

Exercise Program for Nursing Home Residents with Alzheimer's Disease: A 1-Year Randomized, Controlled Trial

Yves Rolland, MD, PhD,^{*†‡§} Fabien Pillard, MD,[†] Adrian Klapouszczak, MD,[†]
Emma Reynish, MD,^{*§} David Thomas, MD,[‡] Sandrine Andrieu, MD, PhD,[§]
Daniel Rivière, MD[†] and Bruno Vellas, MD, PhD^{*§}

OBJECTIVES: To investigate the effectiveness of an exercise program in improving ability to perform activities of daily living (ADLs), physical performance, and nutritional status and decreasing behavioral disturbance and depression in patients with Alzheimer's disease (AD).

DESIGN: Randomized, controlled trial.

SETTING: Five nursing homes.

PARTICIPANTS: One hundred thirty-four ambulatory patients with mild to severe AD.

INTERVENTION: Collective exercise program (1 hour, twice weekly of walk, strength, balance, and flexibility training) or routine medical care for 12 months.

MEASUREMENTS: ADLs were assessed using the Katz Index of ADLs. Physical performance was evaluated using 6-meter walking speed, the get-up-and-go test, and the one-leg-balance test. Behavioral disturbance, depression, and nutritional status were evaluated using the Neuropsychiatric Inventory, the Montgomery and Asberg Depression Rating Scale, and the Mini-Nutritional Assessment. For each outcome measure, the mean change from baseline to 12 months was calculated using intention-to-treat analysis.

RESULTS: ADL mean change from baseline score for exercise program patients showed a slower decline than in patients receiving routine medical care (12-month mean treatment differences: ADL = 0.39, $P = .02$). A significant difference between the groups in favor of the exercise program was observed for 6-meter walking speed at 12 months. No effect was observed for behavioral disturbance, depression, or nutritional assessment scores. In the intervention group, adherence to the program sessions in exploratory analysis predicted change in ability to perform ADLs. No adverse effects of exercise occurred.

From the ^{*}Internal Medicine Service and Gerontology Clinic, Hôpital La Grave-Casselardit, Toulouse, France; [†]Department of Exploration of Respiratory Function and Sports Medicine, Hôpital Larrey, Toulouse, France; [‡]Geriatric Research, Education and Clinical Center, St. Louis VA Medical Center, St. Louis, Missouri; and [§]Inserm Unit 558, Toulouse, France.

Address correspondence to Yves Rolland, Service de Médecine Interne et de Gériatrie Clinique, Pavillon Junot, 170 avenue de Casselardit, Hôpital La Grave-Casselardit, Toulouse, France. E-mail: yvesmrolland@yahoo.fr

DOI: 10.1111/j.1532-5415.2007.01035.x

CONCLUSION: A simple exercise program, 1 hour twice a week, led to significantly slower decline in ADL score in patients with AD living in a nursing home than routine medical care. *J Am Geriatr Soc* 55:158–165, 2007.

Key words: Alzheimer's disease; nursing home; physical activity; RCT; disability

Alzheimer's disease (AD) results in a progressive deterioration in the ability to perform activities of daily living (ADLs).¹ During the last decade, considerable effort has been applied to develop therapeutic agents to slow the gradual impairment in cognitive function that comes with AD. Slowing the loss of ability to perform ADLs has received less attention. The loss of ADLs is a key determinant of a patient's quality of life,² institutionalization,³ risk of death,⁴ and burden for the caregiver and the community.⁵

Benefits of nonpharmacological approaches in the management of people with AD have been highlighted,^{6,7} but randomized, controlled trials are scarce. Interventions, such as an exercise program, have been shown to improve function even in frail nursing home residents⁸ and may yield an important and potent protective factor against ADL decline. Moreover, an exercise program may yield benefits in the management of falls,⁹ malnutrition,¹⁰ behavioral disturbances,¹¹ and depression¹²—key problems for people with AD. Exercise programs may be all the more relevant for people with AD living in nursing homes, because they spend a protracted period in the nursing home,¹³ with a high rate of functional decline;¹⁴ they are frequently physically inactive;¹⁵ and long-term exercise programs are easier to organize in institutions than in the community. To the authors' knowledge, the effect of an exercise program on the ability of people with AD to perform ADLs has not previously been studied. The effectiveness of an exercise program in nursing homes could lead to altered standards of care for institutionalized people with AD.

The aim of this study was to determine whether an exercise program would reduce ADL decline in people with AD living in nursing homes over a 12-month period in a

randomized, controlled trial. It was also hypothesized that an exercise program could improve physical performance and nutritional status and reduce psychological disturbance.

METHODS

Study Design

This study was a 12-month multicenter, randomized, controlled, single-blind study of parallel groups of ambulatory subjects with AD living in five nursing homes in Toulouse, France. Written consent was obtained from patients and caregivers or legal guardians. The institutional review boards of the nursing homes involved approved the study.

After a screening visit and informed consent, subjects were randomly assigned to the exercise program or to routine medical care (Figure 1). Staff not involved in intervention or assessment performed separate randomization at each site by lottery draw. Subjects, rather than nursing homes, were randomized to intervention to avoid confounding effects of the setting area. A single geriatrician (AK) who was blinded to the intervention assignment measured outcomes at baseline, 6 months, and 12 months on different days from the intervention.

