2009

Methods	12-week randomly-assigned experimental trial
Participants	Country: USA Location: home Diagnosis: mild to moderate AD Participants: 27 at baseline (19 women and 8 men) all of whom completed; information about education level not provided Experimental Group: n = 14; mean age (SD) = 76.5 years (3.9); mean MMSE (SD) = 20.1 (5.1) Control Group: n = 13; mean age (SD) = 74.0 years (8.1); mean MMSE (SD) = 15.5 (5.4) Inclusion criteria: probable AlD using Alzheimer Disease of National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association criteria; MMSE ≥ 10; residing in community; stable health and medical history; caregiver that was spending a minimum of 10 hours per week with the person with AD Exclusion criteria: residing in assisted-living facility
Interventions	Experimental Group: exercise program consisting of aerobic, strength, balance, and flexibility training Type of physical activity: aerobic, strength, balance Frequency: daily, exercise duration not specified. Participants were given points for each activity performed. The weekly exercise goal was obtained when the participant collected 6 aerobic points, and 4 strength and balance points Time period: 12 weeks Control Group: social contact, e.g. received home safety assessment that included 2 home visits. In addition, participants recorded 3 activities they performed regularly at home
Outcomes	Cognition outcome: 1-h cognitive battery that included the Boston Naming Test, MMSE, and Hopkins Verbal Learning Test Depression outcomes 1. Neuropsychiatric Inventory: total score and depression subscore 2. Cornell Scale for Depression in Dementia Caregiver Burden outcome: Screen for Caregiver Burden
Notes	The necessary data were not reported on attrition, cognition, depression, or caregiver burden, and the authors did not provide them upon request. Adherence of participants was reflected by receipt of 59% of the diaries and 75% of the exercise group met their goals

Risk of bias

Bias	Authors' judgement	Support for judgement

Steinberg 2009 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Stratified randomization by age and gender. Emailed 13 March 2012, 10 April 2012, and 9 May 2012, to clarify randomization, but no answer received
Allocation concealment (selection bias)	Unclear risk	No description of methods used to conceal allocation
Blinding (performance bias and detection bias) All outcomes	High risk	Not possible to blind participants and the personnel to the intervention allocated
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "All tests were administered by the same rater, who was masked as to treatment assignment"
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Attrition not reported. Requested attrition data 13 March 2012, 10 April 2012, 9 May 2012, and 3 July 2012, but data not provided. Performed ITT analyses using linear random effects models
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	None apparent

Stevens 2006

Methods	12 week, pre- and post-test RCT
Participants	Country: Australia Multicentre: 6 aged-care facilities, nursing homes Diagnosis: mild to moderate dementia (type of dementia not specified) Participants: 120 at baseline, and 75 completed Completed: 75 (56 women and 19 men), mean age = 80.5 years; mean MMSE not provided 3 groups: Group 1 received no intervention, Group 2 received a social visit, and Group 3 was the exercise program. Of the 2 control groups, only Group 1 was included in this review Experimental Group: n = 24, mean age = 79 years Control Group: n = 30, mean age = 81 years Inclusion criteria: mild to moderate dementia as assessed by local Aged Care Assessment Team; those with confirmed diagnosis of dementia, or MMSE < 23 were considered to have dementia; lived in aged-care facility; capable of providing informed consent legally and competently, or consent obtained from legal guardian; able to respond verbally and appropriately to majority of questions; assessed by Age Care Facility as being physically able to complete exercise Exclusion criteria: severe dementia with MMSE of 0-9
Interventions	Experimental Group: activity was based on joint and large muscle group movement with the intention of creating gentle aerobic exertion Type of physical activity: aerobic Frequency: 3 times per week, duration = 30 minutes

Stevens 2006 *(Continued)*

	Time period: 3 months Control Group: usual care
Outcomes	Behaviour outcome: Revised Elderly Persons Disability Scale Cognitive Symptoms outcome: Clock Drawing test
Notes	The necessary data were not reported on cognition and the authors did not provide them upon request Data analysed from residents with 75% or more attendance. Frequency of attendance varied due to ill health, other obligations, disinterest and death

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Lottery method
Allocation concealment (selection bias)	Unclear risk	Simply stated that subjects were randomly allocated by a lottery method
Blinding (performance bias and detection bias) All outcomes	High risk	Not possible to blind participants and the personnel to the intervention allocated
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear whether outcome assessors blinded to group allocation
Incomplete outcome data (attrition bias) All outcomes	High risk	Attrition rate was 37.5%; reason(s) for attrition not provided
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	None apparent

Van de Winckel 2004

Methods	3-month RCT
Participants	Country: Belgium Centre: public psychiatric hospital Diagnosis: moderate to severe multiple infarct dementia (3 participants) and Alzheimer's disease (22 participants) Participants: 25 at baseline, and 24 completed Baseline: 25 (all women) Experimental Group: n = 15; mean age (SD) = 81.33 years (4.24); mean MMSE (SD) = 12.87 (5.01) Control Group: n = 10 mean age (SD) = 81.90 years (4.18); mean MMSE (SD) = 10.8 (5.01)

Van de Winckel 2004 *(Continued)*

	Inclusion criteria: diagnosed with probable AD using NINCDS-ARDRA criteria or multiple infarct dementia; MMSE < 24; able to follow verbal and visual commands; mimic movements; and hear music. Medically cleared by physician; consent signed by family Exclusion criteria: unable to sit in chair for 30 minutes; apathetic; would require change in medication during intervention
Interventions	Experimental Group: intervention focused on strength training, balance, trunk movements and flexibility. Exercise routine supported with music Type of physical activity: strength, balance Frequency: daily, duration = 30 minutes Time period: 3 months Control Group: social contact 1-on-1 conversation with therapist Frequency: daily, activity duration = 30 minutes Time period: 3 months
Outcomes	Behaviour outcome: Beoordelingsschaal voor Oudere Patienten/Evaluation Scale for Elderly Patients Cognitive Function outcomes: 1. MMSE 2. Amsterdam Dementia Screening Test 6
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Coin flipping
Allocation concealment (selection bias)	Unclear risk	No description of methods used to conceal allocation
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not possible to blind participants and the personnel to the intervention allocated
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "The physiotherapist who was conducting both treatments evaluated the patients on cognition. However, the nurses who scored the patients on behaviour were all blind to the group assignment"
Incomplete outcome data (attrition bias) All outcomes	Low risk	1 participant in control group unable to complete 3-month MMSE and ADS 6 due to hip fracture
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Attendance and adherence not stated

Venturelli 2011

Methods	6-month, randomly assigned experimental trial
Participants	Country: Italy Centre: nursing home, specifically Alzheimer care unit Diagnosis: moderate to severe AD Participants: 24 at baseline, 21 completed Baseline: 24 (all women) Experimental Group: n = 12; mean age (SD) = 83 years (6) Control Group: n = 12; mean age (SD) = 85 years (5) Inclusion criteria: 65 years or older; dependent on assistance in 2 or more personal ADLs according to the Barthel index; MMSE maximum score of 15 and minimum of 5; absence of mobility limitations, minimum score of 23, according to the Performance Oriented Mobility Assessment (POMA) index; and constant oxygen saturation during walking (SpO_2 > 85%). According to the clinical dementia rating scale, all nursing home residents had to be in the later stages (CDR3-CDR4) of AD Exclusion criteria: none stated
Interventions	Experimental Group: a minimum of 30 minutes of moderate walking 4 times a week for 6 months Type of physical activity: aerobic Control group: usual care at the home, which consisted of bingo, sewing, music therapy
Outcomes	Cognitive function outcomes: MMSE Activities of daily living outcome: Barthel Index for ADLs
Notes	Adherence of participants in the intervention was 93%

