# **Physical Therapy Reviews**

# Can physical activity be used to maintain cognitive function in nursing home residents with Dementia? A literature review. --Manuscript Draft--

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Abstract:	Background: Dementia is a noncommunicable disease with no effective prevention, treatment or cure. Evidence is emerging for the use of exercise to decelerate cognitive decline; however, few studies exist among nursing home residents and an optimum exercise protocol has yet to be determined. Objectives: To determine the effectiveness of physical activity in maintaining cognitive function in nursing home residents with Dementia. Methods: Databases searched included CINAHL, MEDLINE complete, SPORTDiscus and ScienceDirect. Six relevant studies were identified and critically appraised using the Effective Public Health Practice Project Quality Assessment Tool. Results: All trials included different exercise programmes with various activity types and duration; all control interventions were social activities. Three studies demonstrated improved cognition in the intervention group, whilst one study observed a slower decline. Four studies found statistically significant cognitive decline in the control groups. Overall, there is moderate-to-strong evidence that physical activity can effectively maintain cognitive function in nursing home residents with Dementia. Conclusions: All interventions had a favourable effect on cognition. Results suggest that aerobic exercise of longer duration may be most effective for those with mild-to-moderate cognitive impairment; whilst multimodal programmes may be most effective for moderate-to-severe Dementia. Combining an exercise programme with standard daily activities appears no more effective than exercise alone. Future research should aim to determine an optimum exercise protocol and whether the positive effects on cognition can be maintained long-term with continued exercise.
Funding Information:	

# <u>Title</u>

# Can physical activity be used to maintain cognitive function in nursing home residents with Dementia? A literature review.

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Tel: +44 (0)1202 962478 e-mail: jwilliams@bournemouth.ac.uk I enjoyed reading this literature review on the use of physical activity to maintain cognitive function in residential care. Overall, this was a very well written article. I note that the authors have addressed the first reviewers comments, however reading the revised manuscript, there is still potential to improve the balance between the Results and Discussion (see first reviewer comments 4 and 5).

I would suggest including more narrative detail on the participants and interventions in the Results section. Participant age, sex, baseline cognitive score and activity/frailty level, and specifics on the nature of the interventions (what was in a multi-modal programme?) - the 'ins and outs of type and duration' of the interventions should all be in the Results. It will then be easier to synthesise this information in the Discussion section to give a more concise, cohesive message. There are some important points made in the Discussion, such as the need to consider frailty when prescribing physical activity, so reducing the length of the Discussion section will allow these key messages to stand out.

Many thanks for these comments.

The results sections has been modified to include the details suggested.

The discussion has been edited to reduce its length whilst maintaining the key messages.

- 1 Can physical activity be used to maintain cognitive function in nursing home
- 2 residents with Dementia? A literature review.
- 3

### 4 Background

- 5 Dementia is a noncommunicable disease with no effective prevention, treatment or cure.<sup>1</sup>
- 6 Alzheimer's disease (AD) is the most common type of dementia with twenty-six million people
- 7 affected worldwide; consequently, this is described as a global epidemic which is projected to
- 8 increase as a result of aging populations.<sup>2</sup> Many animal studies have demonstrated that
- 9 physical activity can attenuate neuropathology associated with AD,<sup>2</sup> whilst emerging evidence
- 10 has shown improvements in cognitive and motor function and performance of activities of daily
- 11 living by increasing the amount of exercise in community-dwelling older adults with AD.<sup>3,4</sup>
- 12 However, few studies exist among nursing home residents and an optimum exercise protocol
- 13 has yet to be determined. Subsequently, current UK guidelines provide limited
- 14 recommendations on exercise or long-term management of dementia, with physiotherapy
- assessment and advice not considered routine care.<sup>5</sup> Therefore, there is a need for a systematic
- 16 review of the literature synthesising contemporary knowledge. The aim of this systematic
- 17 review was to determine the effectiveness of physical activity in maintaining cognitive function
- 18 in nursing home residents with dementia and explore the literature for recommendations on
- 19 exercise protocol development.

# 20 Methods

# 21 Search Strategy

This review systematically searched the databases Science Citation Index, Social Sciences
Citation Index, PsycINFO, CINAHL, MEDLINE complete, PsycARTICLES, SocINDEX, SPORTDiscus,
ScienceDirect and Education Source in November 2015. Search terms included Dementia,
"physical activity", "cognitive function" and "nursing home". All search terms incorporated
Boolean logic (Table 1). The search generated 149 potential articles published between 2000
and 2016 which was subsequently limited to the English language and peer reviewed journals.

