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Exercise Plus Behavioral Management in Patients With Alzheimer Disease A Randomized Controlled Trial

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T IS WELL-KNOWN THAT ALZHEIMER disease adversely affects cognitive, emotional, and behavioral functioning.1 Less well-known are the deleterious effects of Alzheimer disease on physical conditioning. However, there are a number of studies linking Alzheimer disease with physical deterioration. For example, when compared with age-matched controls, Alzheimer disease patients show more signs of undernutrition,² higher risk of falls and fractures,³⁻⁶ and more rapid decline on measures of mobility.7,8 Once injured, Alzheimer disease patients are at greater risk of subsequent injury than age- and sex-matched controls.3 Reduced muscle mass has also been associated with loss of independence.9 Consequently, improved physical conditioning for patients with Alzheimer disease may extend their independent mobility and enhance their quality of life despite progression of the disease.

Research is accumulating to suggest that even the oldest adults can improve cardiovascular function and in**Context** Exercise training for patients with Alzheimer disease combined with teaching caregivers how to manage behavioral problems may help decrease the frailty and behavioral impairment that are often prevalent in patients with Alzheimer disease.

Objective To determine whether a home-based exercise program combined with caregiver training in behavioral management techniques would reduce functional dependence and delay institutionalization among patients with Alzheimer disease.

Design, Setting, and Patients Randomized controlled trial of 153 communitydwelling patients meeting National Institute of Neurological and Communicative Diseases and Stroke/Alzheimer Disease and Related Disorders Association criteria for Alzheimer disease, conducted between June 1994 and April 1999.

Interventions Patient-caregiver dyads were randomly assigned to the combined exercise and caregiver training progam, Reducing Disability in Alzheimer Disease (RDAD), or to routine medical care (RMC). The RDAD program was conducted in the patients' home over 3 months.

Main Outcome Measures Physical health and function (36-item Short-Form Health Survey's [SF-36] physical functioning and physical role functioning subscales and Sickness Impact Profile's Mobility subscale), and affective status (Hamilton Depression Rating Scale and Cornell Depression Scale for Depression in Dementia).

Results At 3 months, in comparison with the routine care patients, more patients in the RDAD group exercised at least 60 min/wk (odds ratio [OR], 2.82; 95% confidence interval [CI], 1.25-6.39; P=.01) and had fewer days of restricted activity (OR, 3.10; 95% CI, 1.08-8.95; P<.001). Patients in the RDAD group also had improved scores for physical role functioning compared with worse scores for patients in the RMC group (mean difference, 19.29; 95% CI, 8.75-29.83; P<.001). Patients in the RDAD group had improved Cornell Depression Scale for Depression in Dementia scores while the patients in the RMC group had worse scores (mean difference, -1.03; 95% Cl, -0.17 to -1.91; P=.02). At 2 years, the RDAD patients continued to have better physical role functioning scores than the RMC patients (mean difference, 10.89; 95% CI, 3.62-18.16; P=.003) and showed a trend (19% vs 50%) for less institutionalization due to behavioral disturbance. For patients with higher depression scores at baseline, those in the RDAD group improved significantly more at 3 months on the Hamilton Depression Rating Scale (mean difference, 2.21; 95% CI, 0.22-4.20; P=.04) and maintained that improvement at 24 months (mean difference, 2.14; 95% CI, 0.14-4.17; P=.04).

Conclusion Exercise training combined with teaching caregivers behavioral management techniques improved physical health and depression in patients with Alzheimer disease.

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crease flexibility, balance, and strength with systematic exercise training.^{10,11} In one uncontrolled study of 11 patients with Alzheimer disease, patients benefited from a hospital-based exercise program.¹² Furthermore, exercise programs have been shown to improve function even in frail nursing home residents.^{10,11}

Exercise can yield additional benefits for elderly dementia patients. In elderly individuals without dementia, randomized controlled clinical trials have demonstrated that exercise successfully reduces depression.¹³⁻¹⁶ Between 17% and 86% of dementia patients are depressed.¹⁷ Exercise may provide the added benefit of reducing their levels of depression.

