Physical performance and cognition in older adults with and without dementia

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Review of effects of physical activity on strength, balance, mobility, and ADL performance in elderly with dementia

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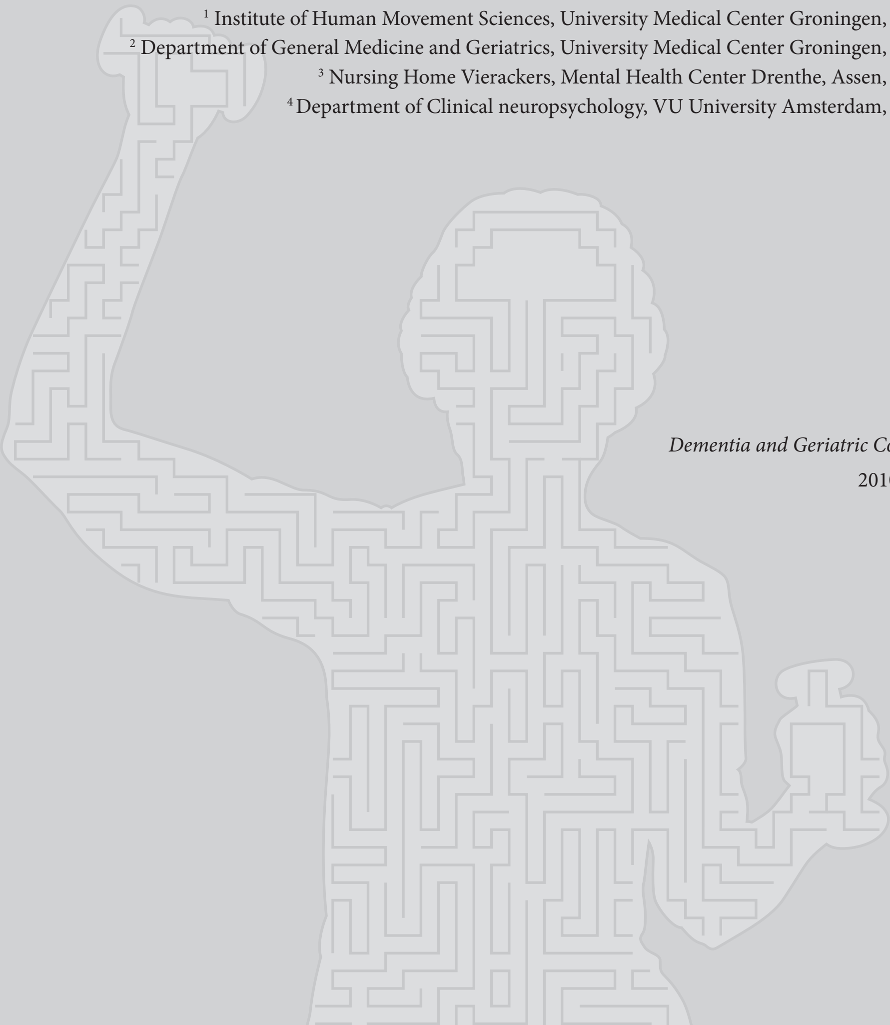

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Abstract

Background/Aims: Elderly with dementia are vulnerable for a decline in physical functioning and basic activities of daily living (BADL) which can lead to a decline in autonomy and participation. This study reviews the effect of physical activity on physical functioning and BADL in elderly with dementia.

Methods: A systematic search of the literature was performed. Keywords related to elderly, dementia, exercise interventions, and physical outcome measures were used.

Results: Sixteen studies were included. It was found that physical activity was beneficial in all stages of dementia. Multicomponent interventions (e.g. a combination of endurance, strength, balance) led to larger improvements in gait speed, functional mobility, and balance, compared to progressive resistance training alone. BADL and endurance improved but were only assessed in multicomponent interventions. Lower limb strength improved equally in multicomponent interventions and progressive resistance training.

Conclusion: Multi-component interventions can improve physical functioning and BADL in elderly regardless of the stage of dementia. The best results were obtained in the interventions with the largest training volume. However, the small number of high quality studies, and heterogeneity of the participants and interventions prevent us from drawing firm conclusions. Recommendations are given with respect to methodological issues, further research, and practical guidelines.

2.1 Introduction

At this moment there are 24.3 million people with dementia of multiple etiologies, e.g., Alzheimer's disease, vascular dementia, fronto-temporal dementia, worldwide. It is estimated that this number will double every twenty years to 81.1 million in 2040 (Ferri, Prince et al. 2005). Since there is no cure for dementia (Geldmacher, Frolich et al. 2006), the increase in the number of people with dementia will have a great impact on our national health care systems (Schölzer-Dorenbosch 2005). In addition to disturbances in cognition and behavior (Lovheim, Sandman et al. 2008), dementia leads to a deterioration in the performance of Activities of daily living (ADL; Gaugler, Duval et al. 2007, Feldman, Van Baelen et al. 2005). ADL can be divided in Instrumental ADL (IADL), which includes activities like light housework, preparing meals, taking medication; and basic ADL (BADL) such as bathing, eating, and dressing (Iavarone, Milan et al. 2007). The deterioration in the performance of BADL, especially, leads to a decline in autonomy (Iavarone, Milan et al. 2007) and is, consequently, an important cause of institutionalization (Gaugler, Duval et al. 2007, Galasko, Kershaw et al. 2004). Some argue that the decline in BADL is a greater burden for caregivers than the decline in cognition (Boersma, Van Den Brink et al. 1999). Moreover, the decline in BADL in particular accelerates in moderate dementia (Folstein, Folstein et al. 1975, Feldman, Schmitt et al. 2006). Therefore it is important to improve or stabilize the ability to perform BADL.

The model of the International Classifications of Functioning, Disability and Health (ICF; Figure 2.1; World Health Organization 2001), can describe the consequences of dementia that eventually lead to deterioration in BADL and loss of autonomy. In the context of this review, dementia (Health condition) has a negative influence on mobility, endurance, lower extremity strength, and balance (Body Functions and Body structures). Those body functions are important for BADL functioning (Activity). Depending on the quality of the BADL performance, patients are less or more restricted in their participation (Participation). Improvement in the other components is a prerequisite for improvement in participation. Unfortunately, dementia cannot be cured, but the consequences may be influenced. The body functions of people (e.g. mobility, lower extremity strength, balance and walking endurance) are highly trainable in cognitively intact older adults (Binder, Schechtman et al. 2002, Vaitkevicius, Ebersold et al. 2002), and can lead to an improvement in ADL (Yokoya, Demura et al. 2009). By training physical components underlying ADL, or by a direct influence of exercise on ADL, healthy elderly can stabilize or improve their

ADL score (Yokoya, Demura et al. 2009).