Following removal of duplicates, studies were screened by titles and abstracts against inclusion
and exclusion criteria. The same process was then adopted to review full texts of remaining
studies. No reference lists from selected articles were screened for additional references. The
search strategy is presented via the flow chart in figure 1.

32

33 [Figure 1 near here].

34 [Table 1 near here].

35

#### 36 Inclusion and Exclusion Criteria

37 Only Randomised Controlled Trials (RCTs) or Controlled Clinical Trials (CCTs) were included in this review as the aim was to explore the efficacy of an intervention. Participants in both 38 intervention and control groups needed to have a formal diagnosis of dementia and be residing 39 40 in a nursing home from the start of the trial. Therefore, studies were excluded if participants were community-dwelling older adults with mild cognitive impairment or no clinical diagnosis 41 42 of dementia. Studies were considered for inclusion if they investigated the effectiveness of any 43 physical activity on cognitive function. Although the type of exercise was not specified, the intervention had to be a structured programme incorporating gross motor activity that was 44 45 instead of, or as well as, the participants' usual activities. Consequently, trials that included fine motor movements only or combined exercise with another new intervention were excluded. 46 47 Cognitive function had to be assessed prior to, and immediately after treatment. Follow-up times were not limited. Studies testing more than one outcome measure were included if the 48 49 results relating to cognition were presented separately from the other measures.

#### 50 Quality Index

The Quality Assessment Tool for Quantitative Studies was used to assess the methodological quality of the selected studies.<sup>6</sup> Previous studies have demonstrated the effectiveness of this tool with excellent inter-rater reliability.<sup>7</sup> All studies were reviewed by the lead investigator with uncertainty resolved by consensus.

#### 55 Results

The search provided five RCTs and one CCT which matched the inclusion criteria. Data extractedfrom these studies are presented in Table 3.

Four RCTs scored strong and one RCT scored moderate on the EPHPP Quality Assessment Tool.<sup>6</sup>
 However, the CCT was rated weak which subsequently reflects the hierarchy of evidence scale
 (Table 2).<sup>8</sup>

61 The studies included in this review had small sample sizes and the three trials with the least participants did not conduct a power analysis,<sup>9,11,12</sup> whereas those with larger samples 62 did.<sup>10,13,14</sup> Although, it should be mentioned that Stevens and Killeen<sup>10</sup> did not achieve the 63 numbers calculated from the power analysis; perhaps reflecting the fact this was the only RCT 64 to be rated moderate by the quality assessment tool.<sup>6</sup> Additionally, participants were not 65 randomly selected to enter the trials from their respective nursing homes and thus could only 66 67 be scored as 'somewhat likely' to be representative of the target population.<sup>6</sup> Therefore, it is 68 possible that both selection bias and small sample sizes reduce the generalisability of findings. 69 Nevertheless, the included participants do represent widely accepted statistics on the prevalence of AD, namely relating to age and gender. 81% of people with AD are aged over 70 seventy-five, whilst AD and other dementias are more prevalent in women.<sup>16</sup> This is echoed in 71 all studies which included more females and had average ages of participants above eighty. 72 Additionally, there were consistent results across the six studies which were all conducted in 73 74 different countries. Still, two studies only had 60-79% of participants completing the study and neither used intention-to-treat analyses.<sup>10,11</sup> Whilst this may increase the risk of attrition bias, 75 these two studies were rated weakest by the quality assessment tool and thus the results may 76 be more questionable. Out of the remaining four studies, only Telenius *et al.*<sup>14</sup> state whether 77 there were significant differences in characteristics between those who completed the study 78 and those who dropped out. This decreases the generalisability of findings as attrition may 79 preferentially select for those responding to the intervention.<sup>9,12,13</sup> Finally, no study reported 80 that participants were blinded to the research question or group allocation. The importance of 81 82 this methodological flaw could be questioned as this method reflects patients in practice whom are aware of the treatment they receive and the intended outcomes. 83

84 [Table 2 near here].