Study Participants

All resident charts were first screened for diagnosis of AD or a Mini-Mental State Examination (MMSE) score of less

than 25.¹⁶ A trained geriatrician (AK) then confirmed the diagnosis of AD for all subjects. In case of doubt, a second opinion was obtained. To be eligible for inclusion, subjects were required to meet the National Institute of Neurological and Communicative Diseases and Stroke/Alzheimer Disease and Related Disorders Association criteria¹⁷ for probable or possible AD, to have lived in the nursing home for at least 2 months, and to be able to transfer from a chair and walk at least 6 meters without human assistance. Subjects were excluded if there was evidence of vascular dementia or Parkinson's disease, planned transfer from the nursing home for surgery in the year to come, a cardiac condition that might deteriorate during exercise, or diagnosis of a terminal illness with a life expectancy of less than 6 months. Enrollment lasted 2 weeks.

Of a total population of 429 nursing home residents, 242 met study criteria. Informed consent was obtained for 134 residents (33, 43, 32, 10, and 16 in each nursing home).

Physical Exercise Program

The same occupational therapist conducted all exercise sessions. Each exercise group consisted of two to seven subjects (mean 5.2) selected according to their baseline physical performance scores, MMSE score, and behavior disturbances and affinity between participants. Changes in exercise group composition occurred during the year depending on acute events such as illness, behavioral disturbance, or changes in physical performance.

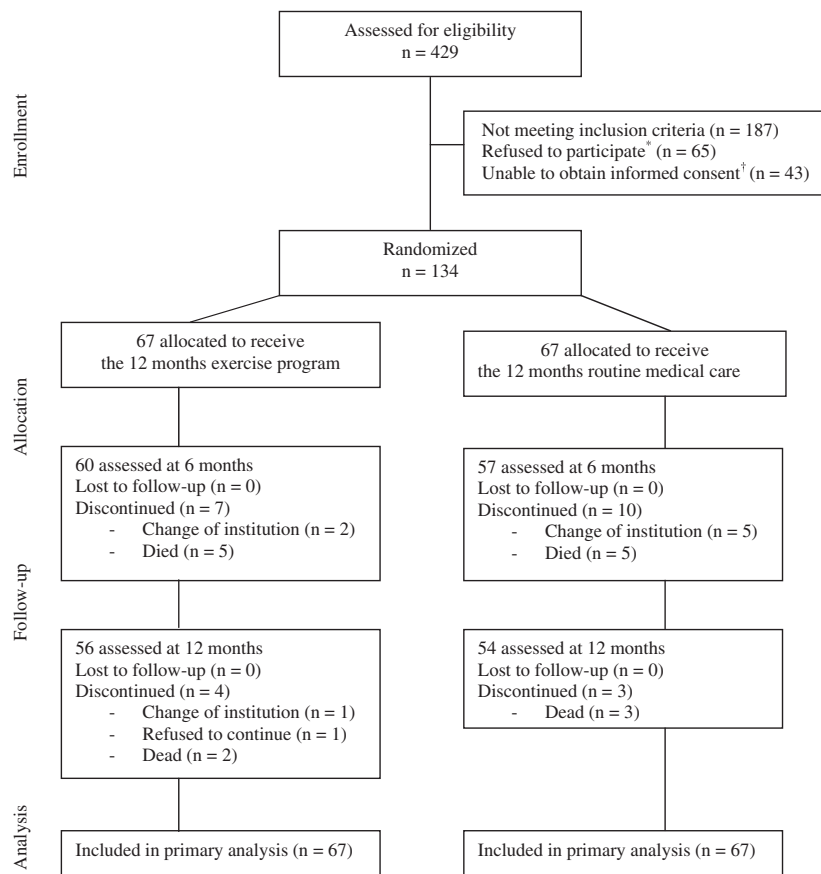


Figure 1. Progress of the participants through the 12-month exercise program. *Refused by the resident. †From the caregiver or the legal guardian.

To enhance adherence to the exercise program and based on previous experience,¹⁸ exercises began at light intensity and gradually increased over the first month of the intervention. Exercises were individualized, based on the participants' behavioral readiness for the proposed program. Music accompanied the sessions.¹⁹

The exercise program consisted of one session of 1 hour during the afternoon, twice a week, separated by at least 2 days (except during vacation or absence of the occupational therapist). Between February 2004 and February 2005, a total of 88 sessions were proposed to each participant.

The exercise program included aerobic, strength, flexibility, and balance training. It was based on previous experience¹⁸ and interventions described by others^{20,21} for frail and cognitively impaired subjects.

During enrollment in each nursing home, an inside circular walking trail was created and adapted for each exercise group. This trail went past the room of each exerciser to enhance adherence to the session. Participants were grouped on the course and encouraged by the occupational therapist. The same trail was used during the 12 months to ritualize the session and encourage confidence.

