Effectiveness of Collaborative Care for Older Adults With Alzheimer Disease in Primary Care

A Randomized Controlled Trial

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Context Most older adults with dementia will be cared for by primary care physicians, but the primary care practice environment presents important challenges to providing quality care.

Objective To test the effectiveness of a collaborative care model to improve the quality of care for patients with Alzheimer disease.

Design, Setting, and Patients Controlled clinical trial of 153 older adults with Alzheimer disease and their caregivers who were randomized by physician to receive collaborative care management (n=84) or augmented usual care (n=69) at primary care practices within 2 US university-affiliated health care systems from January 2002 through August 2004. Eligible patients (identified via screening or medical record) met diagnostic criteria for Alzheimer disease and had a self-identified caregiver.

Intervention Intervention patients received 1 year of care management by an interdisciplinary team led by an advanced practice nurse working with the patient's family caregiver and integrated within primary care. The team used standard protocols to initiate treatment and identify, monitor, and treat behavioral and psychological symptoms of dementia, stressing nonpharmacological management.

Main Outcome Measures Neuropsychiatric Inventory (NPI) administered at baseline and at 6, 12, and 18 months. Secondary outcomes included the Cornell Scale for Depression in Dementia (CSDD), cognition, activities of daily living, resource use, and caregiver's depression severity.

Results Initiated by caregivers' reports, 89% of intervention patients triggered at least 1 protocol for behavioral and psychological symptoms of dementia with a mean of 4 per patient from a total of 8 possible protocols. Intervention patients were more likely to receive cholinesterase inhibitors (79.8% vs 55.1%; $P=.002$) and antidepressants (45.2% vs 27.5%; $P=.03$). Intervention patients had significantly fewer behavioral and psychological symptoms of dementia as measured by the total NPI score at 12 months (mean difference, –5.6; $P=.01$) and at 18 months (mean difference, –5.4; $P=.01$). Intervention caregivers also reported significant improvements in distress as measured by the caregiver NPI at 12 months; at 18 months, caregivers showed improvement in depression as measured by the Patient Health Questionnaire-9. No group differences were found on the CSDD, cognition, activities of daily living, or on rates of hospitalization, nursing home placement, or death.

Conclusions Collaborative care for the treatment of Alzheimer disease resulted in significant improvement in the quality of care and in behavioral and psychological symptoms of dementia among primary care patients and their caregivers. These improvements were achieved without significantly increasing the use of antipsychotics or sedative-hypnotics.

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MOST OLDER ADULTS, including those with dementia, receive their health care from generalist physicians.[1,2] Although primary care physicians prescribe the majority of the psychoactive medications to older adults,[3] the primary care setting appears to be poorly designed and underresourced to provide comprehensive management approaches for dementia.[2,4-6] Over the past decade, quality improvement efforts for geriatric syndromes in primary care have focused on decision support, care management, and other systems-level innovations to deliver guideline-level care.[7,8] Despite recent evidence that early recognition and treatment of cognitive impairment may improve patient outcomes,[9] there is continued controversy about the cost and utility of screening and early diagnosis, and continued debate about the effectiveness of cholinesterase inhibitors.[10-14] Current pharmacological treatment of behavioral symptoms such as aggression or psy-

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chosis is limited by modest efficacy and important adverse effects.[3,15] Nonpharmacological management of behavioral symptoms is recommended as an initial approach but caregivers and clinicians often do not have the resources to provide this care.

Indeed, behavioral and psychological symptoms of dementia represent a major challenge in the care of older adults with Alzheimer disease. These symptoms, which include a broad range of distressing behaviors and psychological reactions, affect the health and quality of life of both the patient and his/her caregiver. More than 90% of patients with dementia will experience behavioral and psychological symptoms of dementia at some point during the course of their illness.[16] Behavioral and psychological symptoms of dementia are not simply a manifestation of end-stage dementia. Older adults with mild cognitive impairment also experience clinically significant behavioral and psychological symptoms.[17] Leaving patients' behavioral and psychological symptoms of dementia untreated has been associated with caregiver burnout, nursing home placement, poor management of comorbid conditions, and excess health care costs.[18-20]

Several authoritative groups have published consensus guidelines for the care of patients with Alzheimer disease.[21-24] Ten factors (BOX) are shared across these guidelines. The effectiveness of this comprehensive package of care has never been tested. Given the major system redesign needed to adopt these recommendations in primary care, such a field test is needed.[12] We previously reported findings describing the problems and prospects of a comprehensive dementia screening and diagnosis program in primary care.[6] The purpose of the current study was to conduct a randomized controlled trial to test the effectiveness of collaborative care management for older adults with Alzheimer disease compared with augmented usual care. Notably, the design of this trial assumes the perspective of the primary care physician and thus targeted the heterogeneous population of older adults with Alzheimer disease and multiple comorbid conditions that is typically found in primary care. For this reason, we hypothesized that the intervention's primary effect would be improvement in neuropsychiatric symptoms rather than cognitive function.