All studies used the Mini Mental State Examination (MMSE) to screen participants' stage of 85 dementia for inclusion. Venturelli et al.<sup>12</sup> included five male and thirty female participants with 86 moderate-to-severe cognitive impairment, an average age of eighty-four ± five and no mobility 87 limitations. The CCT<sup>11</sup> entered four male and eleven female participants with mild-to-severe 88 cognitive impairment, ages ranging from seventy-four and ninety-two. These participants were 89 very frail, relying partly or constantly on walking aids. Kemoun et al.<sup>9</sup> included eight males and 90 91 twenty-three females with moderate-to-severe cognitive impairment, an average age of  $81.8 \pm$ 5.3 and the ability to mobilise ten meters without assistance. Another RCT<sup>14</sup> entered forty-three 92 93 male and one hundred and twenty female participants with moderate cognitive impairment, an average age of 86.7 ± 7.4 and walking six meters with or without a walking aid. Stevens and 94 Killeen<sup>10</sup> included nineteen males and fifty-six females with mild-to-moderate cognitive 95 impairment, an average age of 80.5 and were physically capable of undertaking gentle exercise 96 97 (this included frail persons and wheelchair users). Finally, another RCT<sup>13</sup> entered eighteen male 98 and seventy-nine female participants with mild-to-moderate cognitive impairment, an average age of 85.4 and walking short distances with or without a walking aid. 99

100 All trials included different exercise programmes with various activity types and duration; 101 however, all control interventions were social visits or activities. Venturelli et al.<sup>12</sup> conducted a 102 twenty-four week walking programme for thirty minutes, four times per week; whilst another 103 study followed the same intervention with thirty minute sessions, five times per week, for six weeks<sup>13</sup>. Steven and Killeen<sup>10</sup> included a twelve-week programme consisting of thirty-minute 104 aerobic exercise sessions, three times per week; the participants in the study by Telenius et al.<sup>14</sup> 105 undertook a twelve week strength and balance programme for fifty-to-sixty minutes, twice per 106 week. Kemoun et al.<sup>9</sup> combined walking, equilibrium and stamina exercises for one hour, three 107 108 times per week, for fifteen weeks; whilst Thurm et al.<sup>11</sup> also conducted a multimodal 109 programme including strength, co-ordination, balance, flexibility and stamina exercises; 110 however these were chair-based with forty-five minute sessions, twice per week, for ten weeks.

Only Kemoun *et al.*<sup>9</sup> demonstrated a statistically significant improvement in cognition following the exercise intervention, whilst two studies found improvements but which did not reach statistical significance.<sup>10,11</sup> Venturelli *et al.*<sup>12</sup> demonstrated a slower decline in cognition for the intervention group but these changes were not statistically significant, although they do suggest a stabilization of cognitive decline. However, four studies showed significant cognitive decline in the control groups following the trials.<sup>9-12</sup> Two studies observed no significant changes in either the intervention or control groups.<sup>13,14</sup>

- 118 Overall, there is moderate evidence that physical activity can effectively maintain cognitive
- 119 function in nursing home residents with dementia.<sup>15</sup>
- 120 [Table 3 near here].

#### 121 Discussion

#### 122 Exercise Interventions (Type, Frequency, Intensity, Duration)

123 The results suggest that certain exercise types may be more beneficial at different stages of dementia. [Two studies investigated the effects of aerobic exercise in those with mild-to-124 moderate cognitive impairment.<sup>10,13</sup> Since similar frequency and duration of sessions were also 125 used, it appears that Stevens and Killeen<sup>10</sup> achieved better outcomes with a longer programme 126 127 (twelve weeks). This same programme duration, also for those with moderate dementia, was used by Telenius et al.<sup>14</sup> but incorporating a strength and balance programme. However, 128 Stevens and Killeen<sup>10</sup> again demonstrated greater improvement. Therefore,] it appears that 129 130 aerobic exercise of a longer duration may be more effective than a strength and balance 131 programme in maintaining cognitive levels in those with mild-to-moderate dementia. In contrast, although not significantly, those with moderate-to-severe dementia demonstrated 132 cognitive decline with aerobic exercise alone,<sup>12</sup> but significant improvement via a multimodal 133 programme of a shorter duration.<sup>9</sup> This suggests that multimodal exercise could have more 134 beneficial effects on cognition than single exercise interventions for those with moderate-to-135 severe cognitive impairment. Overall these results provide evidence of a varied effect based on 136

baseline cognition and exercise type, suggesting a stratified approach may be necessary tooptimise the effect.