Because caregivers are responsible for structuring the patient's day-to-day activities and providing ongoing care, teaching them effective caregiving strategies to encourage exercise and avoid behavioral problems associated with increased activity may make exercise training most effective and most reasonable given the circumstances. Caregivers have been successfully trained to reduce patient depression,18 agitation,19,20 and delay institutionalization.²¹ The attention and activity inherent in exercise programs can be an opportunity to improve patientcaregiver interactions. If positive behavioral strategies are used for encouraging exercise participation, exercise may increase opportunities for pleasant interactions between patient and caregiver and conflicts may be reduced. Thus, a caregiver-supervised exercise program for patients with Alzheimer disease may yield significant improvements in physical health, affect, and behavioral distress.

This study was undertaken to determine whether a home-based exercise program combined with caregiver training in behavioral management techniques would reduce functional dependence and delay institutionalization among patients with Alzheimer disease. The Reducing Disability in Alzheimer Disease (RDAD) program was compared with routine medical care in a randomized controlled clinical trial. It was hypothesized that patients in the RDAD program would show significant improvement on measures of physical frailty and depression compared with those obtained among patients in the routine care group.

METHODS Patients

A total of 153 patients were randomized from an ongoing, communitybased Alzheimer disease patient registry²² and through referrals from physician practices and community advertisements. Enrollment began in June 1994 and follow-up ended in April 1999. The study was approved by institutional review boards of both the University of Washington and Group Health Cooperative. Written consent was obtained from both patient and caregiver. Additionally, caregivers (next of kin or legal guardians) provided consent on behalf of patients. All patients received a comprehensive, multidisciplinary diagnostic evaluation, and results were reviewed at consensus meetings attended by a geriatrician, neurologist, psychologist, epidemiologist, nurse, and research staff.

All patients met National Institute of Neurological and Communicative Diseases and Stroke/Alzheimer Disease and Related Disorders Association criteria²³ for probable or possible Alzheimer disease, were required to be communitydwelling, ambulatory, and to have a caregiver who was willing to participate in training sessions. Patients ranged in age from 55 to 93 years, were predominantly male (59%), white (89%), and had dementia for an average of 4.3 years. Patients' mean (SD) Mini-Mental State Examination (MMSE) score was 16.8 (7.1), which placed them in the moderate to severe range of cognitive impairment.

Caregivers

The caregivers were spouses or adult relatives who lived with or spent a minimum of 4 hours every day with the patient. Caregivers' ages ranged from 24 to 91 years; 70% were female, 87% were white, and 80% were spouses.

Procedures

Patient-caregiver dyads were randomly assigned to exercise plus behavior management techniques (RDAD program) or routine medical care. The random allocation sequence was obtained from a computer program that blocked groups of 8 patients. Dyads were randomized after the baseline assessment by research coordinators. Assessments were conducted at screening, baseline, after 3 months (posttreatment) and at 6, 12, 18, and 24-month follow-up by interviewers blind to treatment assignment (FIGURE).

Trial Groups

The active treatment program (RDAD) was adapted from 2 previously established treatments-one to reduce behavioral problems in Alzheimer disease¹⁸ and one to increase exercise among older adults.²⁴ Patient-caregiver dyads assigned to this program were seen in their own homes for 12 hour-long sessions on a schedule of 2 sessions per week for the first 3 weeks, followed by weekly sessions for 4 weeks, and then biweekly sessions over the next 4 weeks. Three follow-up sessions were conducted over the next 3 months to answer questions and consolidate treatment gains. Home health professionals experienced in dementia care conducted all sessions.

The exercise component of the RDAD program included aerobic/endurance activities, strength training, balance, and flexibility training. The goal was for patients to engage in a minimum of 30 min/d of moderate-intensity exercise. In the behavioral management component of the RDAD program, caregivers were taught to identify and modify patient behavioral problems that impaired day-to-day function and adversely affected patient-caregiver interactions. Caregivers were given specific instructions about how to reduce the occurrence of these problems while also teaching them skills to identify and modify precipitants of patient distress. Caregivers were also educated about dementia, its impact on patient behavior and function, and how to modulate their

²⁰¹⁶ JAMA, October 15, 2003-Vol 290, No. 15 (Reprinted)

own responses to problems. The caregivers were encouraged to identify pleasant activities for their patients to encourage positive interactions and to increase physical and social activity.