Walking was required for at least half of the session. After stretching warm-up, subjects were encouraged to walk fast to reach moderate breathlessness but not exhaustion. The session was interspersed with strength, flexibility, and balance training at predetermined stations along the trail where guardrails in the corridor or foam rubber ground sheets could be used for safety.

Strength training was adapted to the participant and focused on lower extremity strength.²² Exercises included squatting at different levels (or repeated stand ups from a chair), lateral elevation of the legs in a standing position, and rising on the toes. Participants were asked to imitate simple flexibility exercises demonstrated by the occupational therapist. Balance training consisted of small step trial exercises using cones and hoops on the ground and one- or two-leg balance exercises on the ground or on foam-rubber ground sheets.

Control Group

Participants assigned to the control group received routine medical care. This group had no exercise or specific behavior management training. The study design stipulated no restriction in nursing, physiotherapy, medical care, advice, or any other healthcare support.

Primary Outcome Measure

The primary effectiveness outcome was decline from baseline in Katz ADL score²³ of exercise participants compared with decline in ADL score of the control group at 12 months of follow-up. The Katz Index of ADLs²³ was used to address the question of whether exercise may prevent the worsening of disabilities in nursing home residents suffering from AD. This scale is robust, sensitive to change over time, and appropriate in evaluating a clinically meaningful effect of the intervention. Each item (eating, transferring from bed to chair, walking, using the toilet, bathing, and dressing) was scored from 0 to 1 (0 = unable to perform the activity without complete help, 0.5 = able to perform the activity

with little help, 1 = able to perform the activity without any help). The scoring system gave a score range from 0 to 6.

Secondary Outcome Measures

The secondary effectiveness outcomes included ADL score at 6 months, measures of physical performance, nutritional status, behavioral disturbance, and depression.

Physical performance was assessed using 6-meter walking speed,²⁴ get-up-and-go test,²⁵ and one-leg balance test.²⁶ In a population with AD, the intraclass correlation coefficient for the time to walk 25 feet, a test similar to the 6-meter walk test, ranged from 0.57 to 0.97.²⁴ The get-up-and-go test²⁴ and the one-leg balance test²⁶ have been widely used in frail older people. The get-up-and-go test is a global, subjective validated assessment tool of how a person rises from a standard armchair, walks to a wall 3 meters away, turns, walks back, and sits down again. The score ranged from 1 to 5 (1 = no instability to 5 = very abnormal). The one-leg balance test was abnormal when the time was less than 5 seconds.²⁶ The better of two tasks was used for the analysis.

Nutritional status was evaluated using body weight and the Mini-Nutritional Assessment (MNA). This scale has been widely used in cognitively impaired subjects.²⁷ Sensitivity and specificity of the MNA to predict elderly patients with adequate nutritional status (MNA \geq 24.0), protein-calorie malnutrition (MNA <17.0), or risk of malnutrition (MNA 23.5–17.0) have been shown to be 96% and 98%, respectively.²⁸

Behavior disturbances were evaluated using the Neuropsychiatric Inventory (NPI).²⁹ Patients with a total NPI score greater than 11 points arising from at least three domains were considered to have marked neuropsychiatric symptoms.³⁰

Depression was evaluated using the Montgomery-Asberg Depression Rating Scale (MADRS), a validated, reliable tool for detecting depression in a AD population.³¹ This scale has been shown to be sensitive to change in demented patients.³² Patients with a score of 18 or higher were considered to be depressed.

Other Variables

Baseline age, sex, current medication (number of medication and use of cholinesterase inhibitors and psychotropic treatments (anxiolytics, neuroleptics, serotonin reuptake inhibitors, and other antidepressants)), and visual and hearing impairment (assessor's subjective assessment from 1 = good to 5 = blind or deaf, respectively) were recorded. Patients with a score of 3 or higher were considered to have visual or hearing impairment. The MMSE¹⁶ was used to quantify dementia severity. Comorbid disease, history of past surgery or trauma, and depression were recorded from the medical records.

Adverse events, falls, fractures, hospitalization, and death were recorded daily for the whole cohort during the 12 months in a register completed by the occupational therapist and the nursing home staff. Malaise and syncope during the sessions and reason for withdrawal from an exercise session (acute disease, disagreement or unwillingness to continue, behavioral disorders, increased disability in ADLs, or other) were recorded. Adherence to treatment was

recorded as the proportion of actual treatment to intended treatment.

Statistical Methodology

The power calculations were computed based on expected changes in ADLs. With 134 participants, this study was designed to have greater than 80% power to detect a relative improvement of 0.5 points or more in total ADL score at 12 months in the exercise program group than in the routine medical care group (with a two-sided type I error rate of 0.05).

At baseline, mean covariate values between the exercise program and the routine medical care groups were compared using *t*, nonparametric Kruskal-Wallis, chi-square, and Fisher exact tests.

Based on the study design, a priori analyses were performed to assess differences in ADL scores based on randomization group. Outcome analysis was performed using the intention-to-treat population principle. An analysis of variance model was used for estimating exercise program effects. (The independent variables were exercise program group or routine medical care group and baseline ADL score.) ADL scores at 6 and 12 months were regressed on groups, controlling for the baseline value of that factor. Baseline values were carried forward for patients missing the 6-month or 12-month test.