Observations of health status may provide explanations for the response to certain exercise 139 types in accordance with the severity of cognitive decline. Interestingly, participants with mild-140 to-moderate cognitive impairment were physically frailer with greater co-morbidities, including 141 cardiovascular disease (Table 3). Therefore, improvements from gentle aerobic exercise alone 142 support the widely accepted notion that the greatest gains are achieved when sedentary 143 people become more active, including better cognitive function.<sup>17</sup> Additionally, the need for a 144 longer aerobic programme perhaps reflects the time required to achieve beneficial effects on 145 the cardiovascular system,<sup>13</sup> with increased cerebral perfusion arguably able to reduce 146 neuronal cell death associated with Alzheimer's disease, as well as promote neuroplasticity.<sup>3</sup> In 147 contrast, studies investigating moderate-to-severe dementia included less co-morbidity or 148 those which could be considered as less life-threatening,<sup>11,12,14</sup> whilst co-morbidities in one 149 150 study were unknown.<sup>9</sup> Participants were also more physically capable with one study only including those with absence of mobility limitations.<sup>12</sup> Perhaps then, a multimodal programme 151 was most effective for these participants as it provided higher intensity exercise targeting 152 153 multiple body systems over and above their previous activity levels. Overall, the stage of 154 Alzheimer's disease and other dementias should be taken into account when selecting the most appropriate exercise type, whilst also considering the pathology's links to other co-morbidities, 155 notably, cardiovascular disease.<sup>16</sup> 156

Comparing all six studies, a fifteen-week multimodal programme proved to be the most 157 effective exercise intervention as this was the only study to achieve statistically significant 158 improvements in cognitive function.<sup>9</sup> Since the frequency, intensity and duration of this 159 programme were all greater than the other studies, and due to the heterogeneity of the 160 interventions, it is difficult to determine whether one, some, or all of these factors are 161 162 responsible for the enhanced effects. Equally, as previously discussed, the participants' 163 cognitive levels and physical capabilities in relation to the intervention may have also had an effect. Nevertheless, the result that a multimodal programme demonstrated the most 164

165 beneficial effects on cognition reflects the American College of Sports Medicine guidelines for 166 older adults,<sup>18</sup> which recommend the inclusion of aerobic, strength and flexibility training 167 within an exercise programme for this age group. The same recommendations are also made by the World Health Organisation and the Department of Health.<sup>17,19</sup> Whilst each of these 168 169 guidelines discuss the importance of tailoring the recommended dosages to individual need and 170 capabilities, including for those with physical and mental disability; the emphasis on retaining 171 cognitive function is placed mainly upon the population at risk of developing dementia, rather than individuals already living with the condition. This arguably limits the appropriateness of 172 these guidelines to the target population of this review. 173

Similarities do exist between some of these recommendations and the findings from this 174 175 review, specifically relating to exercise intensity. The guidelines indicate that moderate-tovigorous intensity activity provides greater health benefits, and this also could be suggested 176 177 from this review, in relation to improving cognitive function in residents with dementia. 178 Although no standardised measure of intensity was used across all six studies it can be assumed 179 that some interventions were more intense than others. Two studies investigated the effects of a walking programme, however, one instructed participants to walk at a self-selected speed 180 with the inclusion of short rest periods,<sup>13</sup> the other to walk at the fastest pace possible without 181 stopping.<sup>12</sup> Whilst both studies maintained cognition levels, the latter of the two (higher 182 intensity programme) maintained cognitive function over a six month period, suggesting this 183 184 intensity can maintain cognitive function in the long term. Similarly, whilst the chair-based 185 multimodal programme demonstrated improvements in cognition, these results were not significant;<sup>11</sup> yet, other multimodal programmes which included walking and the use of an ergo-186 cycle achieved significant improvements in cognitive function.<sup>9</sup> Additionally, both interventions 187 which could be considered higher intensity demonstrated improvements in both cognitive and 188 motor function,<sup>9,12</sup> including specific gait parameters.<sup>9</sup> This suggests that higher intensity 189 190 exercise could have beneficial effects other than improved cognitive function in residents with dementia, for example, a reduced risk of falls.<sup>3,9</sup> Overall, it is difficult to recommend an exact 191 192 optimum exercise protocol from the included studies in this review and the current guidelines; 193 however, it appears that a higher intensity, multimodal programme which includes walking

should be adopted when aiming to maintain or improve cognitive function in nursing homeresidents with dementia.