In each session, exercises were demonstrated and practiced, caregivers were taught how to encourage and help patients with their exercises, and behavioral plans were developed and implemented. A new topic was introduced in each of the first 10 sessions; subsequent sessions focused on solidifying gains and helping caregivers and patients maintain exercise and behavioral management after the study ended. A complete RDAD treatment manual is available from the corresponding author and a description of the intervention has been published previously.25

Patients in the control group received routine medical care, including acute medical or crisis intervention provided at community health care centers. This could include nonspecific advice and support routinely provided by nurses and primary care physicians or community support services. Specific exercise and behavioral management training was not provided to control patients.

Trainers and Training Adherence

Treatment adherence was maintained and monitored by weekly supervision of each trainer by clinical geropsychologists (L.T., S.M.M.) and a physical therapist. Treatment sessions were videotaped and reviewed by independent raters to ensure that trainers followed the treatment protocol.

Primary Outcome Measures

The primary patient outcomes were physical health and function and affective status. We hypothesized that patients receiving RDAD would improve in each area. However, because not all patients entered the study with affective or behavioral disturbance, we believed that these areas would show improvement only in patients for whom such problems were evident at baseline. We also hypothesized that physi-

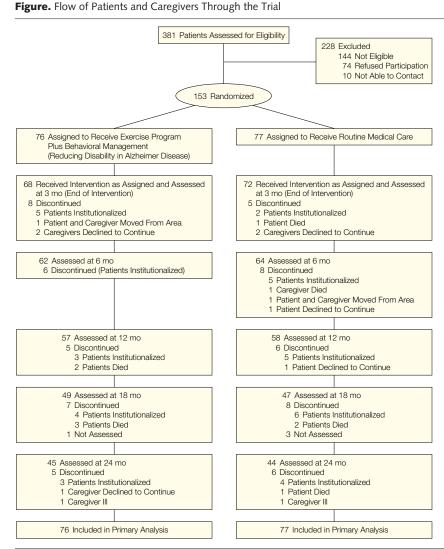
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cal health and function would show the most gain because this domain was relevant across all patients.

Physical Health and Function. Two subscales of the Medical Outcome Study 36-item Short-Form Health Survey (SF-36; physical functioning and physical role functioning) and 3 from the Sickness Impact Profile (SIP; body care and movement, mobility, and home management subscales) were obtained. The SF-36 and SIP assess general health status, are psychometrically sound, and have been used extensively with older adults.^{26,27} Higher SF-36 scores indicate better health functioning; higher SIP scores indicate worse function.

Caregivers completed these measures based on their personal experience with the patients.

Affective Status. Professional interviewers assessed depression based on direct observations of the patient and caregiver interviews. We used the Hamilton Depression Rating Scale^{28,29} and the Cornell Scale for Depression in Dementia,³⁰ which are psychometrically sound measures that have been used to assess depression in older adults with dementia.^{31,32} Higher scores indicate greater impairment. Interviewers were trained and periodically monitored by a clinical geropsychologist (S.M.M.) to ensure interrater reliability.



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Secondary Outcome Measures

Patient performance-based and caregiver-report assessments were obtained. Patient walking speed, functional reach, and standing balance were measured. These measures of physical health and function have been used extensively in trials of healthy older adults.33-35 Caregiver reports included the number of minutes spent walking or doing another aerobic activity for exercise in the past week; the number of restricted activity days and days spent in bed during the past 2 weeks; and falls and near falls during the past month. These measures have demonstrated validity in healthy older adults^{36,37} and are responsive to change.38 To our knowledge, this is the first trial using these measures with dementia patients. To assess the level of patient behavioral disturbance and caregiver distress, the Revised Memory and Behavior Problem Checklist was used. Good psychometric reliability and validity have been reported with use of this checklist.39