The same analyses were performed for the secondary outcomes, and nonparametric Kruskal-Wallis tests were conducted on the change scores. Comparison of the 6-month and 12-month changes in the exercise group and routine medical care was performed.

Multiple logistic regression analyses used the 6-month and 12-month measurement and time, controlling for the baseline value of the outcome. No data were missing from the three observations for any participants who completed the study.

Additional exploratory analyses were performed according to adherence to the exercise program. These analyses were conducted to examine associations between adherence to exercise and change in ADL score. First, the Spearman correlation between the number of sessions of exercise completed during the 12 months and change in ADLs was examined. Second, participants with high adherence (>two thirds of the exercise session for the overall study duration) were compared with participants with intermediate (one third to two thirds) or low (>0 to one third) adherence. Adjustment for confounding baseline characteristics was made.

Analyses were interpreted at the two-sided significance level of .05. Statistical analyses were computed using Stata 6.0 (Stata Corporation, College Station, TX).

RESULTS

Demographic and Baseline Scores

The mean age \pm standard deviation of the participants was 83 ± 7.4 (range 62–103). Participants were predominantly female (75.3%). Subjects had a mean MMSE score of 8.8 ± 6.6 (mild to severe AD) and a mean ADL score of 3.1 ± 1.3 (Table 1). There were no significant differences in

baseline characteristics between the exercise program group and the routine medical care group except for comorbidity.

Rates and Reasons for Dropouts

One hundred ten (82.1%) participants completed the study. Reasons for attrition are reported in Figure 1. In participants who completed the study, there were no significant group differences in baseline characteristics. The number of patients discontinuing was not significantly different between the groups (Fisher exact test, $P = .26$). Kruskal-Wallis and chi-square tests indicated that participants who did not complete the study ($n = 24$) did not differ from other participants ($n = 110$) on any of the baseline variables (except for sex (12/24 men, $P = .001$)). There were no statistically significant differences in male/female dropout in terms of age; comorbidities; or MMSE, ADL, MNA, and NPI scores. Participants who did not complete the study ($n = 24$) did not differ from other participants ($n = 110$) on intervention assignment. Deaths were related to the comorbidities, and none of the deaths were directly or indirectly attributable to an adverse effect of the exercise program. Financial concern (2 in the control group), dissatisfaction of the patients' relatives (1 in each group), and relatives moving to different area of France (2 in each group) motivated change of institution. One resident in the exercise program group withdrew his consent without specific reason.

Adherence to the Exercise Program

Thirteen (19.4%) patients had high adherence (>two-thirds of the sessions, >60 sessions) to the exercise program, 19 (28.4%) had intermediate adherence (one-third to two-thirds of the sessions, 30–60 sessions), 28 (41.8%) had low adherence (<one-third of the sessions, <30 sessions), and seven (10.4%) performed none of the exercise sessions. Of the 56 exercisers who completed the study, mean adherence was $33.2 \pm 25.5\%$ of the 88 sessions. The reasons for nonadherence of the null or low- or intermediate-adherence groups were acute disease (15%), disagreement or unwillingness to continue (35%), behavior disorders (40%), increased disability in ADLs (5%), and others (5%) (reasons may be several).

Intention-to-Treat Outcome Analysis

Primary Effectiveness Assessment

ADL score at baseline, 6 months, and 12 months in the two groups are presented in Table 2. At 6 and 12 months, ADL scores declined significantly in both groups ($P < .001$ for both times and groups). At 12 months, mean ADL score reduction was significantly lower ($P = .02$) in exercisers than in the routine medical care group (no significance at 6 months, $P = .30$). Mean change in ADL score from baseline to 12 months indicated that exercise program group patients declined approximately one-third as much as the routine medical care patients (0.6 ± 1.2 vs 0.9 ± 1.1 , $P = .02$). The treatment did not appear to affect any of the six ADL items significantly, analyzed one by one.

Secondary Effectiveness Assessment

Secondary outcome variables are presented in Table 2. There were no significant differences at baseline for phys-