Nevertheless, it is unclear whether these cognitive benefits can be maintained long-term, with 196 or without continued exercise. None of the included studies conducted follow-up past the end 197 of the intervention. Additionally, the five studies with the shortest programme durations, 198 ranging from six to fifteen weeks, all maintained or improved cognitive function,<sup>9-11,13,14</sup> with 199 200 the fifteen week multimodal programme producing the most significant improvements.<sup>9</sup> 201 Contrastingly, the longest programme (twenty-four weeks) was the only study to show a decline in MMSE scores, although not significantly.<sup>12</sup> Since both the latter two studies 202 203 investigated moderate-to-severe cognitive impairment, it could be suggested that the 204 intervention type and intensity (walking) of the twenty-four week programme was just not effective enough to maintain cognitive levels, as previously discussed. However, perhaps the 205 spread of amyloid plagues and neurofibrillary tangles (primary biological markers of AD) from 206 207 the hippocampus to other brain regions,<sup>2</sup> represent inevitable pathological changes and thus no 208 form of exercise can continue to halt this degenerative condition. To date, the only research which has shown long-term exercise to decrease pathological deposition of these proteins has 209 all been conducted on transgenic mice,<sup>20-22</sup> making the translation of these findings to humans 210 difficult.<sup>23</sup> Overall, future studies should investigate whether a multimodal programme is able 211 to maintain the positive effects on cognitive function at twenty-four weeks and beyond, for all 212 213 stages of dementia.

#### 214 Social Interaction and Control Groups

Initially, it could be suggested that incorporating an exercise programme in addition to standard
daily activities may provide the most beneficial effects on cognition, since both were continued
by the intervention group in the only study to achieve statistically significant improvements.<sup>9</sup>
However, both multimodal programmes were conducted alongside usual activities,<sup>9,11</sup> so whilst
the only difference between the interventions is the dosage of physical activity, this suggests it
is the exercise programme which resulted in the better outcome. Similarly, Stevens and
Killeen<sup>10</sup> produced the same results as Thurm *et al.*<sup>11</sup> through an exercise programme alone,

222 implying that standard activities may have had no effect in the latter study. In addition, four studies demonstrated significant cognitive decline in the control groups, suggesting that daily 223 224 activities alone are unable to maintain cognitive function in residents with dementia.<sup>9-12</sup> Yet, two studies found no change in cognitive scores in either the intervention or control groups, 225 suggesting equal effect.<sup>13,14</sup> However such studies failed to provide optimal exercise 226 intervention. Overall, if an optimum exercise programme is used, then this alone may be able to 227 228 positively affect cognition as well as provide the benefits of standard activities, such as lifting mood, since physical activity is acknowledged as social interaction.<sup>10</sup> Therefore, this may save 229 nursing homes' time and resources as one exercise programme could provide all potential 230 231 benefits. Nonetheless, if resources are available, then other daily activities should be included 232 alongside physical activity to provide ongoing entertainment and stimulation.

#### 233 Limitations

There were a limited number of articles solely targeting nursing home residents, whilst the included studies had relatively small sample sizes. This may reduce the generalisability of the review's findings to the whole population of nursing home residents with dementia. Only English-language studies were included in this review and reference lists of selected studies were not screened for additional references; thus, other relevant articles may have been missed. Moreover, only including nursing home residents also limits the transferability of findings to those with dementia living in the community.

#### 241 Conclusion

242 This review has been unable to determine an optimum exercise protocol; however, there is moderate evidence that physical activity can effectively maintain cognitive function in nursing 243 244 home residents with dementia. Results suggest that aerobic exercise of longer duration may be 245 most effective in maintaining cognitive levels for those with mild-to-moderate cognitive impairment, physical frailties and co-morbidities; whilst multimodal programmes may have the 246 247 same effect for moderate-to-severe dementia and healthier, less frail residents. One 248 multimodal programme did demonstrate significant improvements in cognitive function. It 249 appears interventions should be of a higher intensity and include walking exercises to achieve

the greatest benefits. Moreover, combining an exercise programme with standard daily

activities appears no more effective than exercise alone. Future research should aim to

determine an optimum exercise protocol for this target population and investigate whether the

253 positive effects on cognition can be maintained long-term with continued exercise; thus, trials

with extended follow-ups should be conducted.