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of random selection not described
Allocation concealment (selection bias)	Low risk	Quote:"The head nurse of the ACU (not involved in the residents assessments) did the participants' randomization using StatsPlus for Macintosh"
Blinding (performance bias and detection bias) All outcomes	Low risk	Quote: " . . . members of the research team did not know to which group each participant had been assigned . . . No one on the research team was present during the walking exercise"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "Evaluation was done before and after the experiment period in a blind way" - not described well
Incomplete outcome data (attrition bias) All outcomes	Low risk	Attrition: Experimental Group = 1 (8.4%); Control Group = 2 (16.7%) Reasons for attrition stated for each group
Selective reporting (reporting bias)	Low risk	All outcomes reported

Venturelli 2011 *(Continued)*

Other bias	Low risk	None apparent

Volkers 2012

Methods	18-month RCT
Participants	Country: Netherlands Location: 17 institutions (n = 4 day care centres; n = 6 homes for the elderly, n = 7 nursing homes) Diagnosis: mild cognitive impairment, and mild to severe dementia. A small percentage, 1.4% (mean; 5.6 SDs), had mild cognitive impairment Participants: 148 at baseline, 18 excluded after randomization due to attrition at baseline observation as “they did not complete the minimal EF or memory tests once” Baseline: 130 (94 women and 36 male) Experimental Group: randomized n = 85, included n = 75, mean age (SD) = 82.0 (7.2), mean MMSE (SD) = 15.3 (5.0) Control Group: randomized n = 63, included n = 55, mean age (SD) = 82.3 (7.8) mean MMSE (SD) = 17.1 (6.1) Inclusion criteria: a report of a diagnosis of dementia or presence of cognitive impairment required in the participants' medical status record, able to walk with or without a walking aid Exclusions criteria: diagnosis of personality disorder, cerebral trauma, hydrocephalus, neoplasm, focal brain disorder, and disturbances of consciousness
Interventions	Experimental Group: supervised walks Type of physical activity: aerobic Frequency: 5 times a week, exercise duration = 30 minutes Time period: 18 months Control Group: received usual care Time period: 18 months
Outcomes	Memory: Eight Words Test, Face Recognition, and Picture Recognition
Notes	In 21% of the sessions a mean of at least 30 minutes per walk was obtained and 1.34 ± 1.45 walking sessions were completed per week

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: “This study was a randomized controlled single-blind study” Coin tossing was used for random allocation
Allocation concealment (selection bias)	Unclear risk	Not reported

Volkers 2012 *(Continued)*

Blinding (performance bias and detection bias) All outcomes	High risk	Not possible to blind participants and the personnel to the intervention allocated
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Trained experimenters, blinded to the intervention assignment, administered the neuropsychological tests"
Incomplete outcome data (attrition bias) All outcomes	High risk	The attrition rate and reasons for attrition were unclear Quote: "Selective loss to follow-up measurements of the most impaired participants over time, risks underestimation of the true rates of decline and effect of the intervention" For each neuropsychological test a total of 1036 observations were to be completed, in 148 subjects. However, the "final data set consisted of . . . 573 observations for memory" Percentage of outcome measures completed for each group reported
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	High risk	Compliance to intervention very low Quote: "Overall, participants of the walking group walked 1.34 ± 1.45 times per week with a mean of 36 ± 42 minutes per week per period, varying from 0 to 195 minutes per week. Only 21% of the periods, a mean of at least 30 minutes per walk was obtained"

Vreugdenhil 2012

Methods	4-month RCT
Participants	Country: Australia Location: home Diagnosis: mild to moderate AD Participants: 40 at baseline (24 women and 16 men), all of whom completed; mean age = 74.1 years Experimental Group: n = 20; mean age 73.5 years; mean education = 10.1 years; mean MMSE (SD) = 22.9 (5.0) Control Group: n = 20; mean age 74.7 years; mean education = 10.3 years; mean MMSE (SD) = 21.0 (6.3) Inclusion criteria: diagnosed with dementia using DSM-IV criteria; diagnosed with AD with NINCDS-ARDRA criteria; from outpatient memory disorder clinic; community dwelling with live-in care provider or caregiver that could visit daily Exclusion criteria: physical condition that could prevent participation; evidence of neurodegenerative disorder (other than AD); already in exercise program more than once a week (resistance or aerobic training); started dementia medications in last 3 months
Interventions	Experimental Group: exercises progressively became more challenging, and targeted strength and balance. Also included brisk walking Type of physical activity: aerobic, strength, balance

Vreugdenhil 2012 *(Continued)*

	Frequency: daily, with 10 simple exercises and 30 minutes of brisk walking Time period: 4 months Control Group: usual care
Outcomes	Cognition outcomes 1. Alzheimer's Disease Assessment Scale 2. MMSE ADL outcome: Barthel Index of ADLs Depression outcome: Geriatric Depression Scale Caregiver burden outcome: Zarit Burden Interview
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Used computer-generated random allocation sequence
Allocation concealment (selection bias)	Low risk	Sequentially-numbered, sealed opaque envelopes
Blinding (performance bias and detection bias) All outcomes	High risk	Not possible to blind participants and the personnel to the intervention allocated
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcomes assessors blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	100% of participants completed the trial
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	None apparent

Williams 2008

Methods	16-week, quasi-experimental design, randomly assigned trial
Participants	Country: USA Multicentre: 8 long-term care facilities Diagnosis: moderate to severe AD Participants: 45 at baseline, all of whom completed (89% female); mean age = 87.9 years (5.95); mean MMSE (SD) = 7.3 (6.19)

Williams 2008 *(Continued)*

	Experimental Group 1: n = 16 Experimental Group 2: n = 17 Control Group 3: n = 12 Inclusion criteria: living in long-term care facility; evidence of AD as per NINCDS-ARDRA criteria; able to walk with assistance; CSDD score ≥ 7; dependent in at least 1 of the following: transfers, balance or gait, bed mobility Exclusion criteria: ability to walk unaided for 30 minutes or more
Interventions	Experimental Group 1: exercise focusing on strength, flexibility, and balance. In addition participants walked each session. Type of physical activity: aerobic, strength, balance Frequency: 5 days per week, exercise duration gradually increased to 30 minutes (20 minutes of exercise session was spent walking) Time period: 16 weeks Experimental Group 2: supervised walking Frequency: 5 days per week, exercise duration gradually increased to 30 minutes Time period: 16 weeks Control Group 3: social contact-conversation Frequency: 5 days per week, activity duration equivalent to experimental groups Time period: 16 weeks
Outcomes	Depression outcome: Cornell Scale for Depression in Dementia
Notes	Those who could walk 30 minutes or more without assistance were excluded from the trial

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Participants were assigned a code number, which was drawn by a research assistant who had no access to pre-test results"
Allocation concealment (selection bias)	Unclear risk	Methods used to conceal allocation not described
Blinding (performance bias and detection bias) All outcomes	High risk	Not possible to blind participants and the personnel to the intervention allocated
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Raters were blinded to treatment group allocation"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Attrition rate 20%, details provided, differences in drop-outs between groups were not significant. ITT analysis used