Baseline Descriptive Data and Process Measures

Baseline demographic information was reported for patient and caregiver age, sex, ethnic group, education, and relationship. Patient age at onset and duration of dementia were obtained at screening. In addition, patient cognitive status was assessed using the MMSE.40 No change was hypothesized in the MMSE as a function of treatment; it was obtained for descriptive purposes. Caregivers completed an adverse symptom checklist at each visit. No unexpected or serious adverse events were attributed to the RDAD program, and there was no difference between active and control groups in adverse symptoms. Exercise compliance was assessed using daily exercise logs completed by caregivers, and ratings of exercise homework completed by trainers.²⁵ Completion of assigned behavioral management homework (eg, recommended readings, viewing a training videotape, or implementing a behavioral change plan) was also rated after each session by study trainers.

Statistical Methods

The study was designed to have 80% power (α = .05) to detect at least half SD difference on the primary outcome measure. Between-group comparisons of baseline covariates were conducted using Fisher exact tests, *t* tests, or non-parametric Kruskal-Wallis tests. Cox proportional hazards survival analyses were used to determine which baseline characteristics significantly predicted patient attrition. Hazard ratios and 95% confidence intervals (CIs) were computed.

Outcome analyses compared the RDAD group with the routine care group using generalized estimating equations for linear, logistic, and Poisson regression.⁴¹ Mean (SD) differences, odds ratios, and relative risks were calculated with 95% CIs.

For pretrial and posttrial analyses, the outcome at the 3-month visit (corresponding to the end of the intervention) was regressed on treatment group, controlling for the baseline value of that factor. Pretrial and postrial analyses were based on the intention-to-treat (ITT) principle, using all randomized patients. Baseline values were carried forward for patients missing the posttest. In secondary analyses, these analyses were repeated without imputation for missing posttests, and nonparametric Kruskal-Wallis tests were conducted on the change scores. SAS statistical software was used to perform analyses (Version 6.12; SAS Institute Inc, Cary, NC).

Longitudinal analyses used all 5 posttreatment visits (3, 6, 12, 18, and 24 months) and time, controlling for the baseline value of the outcome. This is a repeated-measures design, with up to 5 observations per person. To account for within-patient correlation of scores at different time points, an autoregressive correlation structure was modeled, which assumed that consecutive visits were more highly correlated than nonconsecutive visits. Time by group interactions were assessed with the same model structure and were reported if significant. Potential confounders (age, sex, MMSE score at baseline, and duration of dementia) were evaluated by entering their baseline values as covariates and noting the change in the estimated treatment coefficient. Changes of more than 15% were considered to be evidence of confounding. Two sets of longitudinal analyses were conducted. The primary longitudinal analyses used all available data for each patient. In the complete follow-up analyses, only patients with 24 months of follow-up were included. In addition, a sensitivity analysis of missing data was conducted. Outcome data were ranked by visit and missing data were assigned the best or the worst rank in the following combinations: (1) all worst, (2) all best, (3) control worst and RDAD best, and (4) control best and RDAD worst.

RESULTS

Demographics and Baseline Scores

There were no significant differences at baseline in any patient or caregiver characteristics (such as age, sex, duration of dementia, and medication use) or assessment measures (TABLE 1).

ITT Outcome Analyses

At 3 months (posttest), significant differences were obtained between groups for the primary measures of physical role function and affective status. In regression analyses, the mean estimated difference for the SF-36 was 19.29 (95% CI, 8.75-29.83; P<.001), and it was -1.03 (95% CI, -0.17 to 1.19; P=.02) for the Cornell Depression Scale. For both outcomes, patients in the RDAD group improved while routine care patients declined. Using ITT, an improvement of 5.9 points on the SF-36 physical role functioning subscale was obtained for RDAD patients compared with a decline of 16.6 points for control patients; on the Cornell scale, an improvement of 0.5 points for RDAD patients compared with a decline of 0.5 for control patients. Significant differences were also obtained on secondary physical and health function measures. At baseline, 56% of those in both the control and RDAD groups reported exercising at least 60 min/wk.