The next question that arises is whether training of mobility, lower extremity strength, balance and walking endurance is also effective, directly or indirectly, in improving ADL performance in older persons with dementia. Therefore, the main goal of this review is to investigate whether physical activity can improve mobility, lower extremity strength, balance, walking endurance, and BADL in elderly with dementia. To formulate recommendations for the most effective training program for elderly with dementia, we will address specific training parameters such as duration, frequency, intensity, and participation rate.

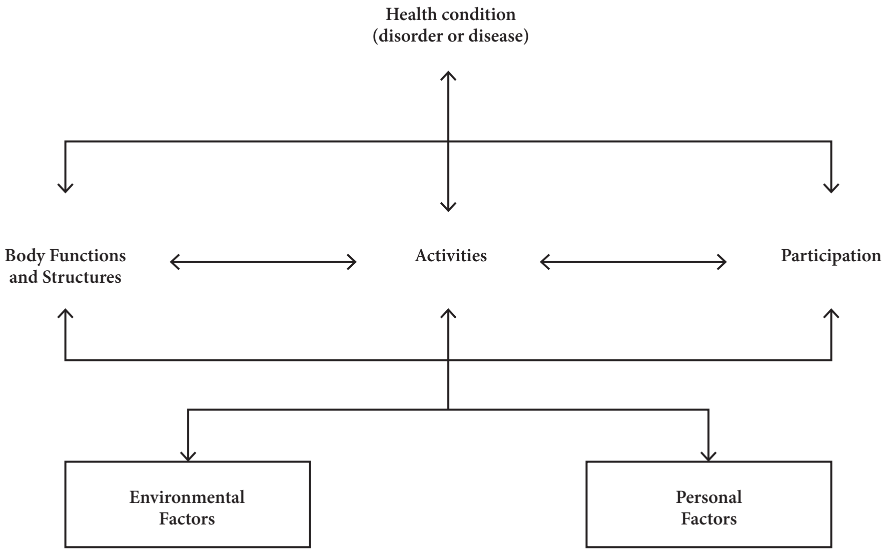

Figure 2.1. International Classification of Functioning, Disability and Health (ICF) Model. Taken from: World Health Organization (WHO; 2001). International Classification of Functioning, Disability and Health. Geneva, Switzerland: WHO.

2.2 Methods

Search strategy

Between September 2009 and March 2010, Embase, PubMed, Web of Science (ISI), PsychINFO, CINAHL, and Biological Abstracts (ISI) were searched for publications on physical activity provided to elderly with dementia. Keywords used in the computerized search included terms from Medical Subject Headings (MeSH) and Embase thesaurus (EMtree) as well as free text terms. For searches in the MeSH database we used the following terms: Motor activity, exercise, physical activity, dementia, aged, musculoskeletal physiological phenomena, physical fitness, Activities of daily living; for the EMtree database search we used, motor activity, exercise, physical activity, dementia, aged, musculoskeletal function, fitness, strength, endurance, aerobic capacity, daily life activity; In both searches the following free text terms were added, physical training, mobility, frail, Alzheimer, balance, functional performance, functional limitations.

Keywords standing for exercise (Motor activity, Exercise, physical activity, physical training) were combined with AND with terms that expressed the population (dementia, Aged, frail, Alzheimer), which were combined with AND for our outcome measures (Musculoskeletal physiological phenomena, musculoskeletal function, strength, mobility, balance, endurance, aerobic capacity, functional performance, functional limitation, physical fitness, Activities of daily living, ADL). In addition, the reference lists of all the selected studies were thoroughly screened for additional studies.

Inclusion criteria

Studies were included if they met the following five criteria: 1) Participants had dementia of any etiology; 2) Participants were on average older than 70, to prevent incorporation of early onset dementia; 3) Solely the effects of physical activity was investigated; 4) The study included outcome measures related to mobility, endurance, lower extremity strength, balance, or ADL performance and 5) Studies were written in English, Dutch, French or German.

Analyses of published studies

A first selection was made on title level and a second selection was made after reading the abstracts. In both steps a conservative approach was used, which means that if there was any doubt, the abstract or full text was screened. Two reviewers independently (CGB & MvH) performed these steps. The process is presented in the flowchart (Figure 2.2). If both reviewers thought a study was irrelevant, this study was excluded. The full text analysis of the different studies was performed by one reviewer (CGB).