Williams 2008 *(Continued)*

Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	None apparent

Abbreviations
> = greater/more than
< = less than
≥ = greater than or equal to
ACU = acute care unit
AD = Alzheimer's disease
ADL = activities of daily living
CDR3-CDR4 = Clinical Dementia Rating scale version 3 - Clinical Demenita Rating scale version 4
CSDD = Cornell Scale for Depression in Dementia
CVA = cerebrovascular accident
DSM-IV = Diagnostic and Statistical Manual of Mental Disorders classification system
ICD-10 = International Statistical Classification of Diseases, 10th revision
ITT = intention-to-treat (analysis)
m = metres
MMSE = Mini Mental Status Examination
MMSE-KC = Mini-Mental Status Examination in Korean version
NINCDS-ARDRA = National Institute of Neurological and Communicative Diseases and Stroke-Alzheimer Disease and Related Disorders Association
RCT = randomized controlled trial

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Abreu 2013	Outcomes related to risk of falling, which is not an outcome of interest
Aman 2009	No randomization
Anon 1986	Participants not diagnosed with dementia (residents of senior citizens' housing)
Arcoverde 2008	No randomization
Batman 1999	Unknown study design (may not be a RCT), unknown age of participants, not able to contact author
Burgener 2008	Treatment included more than exercise (i.e. cognitive behavioural therapy and support group)
Christofoletti 2011	Not a true randomization
Day 2012	Participants did not have dementia, comparison group was not usual care (included flexibility and stretching program)
de Melo Coelho 2013	Not a RCT, only a controlled trial. The methods section states “the procedure was not random” when referring to group allocation
Garuffi 2013	Not a RCT, (quote) "The sample was divided for convenience"
Hariprasad 2013	Participants did not have dementia
Hauer 2012	Outcomes not of interest as related to function and not specifically to ADLs
Heyn 2008	Compared cognitively-impaired with normal older adults

Study	Reason for exclusion
Kerse 2008	Participants were not diagnosed with dementia
Kwak 2008	Participants do not appear to have been randomly assigned to groups
Litchke 2012	Not a RCT
Littbrand 2006	Participants not diagnosed with dementia (older, dependent people)
Littbrand 2011	Did not assess any of the primary or secondary outcomes of this review
Logsdon 2012b	Interventions not solely exercise-based
McCurry 2011	Outcomes not of interest (sleep)
Netz 1994	Participants not diagnosed with dementia (cognitive deterioration or depression, or both)
Netz 2007	Did not assess any of the primary or secondary outcomes of this review
Obisesan 2011	Control group received stretch exercise
Onor 2007	Treatment was not physical activity
Oswald 2007	Treatment was combined cognitive and physical activity
Padala 2012	Outcomes not of interest
Pitkala 2013	The intervention was complex and included 'brain training' tasks as well as physical exercise. Hence groups did not differ in exercise alone
Powell 1974	Participants not diagnosed with dementia (geriatric mental patients)
Roach 2011	Outcomes not of interest. Outcome measures were not ADLs
Rodgers 2002	Participants not diagnosed with dementia (elderly veterans)
Rodriguez-Ruiz 2013	Outcomes not of interest
Scherder 2005	Participants not diagnosed with dementia (mild cognitive impairment)
Schwenk 2010	Dual task training is not one of the types of exercise defined in our inclusion criteria
Suttanon 2013	Outcomes not of interest
Suzuki 2012	Participants had a mild cognitive impairment, not dementia
Tappen 2000	Outcome measured was mobility and not ADLs
Thurm 2011	Not a RCT, (quote) "A controlled study was conducted in two nursing home residences"
van Uffelen 2005	Participants not diagnosed with dementia (mild cognitive impairment)
Viscogliosi 2000	Participants not diagnosed with dementia (mild cognitive impairment)
Williams 2007	This article examined mood and effect and not depression

Study	Reason for exclusion
Yagüez 2011	Intervention was non-aerobic 'Brain Gym'. Outcome measures were sustained attention, visual memory, and working memory

Abbreviations
ADLs: activities of daily living
RCT: randomized controlled trial

Characteristics of ongoing studies *[ordered by study ID]*

Cerga-Pashoja 2010

Trial name or title	Evaluation of exercise on individuals with dementia and their carers: a randomized controlled trial
Methods	Randomized, single-blind controlled trial
Participants	Aiming to recruit 146 people with dementia and their carers
Interventions	Participants will be randomized into 2 groups: 1 trained in a structured, tailored walking program, while the other continues with usual treatment
Outcomes	Not known
Starting date	Not known
Contact information	acerga-pashoja@nhs.net CNWL NHS Foundation Trust Stephenson House 75 Hampstead Road London England NW1 2PL Tel: 020 3214 5886
Notes	Currently at recruitment stage

Cyarto 2010

Trial name or title	The Fitness for the Ageing Brain Study II (FABS II): protocol for a randomized controlled clinical trial evaluating the effect of physical activity on cognitive function in patients with Alzheimer's disease
Methods	Participants will be randomly allocated to 2 treatment groups: usual care group or 24-week home-based program
Participants	The study will recruit 230 community-dwelling participants diagnosed with Alzheimer's disease
Interventions	A 24-week home-based program consisting of 150 minutes per week of tailored moderate physical activity
Outcomes	Not known
Starting date	Not known

Cyarto 2010 *(Continued)*

Contact information	e.cyarto@nari.unimelb.edu.au
Notes	Currently at recruitment stage

Gennep van 2011

Trial name or title	Effects of a program combining walking and cognitive training on memory and behaviour of older persons with dementia www.trailregister.nl/admin/rctview.asp?TC=3121
Methods	Multicentre, randomized, controlled single-blind study
Participants	Target number of participants is 164
Interventions	Participants will be randomized to 1 of 4 interventions 1. Combined intervention: walking and cognitive training (face-name learning) 2. Cognitive training (face-name learning) 3. Walking 4. Social visits
Outcomes	Not known
Starting date	Not known
Contact information	Gennep van, Martin, Netherlands
Notes	Currently enrolling participants, expect to complete in 2014

Hasselbalch 2012

Trial name or title	A multicentre randomized clinical trial of physical exercise in Alzheimer's disease (AD): rationale and design of the ADEX study clinicaltrials.gov/ct2/show/NCT01681602?term=NCT01681602&rank=1
Methods	A multicentre, single-blind, randomized clinical trial
Participants	Estimated enrolment is 192 home-dwelling patients aged 50-90 years with mild to moderate AD
Interventions	The participants will be randomly allocated into 2 groups: An intervention group attending 16 weeks of continuously supervised moderate aerobic exercise 1 hour three times a week and a control group receiving usual care
Outcomes	Not known
Starting date	January 2012
Contact information	kristine.hoffmann@rh.regionh.dk
Notes	

Laks 2012

Trial name or title	Physical exercise as an additional treatment for Alzheimer disease http://clinicaltrials.gov/ct2/show/NCT01515982 Date accessed 6 November 2013
Methods	Randomized controlled trial, double-blinded, with 16-week follow-up
Participants	Estimated enrolment is 60 elderly people with Alzheimer disease
Interventions	Participants will be randomly assigned to an exercise group (on a treadmill) and a control group
Outcomes	Not known
Starting date	Not known
Contact information	jlaks@centroin.com.br Federal University of Rio de Janeiro
Notes	Trial ongoing until December 2013

Lamb 2011

Trial name or title	Physical activity programs for community dwelling people with mild to moderate dementia (DAPA – Dementia And Physical Activity): a multi-centre, randomized controlled trial www.controlled-trials.com/ISRCTN32612072/
Methods	Participants will be randomly allocated to 2 treatment groups: usual care group, or 4-month exercise program with follow-up at 6 and 12 months
Participants	Participants must meet the following criteria 1. Have probable dementia of mild to moderate severity 2. Be able to participate in a structured exercise program: a. able to walk 10 feet without human assistance b. have no serious unstable illness (e.g. unstable angina) c. live in the community, either alone or with a relative, friend or carer, or in sheltered accommodation
Interventions	The trial has 2 groups: 1 group (half the participants) will continue with their current treatment, while the other group (half the participants) will take part in the DAPA exercise program as well as their current treatment. The exercise intervention will be delivered in a group format, with up to 14 participants in each group. The program will be provided in 2, 1-hour sessions per week for 4 months, supplemented with between-session at-home exercises of at least 1 hour per week
Outcomes	Not known
Starting date	November 2011
Contact information	S.Lamb@warwick.ac.uk Warwick Clinical Trials Unit at the University of Warwick
Notes	Trial ongoing until May 2016