Table 1. Characteristics of the Population at Baseline

Characteristic	Exercise Group (n = 67)	Routine Medical Care (n = 67)
Age, mean \pm SD	82.8 \pm 7.8	83.1 \pm 7.0
Sex, n (%)		
Male	19 (28.3)	14 (20.9)
Female	48 (71.7)	53 (79.1)
Activity of daily living score, mean \pm SD*	3.2 \pm 1.3	3.1 \pm 1.3
Eating	0.7 \pm 0.2	0.6 \pm 0.2
Continence	0.3 \pm 0.3	0.3 \pm 0.4
Walking	1	1
Using the toilet	0.6 \pm 0.3	0.6 \pm 0.2
Bathing	0.2 \pm 0.2	0.2 \pm 0.2
Dressing	0.2 \pm 0.3	0.3 \pm 0.3
Mini-Mental State Examination score, mean \pm SD	9.7 \pm 6.8	7.9 \pm 6.4
Medication use		
Medication, n, mean \pm SD [†]	5.4 \pm 2.3	4.8 \pm 2.1
Psychotropic, n, mean \pm SD [‡]	1.9 \pm 1.3	1.8 \pm 1.1
Acetylcholinesterase inhibitor, n (%)	18 (26.9)	14 (20.9)
Comorbidities, n (%) [§]		
1	9 (13.4)	16 (23.9)
2	21 (31.3)	15 (22.4)
≥ 3	26 (38.9)	12 (17.9)
Past depression, n (%)	13 (19.4)	19 (28.4)
Past surgery, n (%)	37 (55.2)	33 (49.3)
Past fracture, n (%)		
All	22 (32.8)	20 (29.9)
Hip fracture	12 (17.9)	10 (14.9)
Hearing impairment, n (%)	27 (40.3)	26 (38.8)
Visual impairment, n (%)	10 (14.9)	7 (10.5)
Walk speed, m/s, mean \pm SD	0.33 \pm 0.14	0.33 \pm 0.14
Get-up-and-go test score, mean \pm SD	2.7 \pm 0.8	2.7 \pm 0.8
Abnormal one-leg balance test score, n (%)	61 (91.0)	62 (92.5)
Weight, kg, mean \pm SD	62.4 \pm 16.2	60.6 \pm 12.7
Mini-Nutritional Assessment score, mean \pm SD	22.2 \pm 3.1	21.8 \pm 2.6
≥ 24.0 , n (%)	32 (47.7)	20 (29.9)
23.5–17.0, n (%)	31 (46.3)	45 (67.1)
< 17.0 , n (%)	4 (6.0)	2 (3.0)
NPI total score, mean \pm SD	10.7 \pm 6.9	11.4 \pm 7.7
Patients with marked neuropsychiatric symptoms, n (%)	18 (26.9)	25 (37.3)
MADRS total score, mean \pm SD	11.9 \pm 6.1	12.3 \pm 6.0
Depressed patients, n (%) [¶]	10 (14.9)	16 (23.9)

Note: All groups comparisons $P > .05$ except for comorbidity ≥ 3 , $P = .04$.

* 0 = dependent, 6 = independent.

[†] Total number of medications minus psychotropics and acetylcholinesterase inhibitors.

[‡] Including anxiolytics, neuroleptics, serotonin reuptake inhibitors, and other antidepressants.

[§] Hypertension, diabetes mellitus, dyslipidemia, chronic obstructive pulmonary disease, coronary heart disease, peripheral vascular disease, cancer, and depression.

^{||} Patients with Neuropsychiatric Inventory (NPI) score > 11 .

[¶] Montgomery-Asberg Depression Rating Scale (MADRS) score ≥ 18 .

SD = standard deviation.

ical performance measures; body weight; or MNA, NPI, or MADRS score between the two groups.

Prespecified analyses demonstrated significant improvement in walking speed in the exercise program group at 6 months ($P < .001$) and 12 months ($P = .006$) and in the routine medical care group at 12 months ($P = .04$). In regression analysis, mean walking speed improvement was significantly higher in exercisers than in the routine medical care group at 6 months ($P = .01$) and 12 months ($P = .002$). During the intervention period, none of the other physical performance measures significantly

changed, and no differences were found between the groups (Table 2).

In regression analysis, no significant differences were noted for mean MNA, NPI, and MADRS scores between the two groups at 6 months and 12 months (Table 2). Categorical analysis of MNA scores demonstrated a similar distribution of the patients between the two groups at baseline, 6 months, and 12 months.

Nonparametric Kruskal-Wallis tests were conducted on the pretrial change scores to verify distribution assumptions. Results were similar.

Table 2. Significant Outcomes

Outcome	6 Months			12 Months		
	Exercise Group	Routine Medical Care	<i>P</i> -value [†]	Exercise Group	Routine Medical Care	<i>P</i> -value [‡]
Activity of daily living disability, mean ± SD*	(n = 60) 2.7 ± 1.4	(n = 57) 2.6 ± 1.5	.43	(n = 56) 2.6 ± 1.5	(n = 54) 2.2 ± 1.5	.65
Physical performance						
Walk speed, m/s, mean ± SD	0.41 ± 0.17	0.37 ± 0.17	.01	0.41 ± 0.16	0.36 ± 0.19	.002
Get-up-and-go test, mean ± SD	3.0 ± 1.1	3.0 ± 1.0	.68	3.1 ± 1.1	3.2 ± 1.2	.31
Abnormal one-leg balance test, n (%)	57 (95.0)	53 (93.0)	.47	53 (94.6)	51 (98.1)	.34
Nutritional status						
Weight, kg, mean ± SD	61.5 (16.4)	58.9 (11.8)	.45	61.9 (15.7)	59.5 (12.5)	.51
Mini-Nutritional Assessment score, mean ± SD	21.6 ± 3.5	21.0 ± 3.7	.26	20.7 ± 3.4	20.4 ± 4.7	.16
≥24.0, n (%)	25 (41.7)	22 (38.6)	.94	17 (30.4)	17 (31.5)	.79
23.5–17.0, n (%)	27 (45.0)	27 (47.4)		31 (55.4)	27 (50.0)	
<17.0, n (%)	8 (13.3)	8 (14.0)		8 (14.3)	10 (18.5)	
Behavioral disturbances and depression						
NPI total score, mean ± SD	8.2 ± 8.0	9.2 ± 8.3	.47	8.3 ± 8.9	8.9 ± 10.4	.78
Patients with marked neuropsychiatric symptoms, n (%) [§]	9 (15)	15 (26.3)	.18	12 (21.4)	11 (20.4)	.82
MADRS-Total, mean ± SD	11.5 ± 6.6	13.3 ± 6.3	.10	13.4 ± 8.0	14.8 ± 7.2	.20
Depressed patients, n (%) [¶]	13 (21.6)	16 (28.1)	.45	15 (26.8)	20 (37.0)	.37