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Table 1. Search terms	
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Key concept	Alternative terms
Dementia	Dementia OR Alzheimer* OR "Alzheimer's disease"
Cognitive function	"Cognitive function" OR "Cognitive decline" OR
	"Cognitive symptoms"
Physical activity	"Physical activity" OR walk* OR exercise OR inactivity OR
	sedentary OR "sedentary lifestyle"
Nursing home	"nursing home"

Questions	Venturelli et al. 2011	Thurm et al. 2011	Kemoun et al. 2010	Telenius et al. 2015	Stevens and Killeen 2006	Eggermont et al. 2008
A) 1.	Somewhat likely	Not likely	Somewhat likely	Somewhat likely	Somewhat likely	Somewhat likely
A) 2.	80-100%	N/A	80-100%	80-100%	80-100%	80-100%
	MODERATE	WEAK	MODERATE	STRONG	MODERATE	MODERATE
B) 1.	RCT	CCT	RCT	RCT	RCT	RCT
B) 2.	YES	NO	YES	YES	YES	YES
B) 3.	YES	N/A	YES	YES	YES	YES
B) 4.	YES	N/A	YES	YES	YES	YES
	STRONG	STRONG	STRONG	STRONG	STRONG	STRONG
C) 1.	NO	NO	NO	NO	Can't tell	NO
C) 2.	N/A	N/A	N/A	N/A	N/A	N/A
	STRONG	STRONG	STRONG	STRONG	WEAK	STRONG
D) 1.	NO	YES	NO	NO	Can't tell	NO
D) 2.	Can't tell	YES	Can't tell	Can't tell	Can't tell	Can't tell
	MODERATE	WEAK	MODERATE	MODERATE	MODERATE	MODERATE
E) 1.	YES	YES	YES	YES	YES	YES
E) 2.	YES	YES	YES	YES	YES	YES
	STRONG	STRONG	STRONG	STRONG	STRONG	STRONG
F) 1.	YES	YES	YES	YES	YES	NO
F) 2.	80-100%	60-79%	80-100%	80-100%	60-79%	80-100%
	STRONG	MODERATE	STRONG	STRONG	MODERATE	STRONG
G) 1.	80-100%	80-100%	80-100%	80-100%	Can't tell	80-100%
G) 2.	YES	YES	Can't tell	YES	Can't tell	Can't tell
G) 3.	NO	NO	YES	NO	NO	NO
H) 1.	Institution	Institution	Institution	Institution	Institution	Institution
H) 2.	Institution	Institution	Institution	Institution	Institution	Institution
H) 3.	YES	YES	YES	YES	YES	YES
H) 4.	Can't tell	NO	Can't tell	YES	NO	YES
GLOBAL RATING	STRONG (1)	WEAK (3)	STRONG (1)	STRONG (1)	MODERATE (2)	STRONG (1)

Table 2. Methodological quality assessment results.

Table 3. Data extraction.

Authors	Study Design	Participants and task	Control	Co-morbidities	Outcome measures	Results	Comments	Critical appraisal score
Venturelli et al. 2011	RCT	5 male and 30 female Age: $84 \pm 5$ Moderate-severe cognitive impairment Duration of residence (months): 21.5 $\pm$ 3.7 (IG) and 20.7 $\pm$ 5.4 (CG) 24-week walking programme (30 minutes, 4 x week)	Routine care incorporating daily organized activities, e.g. bingo, sewing and music therapy	Included: constant SpO <sub>2</sub> >85% during walking, osteoporosis, hypertension, depression Excluded: severe heart disease, low haemoglobin saturation Mobility: Absence of mobility limitations	MMSE	IG had a slower decline in MMSE scores (- 13%) demonstrating no significant change, therefore maintained cognitive levels. CG showed a statistically significant decrease in MMSE scores (-47%)	Maintained constant but fastest walking speed possible (no accelerating or stopping); Average baseline MMSE score stated for IG differed between results table and description of results	Strong = 1
Thurm et al. 2011	CCT	4 male and 11 female Age: 74-92 Mild-severe cognitive impairment 10-week multimodal, chair- based training including Strengthening, coordination, balance, flexibility and stamina (45 minutes, 2 x week) whilst continuing standard daily activities	Standard daily activities, e.g. handicrafts, singing, cooking and movies afternoons	Included: Hypertension, depression Excluded: sensory impairment (hemiplegia, paraplegia) Mobility: Very frail, relied partly or constantly on walking aids	ADAS-Cog	CG showed statistically significant deterioration in total ADAS-cog score (average 3.9 error points) whereas IG had statistically insignificant improvement (average -3.7 error points). IG showed statistically significant improvement in the ADAS-Cog orientation/praxis subscore (average -2.7 error points) whereas CG showed no change	ADAS-cog scores represent difference scores (post minus pre scores). Negative scores indicate improvement; positive scores indicate deterioration in cognitive function	Weak = 3