Logsdon 2012a

Trial name or title	Two interventions for early stage dementia: a comparative efficacy trial clinicaltrials.gov/ct2/show/NCT01550718 Date accessed 6 November 2013
Methods	Randomized, single blind
Participants	Estimated enrolment is 240
Interventions	3 groups: 2 intervention groups (physical activity, and social activity), and 1 usual care control group
Outcomes	Not known
Starting date	Not known
Contact information	logsdon@u.washington.edu University of Washington
Notes	Trial ongoing until December 2013

Potemkowski 2011

Trial name or title	Influence of physical activity on cognitive dysfunction in patients with mild and moderate Alzheimer dementia Neurodegenerative Diseases
Methods	Not known
Participants	240 participants recruited
Interventions	4 groups: study group with mild dementia, study group with moderate dementia, control group with mild dementia, control group with moderate dementia
Outcomes	Not known
Starting date	Not known
Contact information	andrzej.potemkowski@wp.pl
Notes	Study ongoing

Rosendahl 2012

Trial name or title	A high-intensity functional exercise program for older people with dementia and living in residential care facilities (The Umeå Dementia and Exercise Study) ISRCTN: http://isrctn.org/ISRCTN31767087 Date accessed 6 November 2013
Methods	Cluster-randomized controlled trial
Participants	Older people with dementia living in residential care facilities; target number of participants = 183

Rosendahl 2012 *(Continued)*

Interventions	2 groups: exercise, and control (activities while sitting)
Outcomes	Not known
Starting date	Not known
Contact information	erik.rosendahl@physiother.umu.se
Notes	Still collecting data

Tartaglia 2013

Trial name or title	Benefits of Exercise in Alzheimer's Disease clinicaltrials.gov/ct2/show/NCT01935024
Methods	Randomized controlled trial
Participants	Estimated enrolment: 60
Interventions	2 groups: Group 1 (n = 30) out-patient exercise program, Group 2 (n = 30) continue with regular activities over a 6-month period
Outcomes	Unknown
Starting date	August 2013
Contact information	carmela.tartaglia@uhn.ca
Notes	

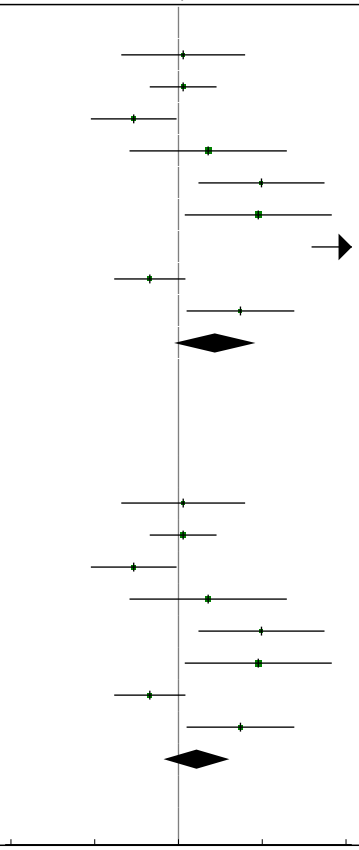
DATA AND ANALYSES

Comparison 1. Exercise vs usual care: cognition

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Cognition	9		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 Cognition: all trials	9	409	Std. Mean Difference (IV, Random, 95% CI)	0.43 [-0.05, 0.92]
1.2 Cognition: excluded moderate-severe dementia	8	388	Std. Mean Difference (IV, Random, 95% CI)	0.21 [-0.18, 0.61]

Analysis 1.1. Comparison 1 Exercise vs usual care: cognition, Outcome 1 Cognition.

Study or subgroup	Exercise N	Exercise Mean(SD)	Usual care N	Usual care Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
1.1.1 Cognition: all trials							
Christofoletti 2008	12	14.9 (2.2)	17	14.8 (1.3)		11.03%	0.06[-0.68,0.8]
Eggermont 2009a	51	0.2 (0.8)	46	0.2 (0.6)		13.47%	0.06[-0.34,0.45]
Eggermont 2009b	30	0.1 (0.4)	31	0.5 (1)		12.73%	-0.53[-1.05,-0.02]
Hwang 2010	10	28.9 (11.9)	8	24 (14.7)		9.54%	0.35[-0.58,1.29]
Kemoun 2010	16	30.4 (7.7)	15	22.2 (8.4)		10.93%	0.99[0.24,1.74]
Van de Winckel 2004	15	15.3 (4.4)	9	11 (4.3)		9.99%	0.95[0.08,1.83]
Venturelli 2011	11	12 (2)	10	6 (2)		7.24%	2.88[1.59,4.17]
Volkers 2012	50	0.1 (0.5)	38	0.4 (0.9)		13.31%	-0.34[-0.77,0.08]
Vreugdenhil 2012	20	23.9 (5)	20	19 (7.7)		11.76%	0.74[0.1,1.38]
Subtotal ***	**215**		**194**			**100%**	**0.43[-0.05,0.92]**
Heterogeneity: Tau^2=0.42; Chi^2=40.9, df=8(P<0.0001); I^2=80.44%							
Test for overall effect: Z=1.75(P=0.08)							
1.1.2 Cognition: excluded moderate-severe dementia							
Christofoletti 2008	12	14.9 (2.2)	17	14.8 (1.3)		11.38%	0.06[-0.68,0.8]
Eggermont 2009a	51	0.2 (0.8)	46	0.2 (0.6)		15.93%	0.06[-0.34,0.45]
Eggermont 2009b	30	0.1 (0.4)	31	0.5 (1)		14.4%	-0.53[-1.05,-0.02]
Hwang 2010	10	28.9 (11.9)	8	24 (14.7)		9.12%	0.35[-0.58,1.29]
Kemoun 2010	16	30.4 (7.7)	15	22.2 (8.4)		11.21%	0.99[0.24,1.74]
Van de Winckel 2004	15	15.3 (4.4)	9	11 (4.3)		9.77%	0.95[0.08,1.83]
Volkers 2012	50	0.1 (0.5)	38	0.4 (0.9)		15.58%	-0.34[-0.77,0.08]
Vreugdenhil 2012	20	23.9 (5)	20	19 (7.7)		12.61%	0.74[0.1,1.38]
Subtotal ***	**204**		**184**			**100%**	**0.21[-0.18,0.61]**
Heterogeneity: Tau^2=0.21; Chi^2=23.15, df=7(P=0); I^2=69.77%							
Test for overall effect: Z=1.07(P=0.28)							