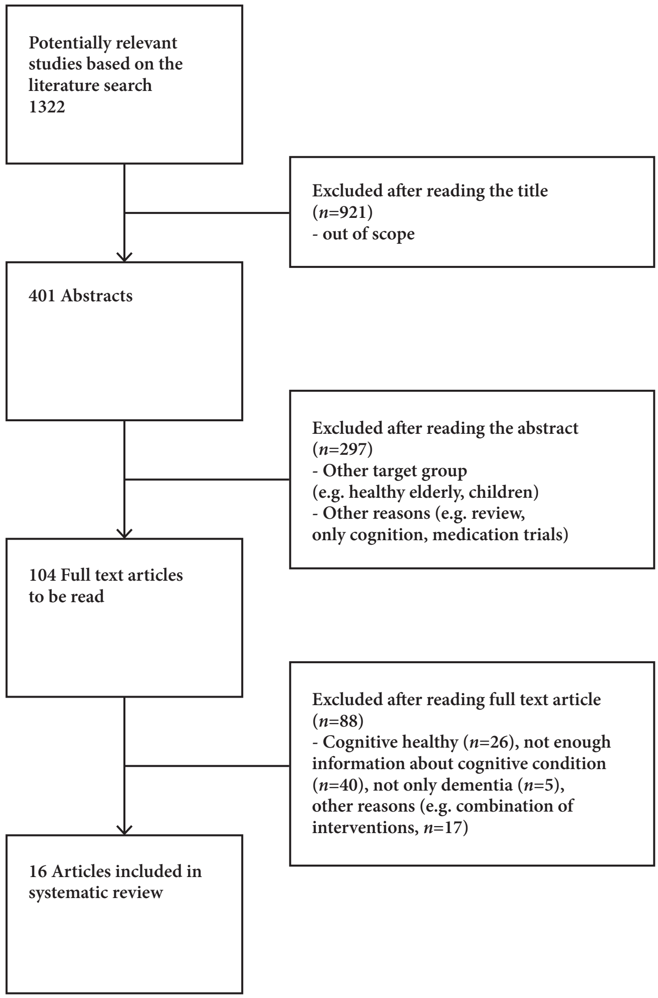

Figure 2.2. Flowchart of Literature Search and Study Selection

Methodological quality

After this initial process, the same reviewer scored the methodological quality of randomized and non-randomized trials using the Downs and Black checklist (Downs, Black 1998). From this validated and reliable checklist 26 questions were used in 4 different domains; reporting (score 0-11), external validity (score 0-3), internal validity-bias, which might indicate a difference between the groups (score 0-7), and internal validity-confounding, which might indicate the existence of a third variable (score 0-6). The maximum score is 27; a higher score indicates a greater methodological quality (Downs, Black 1998).

In addition, we used the list provided by David Sackett (Sackett, Straus et al. 2002). This list provides five different levels of evidence ranging from 1-5 were 1 is the best score available and 5 is the lowest score. Level 1A, systematic reviews of randomized controlled trials; 1B, Individual RCTs with narrow confidence intervals and double blind; 2A Systematic reviews of cohort studies; 2B Individual cohort studies and low-quality RCTs (e.g. single blind RCTs, quasi experimental design or low sample sizes); 3A Systematic reviews of case-control studies; 3B Case-controlled studies; 4 Case series and poor-quality cohort and case-control studies; 5 Expert opinion.

In this field of research it is impossible to perform a double blind intervention; therefore the highest level of evidence that can be reached is 2B.

Data extraction

From the studies selected for full analysis, the following data were extracted: Authors, publication year, study design, study analysis (Intention-to-treat or per-protocol), sample size, the rate of enrolment, the number of drop-outs, the participation rate, percentage of females, mean age, mean cognitive function, data regarding the type of intervention (progressive resistance training, endurance training, or a combination of strength, endurance, and balance training), duration (weeks/months), frequency (number of sessions per week), length of sessions (minutes), and the training intensity (light, moderate or high).

The rate of enrolment is the percentage of participants who met the inclusion and exclusion criteria and participated in the study. Drop-outs were participants who were included in the intervention but who left the program, due to hospitalization, sickness, death, and refusal. The participation rate is calculated based on the attendance of participants who participated in the study.

Statistical analyses

Effect sizes, Cohen's d (Cohen 1988) were calculated. If an effect size was calculated from an RCT the following formula was used (Cohen 1988, Robey 2004);

$$d = \frac{(\mathrm{post_{exp}} - \mathrm{pre_{exp}}) - (\mathrm{post_{cont}} - \mathrm{pre_{cont}})}{\sqrt{\left\{\frac{\left[\frac{\left(s^2_{\mathrm{pre-exp}}(n_{\mathrm{exp}}) + s^2_{\mathrm{pre-cont}}(n_{cont})\right)}{n_{\mathrm{exp}} + n_{\mathrm{cont}}}\right] + \left[\frac{\left(s^2_{\mathrm{post-exp}}(n_{\mathrm{exp}}) + s^2_{\mathrm{post-cont}}(n_{\mathrm{cont}})\right)}{(n_{\mathrm{exp}} + n_{\mathrm{cont}})}\right]}{2}\right\}}}$$

If a control group was not present the following formula was used (Thalheimer, Cook 2002);

$$d = \frac{\text{mean}_{\text{post}} - \text{mean}_{\text{pre}}}{\sqrt{\left[\frac{\left(s_{\text{pre}}^2(n_{\text{pre}}) + s_{\text{post}}^2(n_{\text{post}})\right)}{(n_{\text{pre}} + n_{\text{post}})}\right]}}$$

If the effect size had to be calculated from an F-value the following formula was used (Thalheimer, Cook 2002);

$$d = \sqrt{\left\{\text{F}\left[\left(\frac{(n_{\text{exp}} + n_{\text{cont}})}{(n_{\text{exp}} * n_{\text{cont}})}\right) * \left(\frac{(n_{\text{exp}} + n_{\text{cont}})}{(n_{\text{exp}} + n_{\text{cont}} - 2)}\right)\right]\right\}}$$

The overall effect size is calculated as the mean of individual effect sizes weighted for the sample size.

An effect size of 0.2 was taken to be indicative of a small, 0.5 of a medium, and 0.8 of a large effect size (Cohen 1992). If the effect size could not be calculated due to a lack of information in the article, the level of significance (*p*) is provided.