Kemoun et al. 2010	RCT	8 male and 23 female Age: $81.8 \pm 5.3$ Moderate-severe cognitive impairment 15-week physical activity programme combining walking, equilibrium and stamina exercises (1 hour, 3 x week) whilst continuing standard daily activities	No physical activities; Standard daily activities, e.g. pottery, painting, soft gymnastics and outings	Unknown co- morbidities Mobility: ability to walk 10 meters without technical assistance	French ERFC	IG showed a statistically significant increase in ERFC score (from $26.81 \pm 6.42$ to $30.38 \pm 7.66$ ) compared to the CG for whom scores deteriorated (from $28.33 \pm 7.11$ to $23.23 \pm$ 8.37). A significant correlation between improved ERFC score, walking speed and stride length was also observed.	Soft gymnastics included within standard daily activities may constitute as physical activity	Strong = 1
Telenius et al. 2015	RCT	43 males and 120 females Age: $86.7 \pm 7.4$ Moderate cognitive impairment Duration of residence (months): $26 \pm 24.8$ Included co-morbidities: 12-week high- intensity strengthening and balance exercise programme (50-60 minutes, 2 x week)	Leisure activities including light physical activity, reading, playing games, listening to music and conversations (50-60 minutes, 2 x week)	Included: previous stroke, PD, depression Excluded: medically unstable, psychotic Mobility: able to walk six meters with or without walking aid (1/3 able to walk independently)	MMSE	No significant changes were observed in MMSE scores for IG or CG, therefore cognitive function was maintained	MMSE was not a primary outcome measure	Strong = 1
Stevens and Killeen 2006	RCT	19 male and 56 female Age: 80.5 Mild-moderate cognitive impairment	CG 1 = no intervention CG 2 = social visit from the researcher discussing	Included: vascular and degenerative diseases, e.g. arthritis, PD Mobility:	The Clock- Drawing Test	Both CGs increased in their post-test scores and this score difference was statistically significant for CG 2 (p< .000)	Mean post-test scores were subtracted from mean pre-test scores.	Moderate = 2

		12-week aerobic exercise programme with music (30 minutes, 3 x week)	health-related issues (30 minutes, 3 x week)	physically capable of undertaking gentle exercise (included frail, and wheelchairs users)		IG demonstrated decrease in post-test scores but this improvement was statistically insignificant ( $p = .524$ ) Statistically significant differences existed between IG and CG 2 ( $P = .002$ ) and between the CGs ( $P = .016$ )	Increased post-test scores indicate cognitive decline. Decreased post-test scores suggest improved cognitive function	
Eggermont et al. 2008	RCT	18 male and 79 female Age: 85.4 Mild-moderate cognitive impairment 6-week walking programme (30 minutes, 5 x week)	Social visits (30 minutes, 5 x week)	Included: hypertension, cataract, COPD, arthritis, PVD, tumours, AF, diabetes, myocardial ischaemia, depression Excluded: visual disturbances, hearing difficulties, history of alcoholism, personality disorders, cerebral trauma, hydrocephalus, neoplasm, disturbances of consciousness Mobility: able to walk for short distances with or without a walking aid	Rivermead Behavioural Memory Test (face and picture recognition) Eight words test; digit span; category fluency; letter fluency	No outcome measure revealed a significant time x group interaction effect.	Walked at self- selected speed with short rests included. It was concluded that the intervention lacked beneficial effects on cognition as improvements were not made; however, cognitive function was maintained.	Strong = 1

RCT, randomised controlled trial; MMSE, mini mental state examination; IG, intervention group; CG, control group; ADAS-Cog, Alzheimer Disease Assessment Scale – Cognitive Subscale; ERFC, Rapid Evaluation of Cognitive Function; PD, Parkinson's disease; COPD, chronic obstructive pulmonary disease; PVD, peripheral vascular disease; AF, atrial fibrillation.



Figure 1. PRISMA flow-diagram of search.