* 0 = dependent, 6 = independent.

[†] Comparison of the 6-month changes between exercise group and routine medical care.

[‡] Comparison of the 12-month changes between exercise group and routine medical care.

[§] Neuropsychiatric Inventory (NPI) score > 11.

[¶] Montgomery-Asberg Depression Rating Scale (MADRS) score ≥ 18.

SD = standard deviation.

Safety

There were no significant group differences during the 12 months between the exercise program group and the routine medical care group in observed total number of falls (139 vs 136), fractures (5 vs 2), or deaths (7 vs 8). The mean number of hospitalizations per patient was significantly higher in the exercise program group at 6 months and 12 months (0.3 ± 0.8 vs 0.2 ± 0.6, *P* = .04, and 0.6 ± 1.3 vs 0.2 ± 0.6, *P* = .04, respectively). No malaise or syncope was noted during the exercise sessions. During the study period, five falls occurred during the exercise session. One of them caused a wound of the scalp.

Additional Analysis

The proportion of patients with marked neuropsychiatric symptoms or depression did not change significantly during the interventional period in either group.

In exploratory analyses, the dose-response result on ADL score was further investigated in the intervention group. Increasing number of sessions completed was significantly correlated with less deterioration in ability to perform ADLs (correlation coefficient = 0.37, *P* = .005) (Figure 2). There were no significant differences in baseline characteristics between participants with high, low, and intermediate adherence (data not shown). At 12 months, ADL score declined, although not significantly, in the patients with high adherence. ADL scores of participants with

low or intermediate adherence declined significantly (*P* < .001).

DISCUSSION

This study provides evidence that a moderate exercise program conducted twice a week significantly slows, by approximately one-third, the progressive deterioration in ability to perform ADLs in people with AD living in nursing homes. With a treatment difference of 0.39 points (about a 6.7% benefit relative to the control group) at the study end

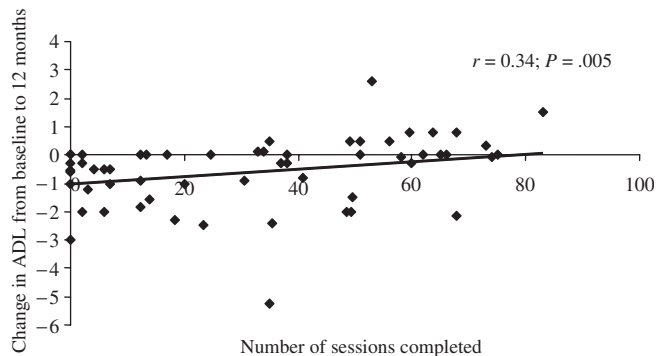


Figure 2. Spearman correlation (*r*) between number of sessions completed and change in activity of daily living (ADL) score from baseline to 12 months in the exercise program group (n = 56).

point, this ADL change corresponds to a small but clinically meaningful benefit of the exercise program. This intervention was associated with improvement in mean walking speed but had no significant effect on nutritional status, behavioral disturbance, or depression measures. The exercise program was safe.

Nonpharmacological randomized, controlled trials with patients with AD are scarce.^{6,7,33} Lack of compliance and difficulty with measurements have led the majority of studies on exercise to exclude people with AD, but the current study suggests that nursing home residents with AD could be a relevant target population for exercise programs. Recently, combined interventions including physical activity have led to better physical health, lower depression, or better functional mobility in an AD population living in the community²⁰ or nursing home.³³ None investigated the effect on basic ADLs. Moreover, although other studies have found that exercise intervention in nursing home residents improved physical performance, few have especially investigated the population with AD.^{34,35} Additionally, most nursing home studies were short-term interventions^{36,37} and involved an intensive intervention staff to maximize exercise participation.³⁶ This more-intensive approach may be more effective but may not be practical in some nursing home settings in the long term. The aim of the current study was to deliver a long-term intervention in a manner translatable to the usual nursing home setting. Thus, these results have broad practical implications. The societal costs of AD are mainly determined by nursing home costs.³⁸ The cost-effectiveness of this intervention has not been evaluated, but it is likely that it exceeded the cost of the decline in the ADL score.