Table 2.1. Study Characteristics and Outcome Measures

Author	Design	*n*, (%♀)	Age M (sd)	MMSE Mean (sd)	Intervention	Functional outcome measure	*p*-value	Cohens' *d*	Analysis	Sackett Level of evidence	Downs & Black
Aman & Thomas, 2009	Case series	EG 40 77.5% CG 10 70%	78.8 (8.7) 81.1 (13.4)	1.4[a] (1.8) 1.7[a] (2.9)	3 weeks, 9 sessions, of 30 minutes, 50% aerobic, and 50% resistance exercises. 270 minutes in total.	Gait speed (6m) ADL	.001 .108	.50 .11	Intention to treat & Per-Protocol	4	Report 8 Ext Val 4 Int Val bias 3 Int Val conf 4 Total 19
Arkin, 2003	Case series	24, 66.6%	78.8 (8.04)	NA	2-8 semesters, 10 weeks each semester, 2 times a week 40-60 minutes. Strength, balance and aerobic exercises. 1600-9600 minutes in total.	6 Minute Walk Test Lower extremity strength	<.001 <.001	3.79 2.73	Per-Protocol	4	Report 3 Ext Val 0 Int Val bias 1 Int Val conf 0 Total 4
Binder, 1995	Case series	14 50%	88.7 (6.9)	14.0 (8.0)	8 weeks, 3 times a week, 50-60 minutes of strength, flexibility, speed of movement exercises. 1200-1440 minutes in total.	Gait speed Sit-to-Stand test Balance	>.05 >.05 .002	.29 .34 .53	Per-Protocol	4	Report 5 Ext Val 1 Int Val bias 3 Int Val conf 0 Total 9
Christofoletti et al., 2008	RCT	EG 17 71% CG 20 70%	72.9 (2.3) 79.4 (2.0)	12.7 (2.1) 14.6 (1.2)	EG, 6 months, 3 times a week, 1 hour a day To stimulate aerobic endurance, strength, balance, motor coordination, agility and flexibility. 4680 minutes in total CG, care as usual.	Timed Up and Go Berg Balance Scale	<.05 <.05	.89 3.02	NA	2B	Report 6 Ext Val 1 Int Val bias 4 Int Val conf 0 Total 11
Hageman & Thomas, 2002	Case series	26 88%	79.2 (6.6)	18.0 (6.2)	6 weeks, 2/3 times a week. Resistance training using therabands. 12 different exercises aimed at improving lower-limb strength 1 set of 15 repetitions. 2700 repetitions in total. Moderate intensity	Gait speed free (6m) Gait speed fast (6m) Timed Up and Go	.128 .045 .753	.20 .19 .06	NA	4	Report 6 Ext Val 1 Int Val bias 2 Int Val conf 0 Total 9
Kwak, 2008	RCT	EG 15 100% CG 15 100%	79.7 (6.64) 82.3 (7.09)	14.5 (5.34) 13.5 (7.04)	EG, 12 months, 2/3 times a week, 30-40 minutes. Start at 30% VO2 max, up to 60% VO2max. Therabands, swiss ball, shoulder wheel, staircase. 4550 minutes in total CG, care as usual	6 Minute Walk Test Muscle strength Muscle endurance Balance ADL	<.01 <.01 <.01 <.05 <.01	1.75 1.20 1.03 .247 1.32	NA	2B	Report 5 Ext Val 3 Int Val bias 4 Int Val conf 2 Total 14

Author	Design	n, (%♀)	Age M (sd)	MMSE Mean (sd)	Intervention	Functional outcome measure	p-value	Cohens' d	Analysis	Sackett Level of evidence	Downs & Black
Kuiack, 2004	Case series	8 63%	79 63-88[b]	17 13-20[b]	12 weeks, 2 days a week. Resistance training 3 sets of 8 repetitions for 5 exercises. Aimed at improving leg extension, shoulder press, hip abductor/adductor, chest/back and abdomen. 2880 repetitions in total.	Gait speed Leg extension Hip abductor Stair climb Chair rise, Balance parallel Balance semi tandem Balance tandem	ns <.01 <.01 ns ns ns ns ns	.18 1.95 3.33 1.18 .22 1.83 2.00 -.24	Per-Protocol	4	Report 4 Ext Val 1 Int Val bias 4 Int Val conf 1 Total 10
Netz et al., 2007	RCT	EG 15 CG 14	76.9 (6.72)	13.3 (5.83)	EG, 12 weeks, 2 times a week, 45 minutes (1080 minutes in total). Range of Motion, strength, coordi-nation, balance exercises for upper and lower body, group of 13-15 participants. CG, care as usual	Timed Up and Go Sit-to-Stand test	ns ns	-.25 -.02	Per-Protocol	2B	Report 7 Ext Val 1 Int Val bias 5 Int Val conf 4 Total 17
Pomeroy et al., 1999	RCT	EG 43 74% CG 38 74%	82.0 (8.0) 81.8 (8.4)	NA	EG, 10 half hour sessions of exercise to improve balance, strength, ROM (300 minutes in total). CG, nonphysical activities.	SMA 2 Minute Walk Test	.017 .048	NA NA	Intention to treat	2B	Report 5 Ext Val 1 Int Val bias 5 Int Vc 2 Total 13
Rolland et al., 2007	RCT	EG 67 72% CG 67 79%	82.8 (7.8) 83.1 (7.0)	9.7 (6.8) 7.0 (6.4)	EG, 12 months, 2 times a week, 60 minutes 88 sessions in total. Aerobic, strength, flexibility and balance training. Encouraged to walk fast. Strength training focused on the lower extremity. 5280 minutes in total CG, care as usual	Gait speed Up and Go One Leg Balance ADL	.002 .31 .34 .02	.32 -.10 NA .22	Intention to treat	2B	Report 11 Ext Val 1 Int Val bias 6 Int Val conf 5 Total 23
Santana-Sosa et al., 2008	RCT	EG 8 63% CG 8 63%	76 (4) 73 (4)	20.1 (2.3) 19.9 (1.7)	EG, 12 weeks, 3 times a week 75 minutes. Joint mobility, resistance and coordination exercises. Individualized. 2700 minutes in total CG, care as usual	Up and Go 2 Minute Step Test Tinetti Sit-to-Stand test ADL Katz ADL Barthel	<.001 .002 <.001 <.001 .019 <.001	2.37 .58 3.59 3.14 NA 5.06	NA	2B	Report 6 Ext Val 1 Int Val bias 5 Int Val conf 5 Total 17