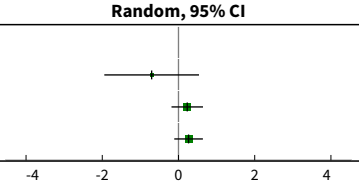


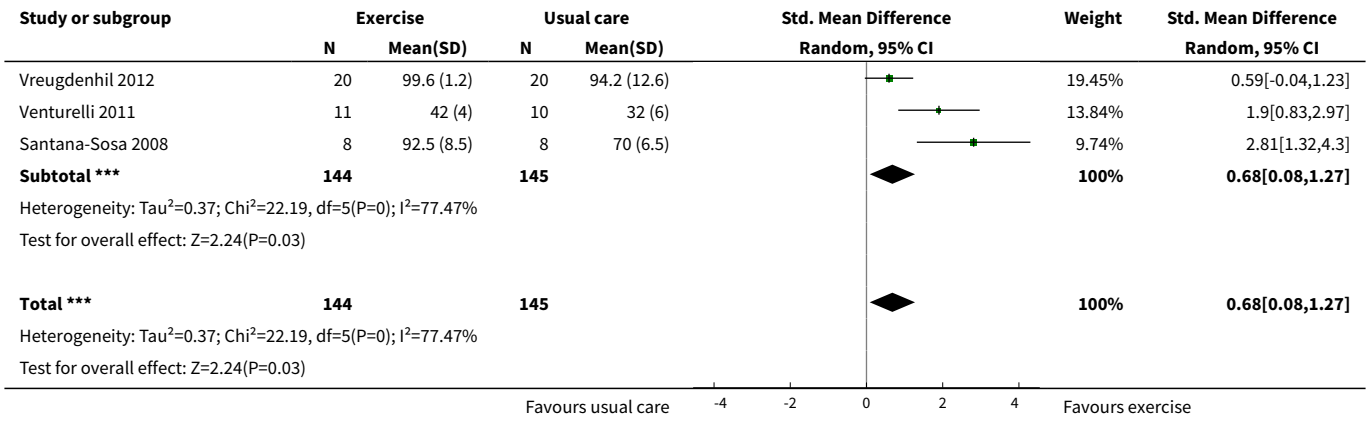
Comparison 2. Exercise vs usual care: Activities of Daily Living (ADL)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Comparison of ADL	6	289	Std. Mean Difference (IV, Random, 95% CI)	0.68 [0.08, 1.27]
1.1 ADL: all trials	6	289	Std. Mean Difference (IV, Random, 95% CI)	0.68 [0.08, 1.27]

Analysis 2.1. Comparison 2 Exercise vs usual care: Activities of Daily Living (ADL), Outcome 1 Comparison of ADL.

Study or subgroup	Exercise N	Exercise Mean(SD)	Usual care N	Usual care Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
2.1.1 ADL: all trials							
Francese 1997	6	24.7 (2.7)	5	26.6 (2.3)		11.96%	-0.7[-1.95,0.54]
Conradsson 2010	43	-1 (2.7)	48	-1.7 (3.2)		22.29%	0.23[-0.18,0.64]
Rolland 2007	56	2.6 (1.5)	54	2.2 (1.5)		22.72%	0.26[-0.11,0.64]

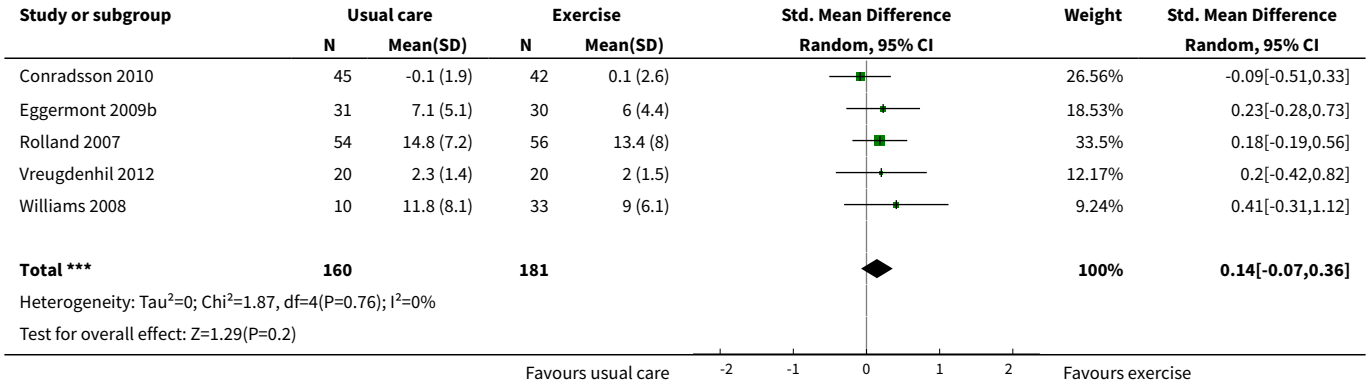




Comparison 3. Exercise vs usual care: depression

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Depression	5	341	Std. Mean Difference (IV, Random, 95% CI)	0.14 [-0.07, 0.36]

Analysis 3.1. Comparison 3 Exercise vs usual care: depression, Outcome 1 Depression.



APPENDICES

Appendix 1. Top-up update searches: August 2012 and October 2013

Source	Search strategy - date limits are for the August 2012 search (appropriate limits were applied to the October 2013 search)	Hits retrieved

(Continued)

1. ALOIS (www.medicine.ox.ac.uk/alois)	"physical activity" OR exercise OR cycling OR swim* OR gym* OR walk* OR danc* OR yoga OR "tai chi" (all dates)	August 2012: 225 October 2013: 8
2. MEDLINE In-process and other non-indexed citations and MEDLINE 1950-present (Ovid SP)	1. exp Dementia/ 2. Delirium/ 3. Wernicke Encephalopathy/ 4. Delirium, Dementia, Amnestic, Cognitive Disorders/ 5. dement*.mp. 6. alzheimer*.mp. 7. (lewy* adj2 bod*).mp. 8. deliri*.mp. 9. (chronic adj2 cerebrovascular).mp. 10. ("organic brain disease" or "organic brain syndrome").mp. 11. ("normal pressure hydrocephalus" and "shunt*").mp. 12. "benign senescent forgetfulness".mp. 13. (cerebr* adj2 deteriorat*).mp. 14. (cerebral* adj2 insufficient*).mp. 15. (pick* adj2 disease).mp. 16. (creutzfeldt or jcd or cjd).mp. 17. huntington*.mp. 18. binswanger*.mp. 19. korsako*.mp. 20. or/1-19 21. exercis*.ti,ab. 22. physical activit*.ti,ab. 23. cycling.ti,ab. 24. swim*.ti,ab. 25. gym*.ti,ab. 26. (walk* or treadmill).ti,ab. 27. danc*.ti,ab. 28. yoga*.ti,ab. 29. "tai chi".ti,ab. 30. exp Exercise/ or Exercise Therapy/ 31. or/21-30	August 2012: 97 October 2013: 93

(Continued)

	32. 20 and 31 33. randomized controlled trial.pt. 34. controlled clinical trial.pt. 35. randomi?ed.ab. 36. placebo.ab. 37. randomly.ab. 38. trial.ab. 39. groups.ab. 40. or/33-39 41. (animals not (humans and animals)).sh. 42. 40 not 41 43. 32 and 42 44. (2011* or 2012*).ed. 45. 43 and 44	
3. EMBASE 1980-2012 August 10 (Ovid SP)	1. exp dementia/ 2. Lewy body/ 3. delirium/ 4. Wernicke encephalopathy/ 5. cognitive defect/ 6. dement*.mp. 7. alzheimer*.mp. 8. (lewy* adj2 bod*).mp. 9. deliri*.mp. 10. (chronic adj2 cerebrovascular).mp. 11. ("organic brain disease" or "organic brain syndrome").mp. 12. "supranuclear palsy".mp. 13. ("normal pressure hydrocephalus" and "shunt*").mp. 14. "benign senescent forgetfulness".mp. 15. (cerebr* adj2 deteriorat*).mp. 16. (cerebral* adj2 insufficient*).mp. 17. (pick* adj2 disease).mp. 18. (creutzfeldt or jcd or cjd).mp. 19. huntington*.mp.	August 2012: 307 October 2013: 519

(Continued)

20. binswanger*.mp.