Although intention-to-treat analyses were performed to preserve the baseline comparability between treatment groups achieved by randomization, several methodological aspects of the study require comment. First, it cannot be excluded that the ADL changes resulted from an interaction between the occupational therapist and the patients in the exercise program group; the lack of a behavior-intervention-only comparison group prevents this study from determining the specific effect of exercise versus the non-exercise intervention. However, the significant improvement in walking speed suggested a direct link between the exercise program and the disability measures. In addition, the controls were not truly a “nontreatment” group, because they received routine medical care. Although none of the nursing homes previously organized an exercise session, because usual care was well done in these nursing homes, that may explain walking speed improvement even in the control group. Moreover, exercisers had more baseline comorbidities and were more frequently hospitalized. Therefore, it is likely that the size of the effect of the exercise program on the change in ADL score might have been less than in a group with fewer baseline comorbidities.

The intervention had no significant effect on nutritional status, behavioral disturbance, or depression measures. Previous nonpharmacological studies have suggested that exercise programs may reduce symptoms of depression in people with AD¹⁷ and behavioral disturbances.³⁴ The results of the current study suggested that a more-targeted approach to behavioral disturbance or nutrition may be necessary.

Whether offering more exercise sessions would have led to better results warrants further investigation, although additional sessions may result in lower adherence. Adherence was already relatively low in this study but was similar to the adherence rate reported in a nursing home training program.³⁷ Exercise adherence was a significant predictor of change in ADL score, and ADL scores of participants with high adherence did not decrease significantly during the intervention period. This result may be due to the fact that subjects with the slowest decline in function were able to adhere to exercise rather than that high adherence to exercise caused a slower decline in function. These results also suggest that the program was sufficient to maintain ability. Future work should focus on efforts to improve adherence.

ADL abilities are a key determinant of the quality of life of people with AD² and of the cost of caring for them.⁵ The findings of the current study demonstrate that an exercise session twice a week can slow the deterioration in ability to perform ADLs in people with AD living in nursing homes.

ACKNOWLEDGMENTS

We thank Mme Cécile Cathala (CHU Toulouse) for the exercise program management and the staff and patients of the nursing homes “Les Roses,” “Les Acacia,” “Alliance,” “Tiers-Temps,” and “Grand Noble” for their assistance and participation. The authors report no conflict of interest.

Financial Disclosure: This study was supported by French National Grant 01,044 03 from the Caisse Nationale d'Assurance Maladie et du Travail and was sponsored by the University Hospital of Toulouse for regulatory and ethic submission.

Author Contributions: Yves Rolland and Adrian Klapouszczak: concept and design, acquisition of subjects and data, analysis and interpretation of data, and preparation of manuscript. Fabien Pillard: concept and design, analysis and interpretation of data, and preparation of manuscript. Emma Reynish and Sandrine Andrieu: analysis and interpretation of data and preparation of manuscript. David Thomas: interpretation of data and preparation of manuscript. Daniel Rivière and Bruno Vellas: concept and design, interpretation of data, and preparation of manuscript.

Sponsor's Role: The sponsor had no role in the design, methods, subject recruitment, data collections, analysis, or preparation of the manuscript.

REFERENCES

1. Aguero-Torres H, Fratiglioni L, Guo Z et al. Dementia is the major cause of functional dependence in the elderly: 3-year follow-up data from a population-based study. *Am J Public Health* 1998;88:1452–1456.
2. Andersen CK, Wittrup-Jensen KU, Lolk A et al. Ability to perform activities of daily living is the main factor affecting quality of life in patients with dementia. *Health Qual Life Outcomes* 2004;2:52.
3. Knopman DS, Berg JD, Thomas R et al. Nursing home placement is related to dementia progression: Experience from a clinical trial. *Alzheimer's Disease Cooperative Study*. *Neurology* 1999;52:714–718.
4. van Dijk PT, Mehr DR, Ooms ME et al. Comorbidity and 1-year mortality risks in nursing home residents. *J Am Geriatr Soc* 2005;53:660–665.
5. Prigerson HG. Costs to society of family caregiving for patients with end-stage Alzheimer's disease. *N Engl J Med* 2003;349:1891–1892.
6. Morley JE, Silver AJ. Nutritional issues in nursing home care. *Ann Intern Med* 1995;123:850–859.