Schnelle et al., 1995	RCT	EG 36 CG 40	85.1 (8.2)	11.6	EG, 8 weeks, 5 times a week, 4 sessions a day. Repetition of exercises specific to functional skills. Ie. Sit to stand exercises, walking a little bit further when going to the toilet. CG, care as usual.	Walking speed Walking endurance	.06 <.05	NA .50	NA	2B	Report 4 Ext Val 2 Int Val bias 3 Int Val conf 3 Total 12
Steinberg et al., 2009	RCT	EG 14 71.4% CG 13 69.2%	76.5 (3.9) 74.0 (8.1)	20.1 (5.1) 15.5 (5.4)	EG, 12 weeks, get 6 aerobic points, 4 strength points and 4 balance points a week. With different exercises, aiming to improve aerobic, strength and balance. CG, home safety review	Gait speed YPAS Sit-to-Stand test	.77 .76 .22	NA NA NA	Intention to treat	2B	Report 6 Ext Val 0 Int Val bias 4 Int Val conf 4 Total 14
Tappen et al., 2000	RCT	EG 20 CG 22	84.3 (7.5) 89.6 (6.5)	10.8 (6.0) 12.5 (5.9)	EG, 16 weeks, 3 times a week, 30 minutes. Walking & conversation. 1440 minutes of walking in total. CG, conversation only	Six minute walk	P=.01	.31	Per-Protocol	2B	Report 7 Ext Val 1 Int Val bias 5 Int Val conf 3 Total 16
Thomas & Hageman, 2003	Case series	28	80.0 (5.57)	17.8 (7.17)	6 weeks, 3 sessions a week. Resistance exercise using therabands. 1 set of 15 repetitions for 12 exercises aimed at improving lower-limb strength. 2700 repetitions in total. Moderate intensity	Gait speed free Gait speed fast Timed Up and Go Knee extensor right Knee extensor left Sit-to-Stand test	.19 .06 .71 .44 .46 .02	-.11 .10 .85 .14 -.04 .50	NA	4	Report 7 Ext Val 2 Int Val bias 4 Int Val conf 2 Total 15
Toulotte et al., 2003	RCT	EG 10 CG 10	81.0 (5.6) 81.9 (4.1)	14.7 (7.6) 18.0 (5.4)	EG, 16 weeks, 2 sessions a week, 45 minutes. Muscular strength, static and dynamic, balance, flexibility and proprioception, exercises. Five persons a group. 1440 minutes in total. CG, care as usual.	Walking speed Timed Up and Go Balance	.015 .001 <.01	NA NA NA	NA	2B	Report 8 Ext Val 0 Int Val bias 4 Int Val conf 3 Total 15

[a] score on the Saint Louis University Mental Status Examination.

[b] range.

MMSE, Mini-Mental State Examination; Report, reporting; Ext Val, External Validity; Int Val bias, Internal validity bias; Int Val conf, Internal validity confounding; EG, Exercise group; CG, Control Group; ADL, Activities of Daily Living; NA, not available; SMA, Southampton mobility assessment; YPAS, Yale physical activity survey.

2.3 Results

Study characteristics

The literature search and hand search of references revealed 1322 potentially relevant studies. After the initial screening on title and abstract level, 104 full text articles were retrieved for further analyses. Finally, a total of sixteen studies met the inclusion criteria and were incorporated in this review (Figure 2.2; Aman, Thomas 2009, Binder 1995, Christofoletti, Oliani et al. 2008, Kuiack, Campbell et al. 2004, Pomeroy, Warren et al. 1999, Schnelle, MacRae et al. 1995, Steinberg, Leoutsakos et al. 2009, Hageman, Thomas 2002, Netz, Axelrad et al. 2007, Rolland, Pillard et al. 2007, Tappen, Roach et al. 2000, Arkin 2003, Santana-Sosa, Barriopedro et al. 2008, Toulotte, Fabre et al. 2003, Thomas, Hageman 2003, Kwak, Um et al. 2008). Details of these studies, the results, effect sizes and level of significance, are presented in Table 2.1. Information about the rate of enrolment, the number of dropouts, and the participation rate are presented in Table 2.2. In total, there were ten randomized controlled trials of level 2B evidence with an average score on the Downs and Black questionnaire (DB) of 15.2 (range 11 - 23). These studies scored 56.3% of the maximum methodological score; reporting, 60.2%; external validity, 36.5%; internal validity bias, 66.1%; internal validity confounding, 51.6%. There were six nonrandomized trials of level 4 evidence and an average score of 11 points on the DB (range 4 - 19). These six studies scored 40.7% of the maximum methodological score; reporting 50%, External validity 44.3%, internal validity bias 44.3%, internal validity confounding 19.5%.

Five studies performed a per-protocol analysis, three performed an Intention-to-treat analysis, and one study performed both analyses, seven studies did not present this information.

Table 2.2. Rate of Enrolment, Number of Dropouts and Participation Rate

Study	Eligible	Rate of enrolment	n_{pre}	Dropouts	Participation rate
Aman & Thomas, 2009	55	91%	50	10; Did not want to exercise	30.7%
Arkin, 2003	NA	NA	24	NA	Student 100%; Caregivers 60% to 80%
Binder, 1995	34	100%	34	9; 8 did not want to exercise, 1 responsible proxy revoked consent	75%
Christofoletti et al., 2008	63	86%	54	13; 3 died, 3 for unknown reasons, 3medication use, 4 clinical instability	NA
Hageman & Thomas, 2002	75	35%	26	NA	NA
Kwak, 2008	NA	NA	30	NA	NA
Kuiack, 2004	13	85%	11	3; unrelated to trainings program	100%
Netz et al., 2007	50	58%	29	4; being moved, getting help at home	>70%
Pomeroy et al., 1999	91	89%	81	NA	80%
Rolland et al., 2007	242	55%	134	24; dead 15, change of institution 8, discontinued 4.	19.4%> 2/3 of sessions. 28.4%, 1/3-2/3 of sessions. 41.8% <1/3 of sessions. 10.4% 0 sessions
Santana-Sosa et al., 2008	NA	NA	16	NA	98.9%
Schnelle et al., 1995	99	95%	94	18; death, transfer, hospitalization	75%
Steinberg et al., 2009	30	90%	27	NA	Overall 75%
Tappen et al., 2000	NA	NA	71	6	Walking + conversation 75%
Thomas & Hageman, 2003	NA	NA	NA	NA	NA
Toulotte et al., 2003	NA	NA	20	NA	NA

NA, Not available

Participants Population

Ten studies provided information about eligible candidates; seven studies showed a rate of enrolment of >85% (Aman, Thomas 2009, Binder 1995, Christofoletti, Oliani et al. 2008, Kuiack, Campbell et al. 2004, Pomeroy, Warren et al. 1999, Schnelle, MacRae et al. 1995, Steinberg, Leoutsakos et al. 2009), three studies had a rate between 35%-58% (Hageman, Thomas 2002, Netz, Axelrad et al. 2007, Rolland, Pillard et al. 2007). Eight studies provided the number of dropouts, of which six studies had a drop-out rate between 18%-27%