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At posttest, 79% of those in the RDAD group and 62% of those in the routine care group reported exercising 60 min/ wk, which is an improvement of 23% for the RDAD group vs 6% for the control group (odds ratio, 2.82; 95% CI, 1.25-6.39; P=.01). Restricted activity days decreased by an average of 0.5 days in the RDAD group, but increased by 0.2 days in the control group (odds ratio, 3.10; 95% CI, 1.08-8.95; P<.001). The percentage of RDAD patients experiencing restricted days was also lower. No other significant differences were obtained. Nonparametric Kruskal-Wallis tests were conducted on the pretrial and posttrial change scores to verify distributional assumptions. Results were similar.

Longitudinal Data for 24 Months

At 24 months of follow-up, significant differences remained between patients in the RDAD group and the control group on the SF-36 physical role functioning subscale (mean difference, 10.89; 95% CI, 3.62-18.16; P=.003). Significant differences between RDAD and routine care patients emerged on the SIP Mobility scale (relative risk, 1.27; 95% CI, 1.03-1.56; P = .02). TABLE 2 presents the observed data before imputation for missing posttests. The longitudinal analyses were repeated with the 89 patients who completed all 24 months of follow-up. Significant differences were again obtained between the RDAD group and the routine care group on the SF-36 physical role functioning subscale (mean difference, 10.59; 95% CI, 2.22-18.96; P=.01) and SIP Mobility scale (relative risk, 1.37; 95% CI, 1.07-1.75; P = .01).

In the sensitivity analyses, the SF-36 physical role functioning scores were robust for most of the possible assumptions about the 22% of patients who were missing data. Under most scenarios, the RDAD intervention improved patients' physical functioning (mean difference, 9.18; 95% CI, 1.57-16.78 [all worst]; mean difference, 8.81; 95% CI, -2.62 to 20.24 [all best]; mean difference, 48.26; 95% CI, 38.67-

57.85 [RDAD group best and control worst]; mean difference, 10.45; 95% CI, 4.06-16.85 [complete data]). Only in the most extreme combination, in which all the missing control patients would have had the best scores and all the missing RDAD patients would have had the worst scores, would the routine care have been better than RDAD intervention. For the SIP Mobility scale, assigning RDAD the best ranks and control the worst retained the significance of the findings.

Rates and Reasons for Dropouts

Of 153 patients who began the study, 140 (92%) completed posttest assessment. Of the 13 who discontinued at 3 months, 8 had been assigned to the RDAD group and 5 to the routine care group (Fisher exact test, P=.40). Eightynine (58%) completed 24-month assessments. Patients who completed this last assessment were less cognitively impaired (baseline MMSE score hazard ratio, 1.36; 95% CI, 1.15-1.61) and had an average MMSE score that was 5 points lower (P<.001). There were no other significant demographic differences between those who completed this assessment and those who did not.

Patient institutionalization was the major reason patients did not complete all assessments, with no significant differences between treatment arms (67% for the control group and 68% for the RDAD group; χ_1^2 =0.04 and *P*=.84). However, the reasons for

Characteristic	Reducing Disability in Alzheimer Disease (n = 76)	Routine Medical Care (n = 77)
Particip	pant	
Age, mean (SD), y	78 (6)	78 (8)
Sex Male	48 (63)	42 (55)
Female	28 (37)	35 (45)
Race/ethnicity Asian/Pacific Islander	1 (1)	3 (4)
Black	8 (11)	5 (6)
White	67 (88)	69 (90)
Married	62 (82)	63 (82)
Years of education, mean (SD)	13 (3)	13 (3)
Duration of dementia, mean (SD), y	4 (3)	5 (3)
Mini-Mental State Examination score, mean (SD)	17.6 (6.8)	15.9 (7.4)
Medication use All psychotropics	16 (21)	18 (23)
Cognitive enhancers	5 (7)	7 (9)
Caregi	ver	
Age, mean (SD), y	70 (13)	70 (13)
Sex Male	20 (26)	26 (34)
Female	56 (74)	51 (66)
Race/ethnicity Native American or Alaska Native	1 (1)	0
Asian/Pacific Islander	3 (4)	3 (4)
Black	7 (9)	5 (6)
Hispanic	1 (1)	0
White	64 (84)	69 (90)
Years of education, mean (SD)	14 (3)	13 (3)
Relationship with participant Spouse	60 (79)	62 (81)
Adult child	4 (5)	5 (6)
Other	12 (16)	10 (13)

*Values are expressed as number (percentage) unless otherwise indicated. All group comparisons P>.05.