21. korsako*.mp.

22. CADASIL.mp.

23. or/1-22

24. exercis*.ti,ab.

25. physical activit*.ti,ab.

26. cycling.ti,ab.

27. swim*.ti,ab.

28. gym*.ti,ab.

29. (walk* or treadmill).ti,ab.

30. danc*.ti,ab.

31. yoga*.ti,ab.

32. "tai chi".ti,ab.

33. exercise/ or stretching exercise/ or anaerobic exercise/ or exercise intensity/ or aerobic exercise/ or treadmill exercise/ or aquatic exercise/

34. or/24-33

35. 23 and 34

36. randomized controlled trial/

37. controlled clinical trial/

38. randomi?ed.ab.

39. placebo.ab.

40. randomly.ab.

41. trial.ab.

42. groups.ab.

43. ("double-blind*" or "single-blind*").ti,ab.

44. or/36-43

45. 35 and 44

46. (2011* or 2012*).em.

47. 45 and 46

4. PsycINFO 1806-August week 1 2012 (Ovid SP)	1. exp Dementia/ 2. exp Delirium/ 3. exp Huntingtons Disease/ 4. exp Kluver Bucy Syndrome/	August 2012: 97 October 2013: 118

(Continued)

5. exp Wernickes Syndrome/

6. exp Cognitive Impairment/

7. dement*.mp.

8. alzheimer*.mp.

9. (lewy* adj2 bod*).mp.

10. deliri*.mp.

11. (chronic adj2 cerebrovascular).mp.

12. ("organic brain disease" or "organic brain syndrome").mp.

13. "supranuclear palsy".mp.

14. ("normal pressure hydrocephalus" and "shunt*").mp.

15. "benign senescent forgetfulness".mp.

16. (cerebr* adj2 deteriorat*).mp.

17. (cerebral* adj2 insufficient*).mp.

18. (pick* adj2 disease).mp.

19. (creutzfeldt or jcd or cjd).mp.

20. huntington*.mp.

21. binswanger*.mp.

22. korsako*.mp.

23. ("parkinson* disease dementia" or PDD or "parkinson* dementia").mp.

24. or/1-23

25. exercis*.ti,ab.

26. physical activit*.ti,ab.

27. cycling.ti,ab.

28. swim*.ti,ab.

29. gym*.ti,ab.

30. (walk* or treadmill).ti,ab.

31. danc*.ti,ab.

32. yoga*.ti,ab.

33. "tai chi".ti,ab.

34. exp Exercise/ or exp Aerobic Exercise/

35. or/25-34

36. 24 and 35

37. random*.ti,ab.

38. exp Clinical Trials/

(Continued)

	39. RCT.ti,ab.	
	40. CCT.ti,ab.	
	41. (placebo or "control group").ab.	
	42. trial.ti,ab.	
	43. groups.ab.	
	44. "double-blind*".ti,ab.	
	45. "single-blind*".ti,ab.	
	46. or/37-45	
	47. 36 and 46	
	48. (2011* or 2012*).up.	
	49. 47 and 48	
5. CINAHL (EBSCOhost)	S1 (MH "Dementia+")	August 2012: 101
	S2 (MH "Delirium") or (MH "Delirium, Dementia, Amnestic, Cognitive Disorders")	October 2013: 107
	S3 (MH "Wernicke's Encephalopathy")	
	S4 TX dement*	
	S5 TX alzheimer*	
	S6 TX lewy* N2 bod*	
	S7 TX deliri*	
	S8 TX chronic N2 cerebrovascular	
	S9 TX "organic brain disease" or "organic brain syndrome"	
	S10 TX "normal pressure hydrocephalus" and "shunt*"	
	S11 TX "benign senescent forgetfulness"	
	S12 TX cerebr* N2 deteriorat*	
	S13 TX cerebral* N2 insufficient*	
	S14 TX pick* N2 disease	
	S15 TX creutzfeldt or jcd or cjd	
	S16 TX huntington*	
	S17 TX binswanger*	
	S18 TX korsako*	
	S19 S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17 or S18	
	S20 TX exercis*	
	S21 TX "physical activit*"	

(Continued)

	S22 TX cycling
	S23 TX swim*
	S24 TX gym*
	S25 TX walk* OR treadmill
	S26 TX danc*
	S27 TX yoga*
	S28 TX "tai chi"
	S29 (MH "Exercise+")
	S30 S20 or S21 or S22 or S23 or S24 or S25 or S26 or S27 or S28 or S29
	S31 S19 and S30
	S32 (MH "Clinical Trials")
	S33 TX trial
	S34 TX RCT OR CCT
	S35 TX placebo*
	S36 TX "double-blind*" OR "single-blind*"
	S37 TX groups OR "control group"
	S38 S32 or S33 or S34 or S35 or S36 or S37
	S39 S31 and S38
	S40 EM 2011
	S41 EM 2012
	S42 S40 OR S41
	S43 S42 AND S39

6. ISI Web of Knowledge (includes: Web of Science (1945-present); BIOSIS Previews (1926-present); MEDLINE (1950-present); Journal Citation Reports)	Topic=(Dement* OR Alzheimer* OR "Lewy body" OR arteriosclerosis OR "Huntington* disease" OR "Kluver Bucy" OR "Pick disease" OR "Wernicke encephalopathy" OR "Korsakoff psychosis") AND Topic=(exercis* OR walk* OR swim* OR "physical activit*" OR aerobic* OR danc* OR "tai chi" OR yoga*) AND Topic=(randomly OR placebo OR groups OR trial OR RCT OR randomized OR randomised) AND Year Published=(2011-2012) Timespan=All Years. Search language=English Lemmatization=On	August 2012: 389 October 2013: 404
7. LILACS (BIREME)	dementia OR alzheimer$ OR demenc$ OR AD OR demência [Words] and exercício OR exercis$ OR walk$ OR swim$ OR aerobic$ [Words] and randomly OR randomised OR randomized OR trial OR ensaio clínico [Words]	August 2012: 11 October 2013: 5
8. CENTRAL (Issue 4, December 2011)	#1 MeSH descriptor Dementia explode all trees #2 MeSH descriptor Delirium, this term only	August 2012: 40 October 2013: 123

(Continued)

#3 MeSH descriptor Wernicke Encephalopathy, this term only

#4 MeSH descriptor Delirium, Dementia, Amnestic, Cognitive Disorders, this term only

#5 dement*

#6 alzheimer*

#7 "lewy* bod*"

#8 deliri*

#9 "chronic cerebrovascular"

#10 "organic brain disease" or "organic brain syndrome"

#11 "normal pressure hydrocephalus" and "shunt*"

#12 "benign senescent forgetfulness"

#13 "cerebr* deteriorat*"

#14 "cerebral* insufficient*"

#15 "pick* disease"

#16 creutzfeldt or jcd or cjd

#17 huntington*

#18 binswanger*

#19 korsako*

#20 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19)

#21 MeSH descriptor Exercise explode all trees

#22 exercis*

#23 "physical activit*"

#24 cycling

#25 swim*

#26 gym*

#27 walk* OR treadmill

#28 danc*

#29 yoga*

#30 "tai chi"

#31 aerobic*

#32 (#21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31)

#33 (#32 AND #20), from 2011 to 2012 [Trials]