(Aman, Thomas 2009, Binder 1995, Christofoletti, Oliani et al. 2008, Kuiack, Campbell et al. 2004, Schnelle, MacRae et al. 1995, Rolland, Pillard et al. 2007); one had a drop-out rate of 14% (Netz, Axelrad et al. 2007) and the last one of 8% (Tappen, Roach et al. 2000). The reasons for dropouts were hospitalization, death, being moved, and refusing to exercise. Not one single study reported dropouts due to negative adverse effects of the intervention. No relationship could be found between the duration of the intervention, i.e. the number of weeks or months, and the dropout rate (r = .301, p = .468, Spearman's rho; Aman, Thomas 2009, Binder 1995, Christofoletti, Oliani et al. 2008, Kuiack, Campbell et al. 2004, Schnelle, MacRae et al. 1995, Netz, Axelrad et al. 2007, Rolland, Pillard et al. 2007, Tappen, Roach et al. 2000). However, there was a moderate to strong, positive, and significant correlation (r = .829; p = .042, Spearman's rho) between the level of global cognitive functioning, measured with the MMSE, and the dropout rate (Binder 1995, Christofoletti, Oliani et al. 2008, Kuiack, Campbell et al. 2004, Netz, Axelrad et al. 2007, Rolland, Pillard et al. 2007, Tappen, Roach et al. 2000). In other words, if participants had a higher score on the MMSE, the chance that they dropped out of the study increased. The participation rate, calculated over eight studies (Binder 1995, Schnelle, MacRae et al. 1995, Steinberg, Leoutsakos et al. 2009, Netz, Axelrad et al. 2007, Tappen, Roach et al. 2000, Arkin 2003, Santana-Sosa, Barriopedro et al. 2008), was 81.4%. In contrast with the dropout rate, the participation rate is higher if the cognitive level increased (seven studies, r = .729, p = .063, Spearman's rho; Binder 1995, Kuiack, Campbell et al. 2004, Schnelle, MacRae et al. 1995, Steinberg, Leoutsakos et al. 2009, Rolland, Pillard et al. 2007, Tappen, Roach et al. 2000, Santana-Sosa, Barriopedro et al. 2008). One study found that the participation rate increased if students were responsible for the execution of the intervention instead of the family caregivers (Tappen, Roach et al. 2000). A second study showed that a conversation during a walking intervention has a beneficial influence on the participation rate (Tappen, Roach et al. 2000). However, one study contrasted sharply with the other studies (Rolland, Pillard et al. 2007). In the latter study only 19.4% of the participants performed more than two-third of the sessions and around 50% of the participants performed more than one-third of the sessions. However, 10% did not participate in any exercise. The participants in this latter study had the lowest score on cognition, and the inclusion and exclusion criteria were not very selective (Rolland, Pillard et al. 2007).

The effect of physical interventions on Gait speed, Endurance, Functional mobility, Lower extremity strength and Balance.

Gait speed was assessed in six different studies, two level 2B studies (Rolland, Pillard et al. 2007, Toulotte, Fabre et al. 2003), with, respectively, 23 and 5 on the Downs and Black questionnaire (DB) and four level 4 studies, with respectively 19, 9, 10, and 15 on the DB (Aman, Thomas 2009, Kuiack, Campbell et al. 2004, Hageman, Thomas 2002, Thomas, Hageman 2003). Only in one level 2B study the effect size (ES) could be calculated (d = *.32*, p = .002; Rolland, Pillard et al. 2007), in the other level 2B a significant improvement in gait speed (p = .015) was observed (Toulotte, Fabre et al. 2003). A moderate ES (d = .50, p <.001) was obtained in a level 4 study (Aman, Thomas 2009). The latter three studies used multi-component interventions (i.e. a combination of strength, endurance, flexibility training) with durations ranging from three weeks to twelve months. In contrast, level 4 studies with progressive resistance training of six and twelve weeks found almost no effect on normal gait speed ($d \leq .2$; Kuiack, Campbell et al. 2004, Hageman, Thomas 2002, Thomas, Hageman 2003). Concerning fast gait speed a low ES was found after progressive resistance training (d = .19, p = .045; Hageman, Thomas 2002). No information was available on the effect of multi-component interventions on fast gait speed.

Endurance was assessed in five studies, four level 2B studies, which had between 13-17 points on the DB (Pomeroy, Warren et al. 1999, Tappen, Roach et al. 2000, Santana-Sosa, Barriopedro et al. 2008, Kwak, Um et al. 2008), and one level 4 study with 4 points on the DB (Arkin 2003). All studies found a positive effect of physical activity on the endurance capacity (Pomeroy, Warren et al. 1999, Tappen, Roach et al. 2000, Arkin 2003, Santana-Sosa, Barriopedro et al. 2008, Kwak, Um et al. 2008). In the multi-component interventions the effect size was larger, if the duration of the intervention was longer, ranging from d = 3.79 after an intervention of one to four years, to d = .58 in an intervention of 12 weeks (Arkin 2003, Santana-Sosa, Barriopedro et al. 2008, Kwak, Um et al. 2008). A solely walking intervention of 16 weeks had the lowest ES (d = .31; Tappen, Roach et al. 2000). No information is available on the effect of progressive resistance training on endurance.

Functional mobility was assessed in eight studies, six level 2B studies, which all existed of multicomponent interventions (Christofoletti, Oliani et al. 2008, Pomeroy, Warren et al. 1999, Netz, Axelrad et al. 2007, Rolland, Pillard et al. 2007, Santana-Sosa, Barriopedro et al. 2008, Toulotte, Fabre et al. 2003) and two level 4 progressive resistance training interventions (Hageman, Thomas 2002, Thomas, Hageman 2003). Only from two level

2B studies ES could be calculated and appeared to be large (*d* = .89, $p < .05$; *d* = 2.37, $p < .001$; Christofoletti, Oliani et al. 2008, Santana-Sosa, Barriopedro et al. 2008). From the remaining four studies two did find a significant improvement (Pomeroy, Warren et al. 1999, Toulotte, Fabre et al. 2003), and two studies did not (Netz, Axelrad et al. 2007, Rolland, Pillard et al. 2007). Possible explanation for the negative results are the short duration of the intervention (Netz, Axelrad et al. 2007) or the qualitative score which might be less suitable then quantitative scores in this specific population (Rolland, Pillard et al. 2007). However, it should be noted that the studies without a significant improvement had a higher score on the DB, which indicates that their methodological quality is higher (17 and 23, compared to 17, 15, 13 and 11 points respectively). Both level four studies did not find an improvement on functional mobility. These two studies used progressive resistance training and had a duration of 6 weeks (Hageman, Thomas 2002).