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Table 2. Significant Outcomes

	No. of Participants	Mean (SD) Score				
		SF-36	SIP Mobility	Cornell Depression in Dementia Scale	Restricted Activity, d	No. (%) of Participants Who Exercised ≥60 min/wk
Baseline Routine medical care	77	67.9 (35.1)	14.2 (13.8)	5.8 (4.5)	0.4 (2.2)	43 (56)
RDAD	76	62.2 (36.6)	16.3 (19.2)	5.7 (3.9)	0.6 (2.2)	43 (56)
Posttest (3 mo) Routine medical care	72 68	50.7 (39.1) 72.1 (33.0)	15.2 (17.1)	6.2 (3.8) 5.2 (3.6)	0.6 (2.5)	45 (62) 56 (82)
6 mo Routine medical care	64	60.9 (35.0)	16.7 (16.2)	6.5 (4.4)	0.6 (2.3)	44 (69)
RDAD 12 mo	62	64.9 (36.1)	17.4 (20.7)	6.4 (3.8)	0.3 (1.8)	40 (64)
Routine medical care	58	62.1 (37.8)	15.9 (14.7)	7.1 (4.5)	0.7 (2.3)	34 (59)
RDAD	57	68.9 (32.8)	16.0 (19.7)	7.0 (4.5)	0.9 (3.3)	36 (64)
18 mo Routine medical care	47	61.2 (34.5)	20.6 (18.7)	7.5 (5.7)	1.1 (3.7)	24 (52)
RDAD	49	71.4 (37.8)	14.6 (17.1)	6.3 (4.3)	0.3 (2.0)	34 (69)
24 mo Routine medical care	44	57.4 (40.2)	21.0 (18.8)	7.4 (5.0)	0 (0.3)	20 (45)
RDAD	45	60.0 (41.1)	18.9 (17.1)	6.4 (4.5)	0.9 (3.2)	23 (51)
Pre (baseline) and post (3 mo) intention-to-treat <i>P</i> Value		<.001	.17	.02	<.001	.01
Longitudinal <i>P</i> Value (all posttreatment visits)*		<.01	.02	.10	.45	.13

Abbreviations: RDAD, Reducing Disability in Alzheimer Disease; SF-36, 36-item Short-Form Health Survey; SIP, Sickness Impact Profile. *Longitudinal analysis used all 5 posttreatment visits.

	Reducing Disability in Alzheimer Disease (n = 76)	Routine Medical Care (n = 77)
Withdrawals	31 (41)	33 (43)
Patient institutionalized	21 (68)	22 (67)
Behavioral problems of patient	4 (19)	11 (50)
Impairment or illness of patient	4 (19)	4 (18)
Increased ADL impairment of patient	5 (24)	6 (27)

III health or death of caregiver 8 (38) Unwilling or unable to continue Caregiver 5 (16) Patient 5 (16) Abbreviation: ADL, activities of daily living. *Values are expressed as number (percentage).

patient institutionalization did differ (TABLE 3). Eleven control patients (50%) were institutionalized because of patient behavioral problems compared with 4 RDAD patients (19%). One control patient (5%) was institutionalized because of caregiver health or caregiver availability compared with 8 RDAD patients (38%).

Additional Analyses

We further investigated patients with preexisting mood disturbance to determine whether those with problems were more or less likely to benefit from intervention. Patients with a score of 6 or greater on the Cornell scale were selected because this score was above our sample mean score at baseline. For these patients, Hamilton Depression Rating scale scores were examined. In ITT analysis, RDAD patients improved at posttest (mean [SD], 2.0 [4.9]) while control patients worsened (mean [SD], 0.6 [5.1]). The mean adjusted difference was 2.21 (95% CI, 0.22-4.20;

1 (5)

5 (15)

6 (18)

P=.04). Over 24 months of follow-up, this difference of 2.14 (95% CI, 0.14-4.17) remained statistically significant (P = .04).