7. Cohen-Mansfield J, Mintzer JE. Time for change: The role of non-pharmacological interventions in treating behavior problems in nursing home residents with dementia. *Alzheimer Dis Assoc Disord* 2005;19:37–40.
8. Lazowski DA, Ecclestone NA, Myers AM et al. A randomized outcome evaluation of group exercise programs in long-term care institutions. *J Gerontol A Biol Sci Med Sci* 1999;54A:M621–M628.
9. Buchner DM, Larson EB. Falls and fractures in patients with Alzheimer-type dementia. *JAMA* 1987;257:1492–1495.
10. White H, Pieper C, Schmader K et al. A longitudinal analysis of weight change in Alzheimer's disease. *J Am Geriatr Soc* 1997;45:531–532.
11. Lyketsos CG, Lopez O, Jones B et al. Prevalence of neuropsychiatric symptoms in dementia and mild cognitive impairment: Results from the cardiovascular health study. *JAMA* 2002;288:1475–1483.
12. Taylor AH, Cable NT, Faulkner G et al. Physical activity and older adults: A review of health benefits and the effectiveness of interventions. *J Sports Sci* 2004;22:703–725.
13. Welch HG, Walsh JS, Larson EB. The cost of institutional care in Alzheimer's disease: Nursing home and hospital use in a prospective cohort. *J Am Geriatr Soc* 1992;40:221–224.
14. Schmeidler J, Mohs RC, Aryan M. Relationship of disease severity to decline on specific cognitive and functional measures in Alzheimer disease. *Alzheimer Dis Assoc Disord* 1998;12:146–151.
15. Ballard C, Fosse J, Chithramohan R et al. Quality of care in private sector and NHS facilities for people with dementia: cross sectional survey. *BMJ* 2001;323:426–427.
16. Folstein MF, Folstein SE, McHugh PR. 'Mini-mental state'. A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;12:189–198.
17. McKhann G, Drachman D, Folstein M et al. 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;34:939–944.
18. Rolland Y, Rival L, Pillard F et al. Feasibility of regular physical exercise for patients with moderate to severe Alzheimer disease. *J Nutr Health Aging* 2000;4:109–113.
19. Mathews RM, Clair AA, Kosloski K. Keeping the beat. Use of rhythmic music during exercise activities for the elderly with dementia. *Am J Alzheimers Dis Other Dement* 2001;16:377–380.
20. Teri L, Gibbons LE, McCurry SM et al. Exercise plus behavioral management in patients with Alzheimer disease: A randomized controlled trial. *JAMA* 2003;290:2015–2022.
21. Jirovec MM. The impact of daily exercise on the mobility, balance and urine control of cognitively impaired nursing home residents. *Int J Nurs Stud* 1991;28:145–151.
22. Guralnik JM, Ferrucci L, Pieper CF et al. Lower extremity function and subsequent disability: Consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. *J Gerontol A Biol Sci Med Sci* 2000;55A:M221–M231.
23. Katz S, Ford AB, Moskowitz RW et al. Studies of illness in the aged. The index of ADL. A standardized measure of biological and psychosocial function. *JAMA* 1963;185:914–919.
24. Tappen RM, Roach KE, Buchner D et al. Reliability of physical performance measures in nursing home residents with Alzheimer's disease. *J Gerontol A Biol Sci Med Sci* 1997;52A:M52–M55.
25. Mathias S, Nayak US, Isaacs B. Balance in elderly patients: the 'get-up and go' test. *Arch Phys Med Rehabil* 1986;67:387–389.
26. Vellas BJ, Rubenstein LZ, Ousset PJ et al. One-leg standing balance and functional status in a population of 512 community-living elderly persons. *Aging (Milano)* 1997;9:95–98.
27. Guigoz Y, Lauque S, Vellas BJ. Identifying the elderly at risk for malnutrition. The Mini Nutritional Assessment. *Clin Geriatr Med* 2002;18:737–757.
28. Vellas B, Guigoz Y, Garry PJ et al. The Mini Nutritional Assessment (MNA) and its use in grading the nutritional state of elderly patients. *Nutrition* 1999;15:116–122.
29. Cummings JL, Mega M, Gray K et al. The Neuropsychiatric Inventory: Comprehensive assessment of psychopathology in dementia. *Neurology* 1994;44:2308–2314.
30. Holmes C, Wilkinson D, Dean C et al. The efficacy of donepezil in the treatment of neuropsychiatric symptoms in Alzheimer disease. *Neurology* 2004;63:214–219.
31. Muller-Thomsen T, Arlt S, Mann U et al. Detecting depression in Alzheimer's disease: Evaluation of four different scales. *Arch Clin Neuropsychol* 2005;20:271–276.
32. Karlsson I, Godderis J, Augusto De Mendonca Lima C et al. A randomised, double-blind comparison of the efficacy and safety of citalopram compared to mianserin in elderly, depressed patients with or without mild to moderate dementia. *Int J Geriatr Psychiatry* 2000;15:295–305.
33. Tappen RM, Roach KE, Applegate EB et al. Effect of a combined walking and conversation intervention on functional mobility of nursing home residents with Alzheimer disease. *Alzheimer Dis Assoc Disord* 2000;14:196–201.
34. Stevens J, Killeen M. A randomised controlled trial testing the impact of exercise on cognitive symptoms and disability of residents with dementia. *Contemp Nurse* 2006;21:32–40.
35. Landi F, Russo A, Bernabei R. Physical activity and behavior in the elderly: A pilot study. *Arch Gerontol Geriatr Suppl* 2004;9:235–241.
36. Ouslander JG, Griffiths PC, McConnell E et al. Functional incidental training: A randomized, controlled, crossover trial in Veterans Affairs nursing homes. *J Am Geriatr Soc* 2005;53:1091–1100.
37. Schnelle JF, MacRae PG, Giacobassi K et al. Exercise with physically restrained nursing home residents: Maximizing benefits of restraint reduction. *J Am Geriatr Soc* 1996;44:507–512.
38. Leon J, Cheng CK, Neumann PJ. Alzheimer's disease care: Costs and potential savings. *Health Aff (Millwood)* 1998;17:206–216.