Lower extremity strength was assessed in seven different studies. There were three level 2B studies with a range of 13-17 points on the DB which used multi-component interventions (Netz, Axelrad et al. 2007, Santana-Sosa, Barriopedro et al. 2008, Kwak, Um et al. 2008) and four level 4 studies, with a range of 4-15 points on the DB (Binder 1995, Christofoletti, Oliani et al. 2008, Arkin 2003, Thomas, Hageman 2003). Two level 2B studies found large effect sizes on lower extremity strength (*d* = 3.14; *d* = 1.20; Santana-Sosa, Barriopedro et al. 2008, Kwak, Um et al. 2008). The other level 2B study, did not find any effect (*d* = -.02; Netz, Axelrad et al. 2007). This latter study had the fewest minutes spend on the intervention from all level 2B studies. There were two level four studies who used a multi-component intervention (Binder 1995, Arkin 2003) and two that only used progressive resistance training (Hageman, Thomas 2002, Thomas, Hageman 2003). Although the interventions differed, the largest ES were found in the interventions with the longest duration. A multi-component interventions of 1-4 years (*d* = 2.73; Arkin 2003) outperformed a multi-component interventions of 8 weeks (*d* = .34; Binder 1995). In accordance, a progressive resistance training of 12 weeks (*d* = 1.95; Kuiack, Campbell et al. 2004) outperformed a progressive resistance training of 6 weeks (*d* = .14) (Thomas, Hageman 2003).

Balance was assessed in seven studies, five multi-component level 2B studies (Christofoletti, Oliani et al. 2008, Rolland, Pillard et al. 2007, Santana-Sosa, Barriopedro et al. 2008, Toulotte, Fabre et al. 2003, Kwak, Um et al. 2008) and two level 4 studies with one using multi-component intervention, and the other using a progressive resistance training (Binder 1995, Kuiack, Campbell et al. 2004). Four of the five level 2B studies found a positive effect on balance with ES varying from low to very high (*d* = .247-3.59). The studies with a longer duration or a higher frequency had a higher ES. In one level 2B study, probably caused by the use of a qualitative score instead of quantitative score no significant improvement was found (Rolland, Pillard et al. 2007). From the two level 4 studies, one multi-component study found a moderate ES after a multicomponent intervention of eight weeks (Binder 1995). The other study used progressive resistance training, and found a high but non-significant ES (*d* = 2.00) after twelve weeks (Kuiack, Campbell et al. 2004).

The effect of physical interventions on BADL

In the majority of the studies selected for this review, BADL was not assessed. Only four studies investigated the effects of exercise on BADL; all these studies used multi-component interventions. There were three level 2B studies, two studies found a very high ES (*d* = 1.32; *d* = 5.78; Santana-Sosa, Barriopedro et al. 2008, Kwak, Um et al. 2008), the other one had a low ES (*d* = .22; Rolland, Pillard et al. 2007). The latter study achieved the highest points on the DB, 23 compared to 14 and 17 for the first two studies. The positive effects of physical activity on BADL was observed in participants with mild (Mean MMSE 20), moderate (Mean MMSE 14), and severe dementia (Mean MMSE 8.8). The interventions ranged from 12 weeks to 12 months. One study, level 4, did not find a significant improvement in BADL performance. However, this latter study had a duration of three weeks with 270 minutes of exercise in total (Aman, Thomas 2009).

The improvements in BADL were supported by improvements in physical functioning in two studies (Santana-Sosa, Barriopedro et al. 2008, Kwak, Um et al. 2008). The third study, did find an improvement in gait speed, but not on balance and mobility. However, the latter finding might be caused by the use of qualitative scores instead of quantitative scores (Rolland, Pillard et al. 2007).

The overall effect of physical activity

To compare overall effects, the mean effect sizes of the different outcome measures were calculated (Table 2.3). It is interesting that the extreme effect sizes, very high or low, correspond with a relatively low methodological quality. Overall, the moderate effect sizes are found in studies with more acceptable methodological scores.

Table 2.3. Mean Effect Sizes and Mean Methodological Quality Weighted with Sample Size.

Outcome measures	Number of Studies	Effect Size (range)	Methodological Quality [a] (range)
Gait speed (normal)	6	0.29 (-.11 – .50)	18.8 (9 – 23)
Gait speed (fast)	2	0.14 (.10 – .19)	12.1 (9 – 15)
Endurance	5	1.08 (.31 – 3.79)	12.7 (4 – 17)
Functional mobility	6	0.28 (-.25 – 2.37)	18.2 (9 – 23)
Lower extr strength	7	0.85 (-.04 – 3.14)	13.3 (4 – 17)
Balance	5	1.76 (-.24 – 3.59)	12.1 (9 – 17)
ADL	4	0.68 (.11 – 5.06)	20.5 (14 – 23)

[a] Score based on Downs and Black, theoretical range 0 (lowest quality) to 26 (highest quality)
Extr, extremity; ADL, Activities of daily living

2.4 Discussion

The first goal of this systematic review was to investigate whether physical activity improves physical functioning, i.e. gait speed, functional mobility, balance, endurance, lower-extremity strength, and BADL in elderly with dementia. A second goal was to formulate guidelines for the most effective training program.

Before we are able to answer these questions properly it is important to get more insight into the participants. Are these persons representative of the total population of elderly persons with dementia? Therefore, it is necessary to know how many people were interested in participating, and how many were allowed to enroll in the intervention program. From this latter group it is well worth it to know how they complied with the protocol. We found that the majority of the participants were willing to participate. Seven out of ten studies found a rate of enrollment of at least 85%. Three studies had a lower rate of inclusion probably caused by more specific inclusion and exclusion criteria regarding cognitive functioning or mobility. Of the participants who started with the intervention, about 20-25% dropped out for different reasons (e.g. death, hospitalization, refusing). Not one dropped out due to adverse effects of the intervention. It is remarkable that participants with higher scores on the MMSE have higher dropout rates, but also higher participation rates. We speculate that people with higher scores on the MMSE have better memories and stronger wills of their own. Therefore a part of this group will indicate that they do not want to continue the program (dropout), but another part will decide, by themselves, that they do want to continue, which results in higher participation. From the participants in the interventions the average participation rate was around 80%, though large differences were found. The participation rate could be increased by talking during the interventions or by using students to guide the participants, instead of family caregivers (Tappen, Roach et al. 2000, Arkin 2003). The results regarding rates of enrollment, drop outs, and participation rates do differ between the different studies, but not enough information is provided to analyze this difference in detail. In the majority of studies, physical exercise is an activity which was performed and sustained by most elderly individuals. Generally, the rates of enrollment and the participation rates suggest that elderly with dementia like to take part in interventions involving physical activity. Although this is important information, less than 70% of the included studies provided information regarding rate of enrollment, drop-out rates and participation rates. We recommend that future studies provide this information.