Baseline cognitive status (MMSE score), patient or caregiver sex, and duration of dementia did not affect results. Analyses of treatment compliance data completed by study trainers showed that 91% of RDAD patients attempted their exercise homework (79% completed >75% of assigned homework). Only 9% of RDAD patients did not complete any homework.

COMMENT

This study demonstrated that an integrated treatment program designed to train dementia patients and their caregivers in exercise and behavioral management techniques was successfully implemented in a community setting. Caregivers were able to learn how to encourage and supervise exercise participation, and patients participating in this program achieved increased levels of physical activity, decreased rates of de-

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pression, and improved physical health and function. Patients in the RDAD group fared significantly better than those in the control group. Scores on the SF-36 Physical Role Functioning subscale, Cornell Depression scale, and the number of restricted activity days all significantly improved. Posttest physical function improvements were maintained at 24-month follow-up and, for those patients entering with higher levels of initial depression, improvements in depression were maintained after 24 months.

The reasons for patient institutionalization throughout the 24-month follow-up period differed between patients in the RDAD group and in the routine care group. Eleven routine care patients (50%) who discontinued the study due to institutionalization did so because he/she experienced an increase of behavioral problems compared with only 4 (19%) of 21 in the RDAD group (Table 3). These numbers are small but suggest that the RDAD program may have influenced patients and caregivers to a significant enough degree to delay institutionalization caused by an inability to manage patient behavioral disturbances.

Adherence to program recommendations was quite high demonstrating that community-dwelling caregivers can be successfully trained to supervise a home exercise program for persons with dementia. Although other studies have found that exercise professionals in structured institutional settings can implement exercise programs, 10,42-44 this is the first to show that a simplified exercise program can be taught to caregivers of dementia patients residing in the community. Furthermore, this study involved a heterogeneous array of patients and caregivers, lending support to the generalizability of these findings.

We included both caregivers and patients in this intervention. We did not, however, assess the degree to which caregivers felt satisfied with what they were learning, nor did we assess the potential outcomes of treatment on caregivers. It became clear as we conducted the study that caregivers were benefiting from participation, but the nature of that benefit and its potential impact on their caregiving was not determined. We also did not investigate the relative efficacy of exercise or behavioral management in producing the results reported herein. We were interested in the combined effect of both treatment components because we were interested in improving both physical and affective health. Now that the combination has been shown efficacious in producing change, we would be interested in exploring the relative effectiveness of each component alone as well as the impact of treatment on caregivers themselves. While we hypothesize that the combination is superior and that caregivers benefit from training, these are empirical questions worthy of inquiry.

Future research is needed to determine whether the effects obtained herein can be replicated or improved. Given that our depressed patients improved, a more targeted approach may show stronger results. That would be consistent with our own earlier work in which we found that a targeted behavioral approach was successful in reducing the levels of depression in dementia patients and their caregivers.18 Because exercise is also associated with reduced depression in adults without dementia, targeting patients with coexisting depression and dementia might enhance treatment effects. Given these results and the consistently strong association between physical exercise and health in older adults without dementia,13-15 the potential health benefits of a simple exercise program for older adults with dementia should not be overlooked.

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Author Contributions: Dr Teri, as principal investigator, had full access to all study data and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Teri, McCurry, Logsdon, Buchner, Barlow, Kukull, LaCroix, McCormick, Larson. Acquisition of data: Teri, McCurry, Logsdon, Barlow, LaCroix. Analysis and interpretation of data: Teri, Gibbons, McCurry, Logsdon, Barlow, Kukull, McCormick, Larson. Drafting of the manuscript: Teri, Gibbons, McCurry, Logsdon, Larson.

Critical revision of the manuscript for important intellectual content: Teri, Gibbons, McCurry, Logsdon, Buchner, Barlow, Kukull, LaCroix, McCormick, Larson. *Statistical expertise*: Teri, Gibbons, Barlow, LaCroix, McCormick.

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