9. Clinicaltrials.gov (www.clinicaltrials.gov)	Interventional Studies | dementia OR alzheimers OR AD OR alzheimer's OR alzheimer OR lewy OR FTLD OR FLD | exercise OR aerobic OR aerobics OR walk-	August 2012: 13

(Continued)

	ing OR swimming OR cycling | Adult, Senior | received from 09/01/2011 to 08/13/2012	October 2013: 19
10. ICTRP Search Portal (http://apps.who.int/trialsearch) (includes: Australian New Zealand Clinical Trials Registry; ClinicalTrilas.gov; ISRCTN; Chinese Clinical Trial Registry; Clinical Trials Registry – India; Clinical Research Information Service – Republic of Korea; German Clinical Trials Register; Iranian Registry of Clinical Trials; Japan Primary Registries Network; Pan African Clinical Trial Registry; Sri Lanka Clinical Trials Registry; The Netherlands National Trial Register)	Interventional Studies | dementia OR alzheimers OR AD OR alzheimer's OR alzheimer OR lewy OR FTLD OR FLD | exercise OR aerobic OR aerobics OR walking OR swimming OR cycling | received from 01/09/2011 to 13/08/2012	August 2012: 50 October 2013: 1
TOTAL before de-duplication		August 2012: 1330 October 2013: 1397
TOTAL after de-duplication		August 2012: 87 October 2013: 41

Appendix 2. Update search: September 2011

Source	Search strategy	Hits retrieved
1. ALOIS (www.medicine.ox.ac.uk/alois)	Keyword search: "physical activity" OR exercise cycling OR swim* OR gym* OR walk* OR danc* OR yoga OR "tai chi" (all dates)	217
2. MEDLINE In-process and other non-indexed citations and MEDLINE 1950-present (Ovid SP)	1. exp Dementia/ 2. Delirium/ 3. Wernicke Encephalopathy/ 4. Delirium, Dementia, Amnestic, Cognitive Disorders/ 5. dement*.mp. 6. alzheimer*.mp. 7. (lewy* adj2 bod*).mp. 8. deliri*.mp.	230

(Continued)

9. (chronic adj2 cerebrovascular).mp.
10. ("organic brain disease" or "organic brain syndrome").mp.
11. ("normal pressure hydrocephalus" and "shunt*").mp.
12. "benign senescent forgetfulness".mp.
13. (cerebr* adj2 deteriorat*).mp.
14. (cerebral* adj2 insufficient*).mp.
15. (pick* adj2 disease).mp.
16. (creutzfeldt or jcd or cjd).mp.
17. huntington*.mp.
18. binswanger*.mp.
19. korsako*.mp.
20. or/1-19
21. exercis*.ti,ab.
22. physical activit*.ti,ab.
23. cycling.ti,ab.
24. swim*.ti,ab.
25. gym*.ti,ab.
26. (walk* or treadmill).ti,ab.
27. danc*.ti,ab.
28. yoga*.ti,ab.
29. "tai chi".ti,ab.
30. exp Exercise/ or Exercise Therapy/
31. or/21-30
32. 20 and 31
33. randomized controlled trial.pt.
34. controlled clinical trial.pt.
35. randomi?ed.ab.
36. placebo.ab.
37. randomly.ab.
38. trial.ab.
39. groups.ab.
40. or/33-39
41. (animals not (humans and animals)).sh.
42. 40 not 41

(Continued)

	43. 32 and 42 44. (2007* or 2008* or 2009* or 2010* or 2011*).ed. 45. 43 and 44	
3. EMBASE 1980-2011 week 35 (Ovid SP)	1. exp dementia/ 2. Lewy body/ 3. delirium/ 4. Wernicke encephalopathy/ 5. cognitive defect/ 6. dement*.mp. 7. alzheimer*.mp. 8. (lewy* adj2 bod*).mp. 9. deliri*.mp. 10. (chronic adj2 cerebrovascular).mp. 11. ("organic brain disease" or "organic brain syndrome").mp. 12. "supranuclear palsy".mp. 13. ("normal pressure hydrocephalus" and "shunt*").mp. 14. "benign senescent forgetfulness".mp. 15. (cerebr* adj2 deteriorat*).mp. 16. (cerebral* adj2 insufficient*).mp. 17. (pick* adj2 disease).mp. 18. (creutzfeldt or jcd or cjd).mp. 19. huntington*.mp. 20. binswanger*.mp. 21. korsako*.mp. 22. CADASIL.mp. 23. or/1-22 24. exercis*.ti,ab. 25. physical activit*.ti,ab. 26. cycling.ti,ab. 27. swim*.ti,ab. 28. gym*.ti,ab. 29. (walk* or treadmill).ti,ab. 30. danc*.ti,ab.	443

(Continued)

	31. yoga*.ti,ab. 32. "tai chi".ti,ab. 33. exercise/ or stretching exercise/ or anaerobic exercise/ or exercise intensity/ or aerobic exercise/ or treadmill exercise/ or aquatic exercise/ 34. or/24-33 35. 23 and 34 36. randomized controlled trial/ 37. controlled clinical trial/ 38. randomi?ed.ab. 39. placebo.ab. 40. randomly.ab. 41. trial.ab. 42. groups.ab. 43. ("double-blind*" or "single-blind*").ti,ab. 44. or/36-43 45. 35 and 44 46. (2007* or 2008* or 2009* or 2010* or 2011*).em. 47. 45 and 46 48. limit 47 to human	
4. PsycINFO 1806-August week 5 2011 (Ovid SP)	1. exp Dementia/ 2. exp Delirium/ 3. exp Huntingtons Disease/ 4. exp Kluver Bucy Syndrome/ 5. exp Wernickes Syndrome/ 6. exp Cognitive Impairment/ 7. dement*.mp. 8. alzheimer*.mp. 9. (lewy* adj2 bod*).mp. 10. deliri*.mp. 11. (chronic adj2 cerebrovascular).mp. 12. ("organic brain disease" or "organic brain syndrome").mp. 13. "supranuclear palsy".mp. 14. ("normal pressure hydrocephalus" and "shunt*").mp.	214

(Continued)

15. "benign senescent forgetfulness".mp.
16. (cerebr* adj2 deteriorat*).mp.
17. (cerebral* adj2 insufficient*).mp.
18. (pick* adj2 disease).mp.
19. (creutzfeldt or jcd or cjd).mp.
20. huntington*.mp.
21. binswanger*.mp.
22. korsako*.mp.
23. ("parkinson* disease dementia" or PDD or "parkinson* dementia").mp.
24. or/1-23
25. exercis*.ti,ab.
26. physical activit*.ti,ab.
27. cycling.ti,ab.
28. swim*.ti,ab.
29. gym*.ti,ab.
30. (walk* or treadmill).ti,ab.
31. danc*.ti,ab.
32. yoga*.ti,ab.
33. "tai chi".ti,ab.
34. exp Exercise/ or exp Aerobic Exercise/
35. or/25-34
36. 24 and 35
37. random*.ti,ab.
38. exp Clinical Trials/
39. RCT.ti,ab.
40. CCT.ti,ab.
41. (placebo or "control group").ab.
42. trial.ti,ab.
43. groups.ab.
44. "double-blind*".ti,ab.
45. "single-blind*".ti,ab.
46. or/37-45
47. 36 and 46
48. (2007* or 2008* or 2009* or 2010* or 2011*).up.