Elderly with dementia can take part in physical activity interventions, but they also benefit from ordinary exercise. Physical activity interventions in elderly with dementia lead to an improvement in physical performance, as presented by overall effect sizes (Table 3). The largest improvements on gait speed, functional mobility, and balance were seen after multi-component interventions, and not after progressive resistance training. A positive improvement was also found in endurance after multi-component interventions. Lower-extremity strength increased after multi-component, as well as progressive resistance training, but it is unclear which interventions lead to the best outcome. In most cases, the largest improvements in physical functioning were found after interventions with the largest training volume. However, it should be noted that only sixteen studies are incorporated in this systematic review, each with different durations, ranging from three weeks to twelve months, and different components within their interventions. Therefore, it is important to get more insight into the effects of different durations, different training volume, and the different components within each intervention (e.g. exercises, intensity), in order to understand the mechanism behind the intervention. With the presented data we are unable to assess the quality of the different components of each intervention by themselves. Therefore it is not possible to determine the dose-response relationship in detail, and consequently, we can only provide more general guidelines. Based on the presented data, the largest improvements are found after interventions with a duration of at least twelve weeks, with a frequency of three times a week, for 45-60 minutes per session. Improvements were seen amongst participants with mild (Santana-Sosa, Barriopedro et al. 2008), moderate (Kwak, Um et al. 2008), and severe (Rolland, Pillard et al. 2007) cognitive problems. This indicates that physical activity is beneficial in each stage of cognitive decline. Our findings are in line with physical activity intervention studies in elderly without cognitive decline, and elderly in long term care institutions (Kolbe-Alexaner, Lambert et al. 2006, Forster, Lambley et al. 2010).

The effect of physical activity on BADL can be hypothesized using the ICF model. An improvement in body functions, such as gait speed, functional mobility, endurance, lower extremity strength, and balance, can lead to an improvement in activities, such as BADL, which might lead to an increase in participation. However, BADL was only assessed in four studies. From these four studies, three studies with the largest training volume and highest methodological quality found improvements in BADL. These improvements were found in patients with mild, moderate, and severe dementia. Among the three studies, two found an improvement in all the other physical measurements, which is in accordance with the relationship between physical performance and BADL. However, one study did not find improvements on all measurements; more specifically it did not find improvements on the qualitative scoring measurement (Up and Go, Single-stance). It might be that due to the characteristics of the population floor effects appeared. Due to the small number and the mixed results it is not possible to determine if an improvement in physical performance would mediate the effect of exercise on BADL. It could also be mediated by cognition, for example. Future studies should focus on the effect of physical activity interventions on physical functioning and BADL, and take other possible mediating factors, like cognition, and moderating factors like depression, apathy and agitation into account. This is necessary to get more insight into the mechanism by which physical activity works.

Although we tried to ensure that all studies referring to elderly with dementia and physical activity were included in this review, we cannot rule out the possibility that we have missed some. For example, in the literature we found some studies that were performed in nursing homes, and we found studies where participants had a score of 24 or lower on the MMSE. However, if we were not absolutely sure that the participants of these latter studies had dementia, these studies were excluded. Therefore, we recommend that future studies try to describe their population as specifically as possible. Preferably, their descriptions should be supported with additional information, such as the etiology of the disease, a measurement of cognition like the MMSE (Folstein, Folstein et al. 1975), global assessment of functioning such as the Clinical Dementia Rating (CDR), or the Global Deterioration Scale (Reisberg, Ferris et al. 1982). Moreover, the studies that were included in this review were, in general, of mediocre quality according to the Blacks and Downs list. For all the level 2B studies compiled, an average of 56% of the maximum methodological score was obtained. Especially on reporting, external validity and internal validity (confounding) information was missing. This indicates the urgent need for high quality intervention studies. Another important aspect is the choice of measurements. Elderly with dementia are a very specific population, and probably for that reason the psychometric qualities of multiple measurements have not been studied thoroughly. We recommend that measurements are chosen in such a way that effect sizes can be calculated and floor effects should not be possible. It is important that measurements are sensitive for change in such a vulnerable population.

2.5 Conclusion

Physical activity can be beneficial in all stages of dementia. However, to get more insight in the mechanism underlying the effects of physical activity we need more high-quality studies. It is of the utmost importance that specific information about the intervention is well documented, such as the participants, the intensity, duration, and the different components. This information is necessary in order to interpret the external validity, possible confounders, and the dose-response relationship in detail. Future studies should focus on the effect of physical activity interventions on physical functioning and on BADL, and should take other mediators, like cognition, into account. Based on the presented data, it can be concluded that multi-component interventions, with a high training volume lead to an improvement in physical performance and BADL, and outperform walking and progressive resistance training intervention in most aspects. The largest improvements were found after interventions with a duration of twelve weeks or more, and a frequency of three times a week, with 45-60 minutes a session. Practical guidelines and recommendations for future studies are summarized in Table 2.4.

Table 2.4. Summary of Recommendations

Classification	Recommendations
Methodological issues	Provide detailed information about the diagnosis, cognition, participation rate of the participants, drop-outs, and rate of enrolment Choose measurements that are sensitive for change, valid, and reliable for the goal population Present the data in such way that more calculation, like ES, can be performed
Questions for further research	Regarding the paucity of studies assessing BADL after physical exercise in elderly with dementia: How can exercise optimally influence BADL? Dose-response relationship: What are the optimal duration, frequency and intensity? Type of activities: Are some components more important than others? What is the best combination of components? Working mechanisms: Can mediating factors be identified (e.g. cognition) Intervention related to cognitive level: Should an intervention be changed if the cognitive level changes?
Practical guidelines	Offer exercise in all stages of dementia Use multicomponent interventions A duration of twelve weeks or more Exercise at least three times a week Exercise 45-60 minutes per session