(Continued)

	49. 47 and 48	
5. CINAHL (EBSCOhost)	S1 (MH "Dementia+")	264
	S2 (MH "Delirium") or (MH "Delirium, Dementia, Amnestic, Cognitive Disorders")	
	S3 (MH "Wernicke's Encephalopathy")	
	S4 TX dement*	
	S5 TX alzheimer*	
	S6 TX lewy* N2 bod*	
	S7 TX deliri*	
	S8 TX chronic N2 cerebrovascular	
	S9 TX "organic brain disease" or "organic brain syndrome"	
	S10 TX "normal pressure hydrocephalus" and "shunt*"	
	S11 TX "benign senescent forgetfulness"	
	S12 TX cerebr* N2 deteriorat*	
	S13 TX cerebral* N2 insufficient*	
	S14 TX pick* N2 disease	
	S15 TX creutzfeldt or jcd or cjd	
	S16 TX huntington*	
	S17 TX binswanger*	
	S18 TX korsako*	
	S19 S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17 or S18	
	S20 TX exercis*	
	S21 TX "physical activit*"	
	S22 TX cycling	
	S23 TX swim*	
	S24 TX gym*	
	S25 TX walk* OR treadmill	
	S26 TX danc*	
	S27 TX yoga*	
	S28 TX "tai chi"	
	S29 (MH "Exercise+")	
	S30 S20 or S21 or S22 or S23 or S24 or S25 or S26 or S27 or S28 or S29	
	S31 S19 and S30	

(Continued)

	S32 (MH "Clinical Trials") S33 TX trial S34 TX RCT OR CCT S35 TX placebo* S36 TX "double-blind*" OR "single-blind*" S37 TX groups OR "control group" S38 S32 or S33 or S34 or S35 or S36 or S37 S39 S31 and S38 S40 EM 2007 S41 EM 2008 S42 EM 2009 S43 EM 2010 S44 EM 2011 S45 S40 or S41 or S42 or S43 or S44 S46 S39 and S45	
6. ISI Web of Knowledge (includes: Web of Science (1945-present); BIOSIS Previews (1926-present); MEDLINE (1950-present); Journal Citation Reports)	Topic=(Dement* OR Alzheimer* OR "Lewy body" OR arteriosclerosis OR "Huntington* disease" OR "Kluver Bucy" OR "Pick disease" OR "Wernicke encephalopathy" OR "Korsakoff psychosis") AND Topic=(exercis* OR walk* OR swim* OR "physical activit*" OR aerobic* OR danc* OR "tai chi" OR yoga*) AND Topic=(randomly OR placebo OR groups OR trial OR RCT OR randomized OR randomised) AND Year Published=(2007-2011) Timespan=2007-2011. Search language=English Lemmatization=On	641
7. LILACS (BIREME)	dementia OR alzheimer$ OR demenc$ OR AD OR demência [Words] and exercício OR exercis$ OR walk$ OR swim$ OR aerobic$ [Words] and randomly OR randomised OR randomized OR trial OR ensaio clínico [Words]	9
8. CENTRAL (Issue 2, 2011)	#1 MeSH descriptor Dementia explode all trees #2 MeSH descriptor Delirium, this term only #3 MeSH descriptor Wernicke Encephalopathy, this term only #4 MeSH descriptor Delirium, Dementia, Amnestic, Cognitive Disorders, this term only #5 dement* #6 alzheimer* #7 "lewy* bod*" #8 deliri*	189

(Continued)

	#9 "chronic cerebrovascular" #10 "organic brain disease" or "organic brain syndrome" #11 "normal pressure hydrocephalus" and "shunt*" #12 "benign senescent forgetfulness" #13 "cerebr* deteriorat*" #14 "cerebral* insufficient*" #15 "pick* disease" #16 creutzfeldt or jcd or cjd #17 huntington* #18 binswanger* #19 korsako* #20 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19) #21 MeSH descriptor Exercise explode all trees #22 exercis* #23 "physical activit*" #24 cycling #25 swim* #26 gym* #27 walk* OR treadmill #28 danc* #29 yoga* #30 "tai chi" #31 aerobic* #32 (#21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31) #33 (#32 AND #20), from 2007 to 2011	
9. Clinicaltrials.gov (www.clinicaltrials.gov)	Interventional Studies | dementia OR alzheimers OR AD OR alzheimer's OR alzheimer OR lewy OR FTLD OR FLD | exercise OR aerobic OR aerobics OR walking OR swimming OR cycling | Adult, Senior | received from 09/01/2007 to 09/05/2011	29
10. ICTRP Search Portal (http://apps.who.int/trialsearch) (includes: Australian New Zealand Clinical Trials Registry; ClinicalTrilas.gov; ISRCTN; Chinese Clinical Trial Registry; Clinical Trials Registry – In-	Interventional Studies | dementia OR alzheimers OR AD OR alzheimer's OR alzheimer OR lewy OR FTLD OR FLD | exercise OR aerobic OR aerobics OR walking OR swimming OR cycling | Adult, Senior | received from 01/09/2007 to 05/09/2011	95

(Continued) dia; Clinical Research Information Service – Republic of Korea; German Clinical Trials Register; Iranian Registry of Clinical Trials; Japan Primary Registries Network; Pan African Clinical Trial Registry; Sri Lanka Clinical Trials Registry; The Netherlands National Trial Register)	
TOTAL before de-duplication	2331
TOTAL after de-duplication and first-assessment	277

WHAT'S NEW

Date	Event	Description
10 April 2015	New citation required and conclusions have changed	An update search was performed on 3 October 2013.The results from this search have been incorporated into the review.The results and conclusions have changed.
10 April 2015	New search has been performed	A new trial was incorporated into this review.The results and conclusions have changed.

HISTORY

Protocol first published: Issue 2, 2007
Review first published: Issue 3, 2008

Date	Event	Description
13 August 2012	New search has been performed	An update search was performed for this review on 13 August 2012.
13 August 2012	New citation required and conclusions have changed	An update search was performed for this review on 13 August 2012. The results from this search have been incorporated into the review.The results and conclusions have changed; the review authors have changed.
4 September 2011	New search has been performed	An update search was performed for this review on 4 September 2011. The results from this search have been incorporated into the review.
28 May 2008	Amended	In additional Table 1: Description of Rating Scales Used in the Included Studies, the abbreviation for Psychogeriatric Dependency Rating Scale has been changed to PGDRS from PGSRS

Date	Event	Description
14 December 2007	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

Dorothy Forbes: conceived, designed, and co-ordinated the review
Catherine Blake: corresponded with trial authors, staff at the Cochrane Dementia and Cognitive Improvement Group, and team members
Dorothy Forbes, Emily Thiessen, Scott Forbes (SCF): selected trials
Dorothy Forbes, Emily Thiessen, Catherine Blake: assessed risk of bias
Dorothy Forbes, Emily Thiessen, Catherine Blake, Scott Forbes, Sean Forbes (SF): extracted data, analysed data, drafted review versions, and reviewed drafts and final submissions

DECLARATIONS OF INTEREST

Dorothy Forbes: none known
Emily Thiessen: none known
Catherine Blake: none known
Scott Forbes: none known
Sean Forbes: none known

SOURCES OF SUPPORT

Internal sources

- University of Alberta, Canada.
- University of Western Ontario, Canada.
- University of Florida, USA.

External sources

- Canadian Cochrane Centre, Canada.

  Sponsored Emily Thiessen's attendance at a five day Cochrane Review workshop
- Nova Scotia Cochrane Centre, Canada.

  Hosted Cochrane Review workshop

INDEX TERMS

Medical Subject Headings (MeSH)

Activities of Daily Living; Caregivers; Cognition; Dementia [psychology] [*rehabilitation]; Depression [rehabilitation]; Exercise; Exercise Therapy [*methods]; Motor Activity; Randomized Controlled Trials as Topic

MeSH check words

Aged; Humans