Box. Common Guideline Recommendations for Diagnosis and Management of Alzheimer Disease and Related Dementias*

Active screening for cognitive impairment coupled with a second stage assessment to diagnose the specific type of dementia

Evaluation for reversible causes of dementia

Referral to patient and caregiver educational programs and/or community support agencies

Consideration for specialty referral

Active case finding and treatment for depression, psychoses, behavioral disturbances, and hazardous activities

Active case finding and treatment for excess disability due to comorbid medical conditions

Consideration for treatment with cholinesterase inhibitors

Facilitated communication among the clinicians both within the health care system and the community

Active surveillance and tracking of patient outcomes with feedback to the health care team

Active monitoring and support of the caregiver's emotional and physical health

*Based on published guidelines.[21-24]

METHODS

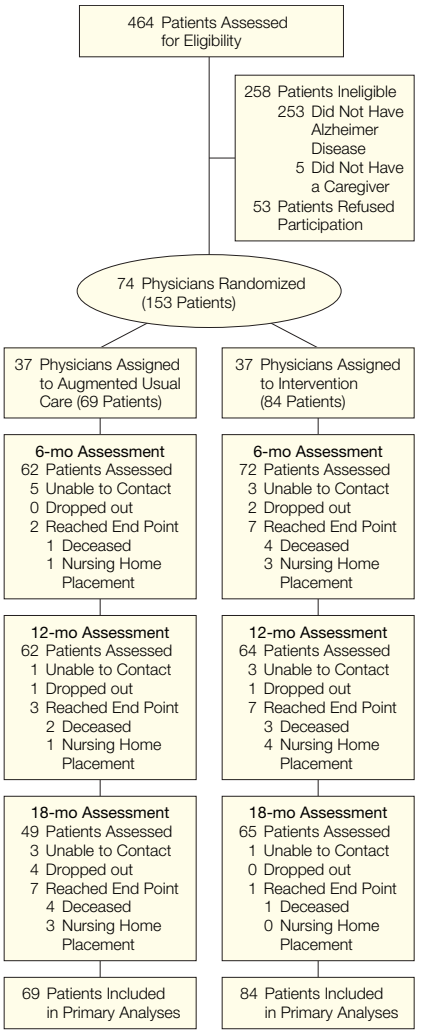
The study was approved by the institutional review board of Indiana University/Purdue University. All participants or their caregivers provided written informed consent for participation. Consent was obtained in 2 stages. Patients first consented to complete the diagnostic evaluation.[6] Among those eligible for the clinical trial following the diagnostic evaluation, additional informed consent was obtained from both the patient and the caregiver. The FIGURE describes the flow of individuals through the study.

Recruitment

Patients were recruited to the clinical trial from 2 large primary care practices from January 2002 through August 2004. The first practice includes 7 community-based health centers affiliated with Wishard Health Services, a university-affiliated urban health care system serving medically indigent patients in Indianapolis, Ind. This practice serves approximately 5000 older adults. The second site included 3 primary care practices at the Indianapolis Veterans Affairs Medical Center. This practice provides primary care to approximately 6000 veterans aged 65 years or older. Patients were recruited to the clinical trial by (1) physician referral following a written prompt from the research team that the patient screened positive on cognitive testing; or (2) physician referral following a written prompt from the research team that the patient may be eligible due to a medical record diagnosis consistent with dementia. All referred patients, regardless of clinic site or method of referral, completed the formal diagnostic evaluation described below. Exclusion criteria included residence in a nursing home, unable to understand English, no access to a telephone, or no caregiver willing to consent to participate in the study.

The diagnostic assessment has been previously described and was de-

Figure. Patient and Physician Participation in Study



signed and implemented in collaboration with faculty at the Indiana Alzheimer Disease Center. The assessment included the neuropsychological battery from the Consortium to Establish a Registry for Alzheimer Disease,[25] a semistructured interview with the caregiver,[26] and a targeted neurological and cardiovascular physical examination. These data were reviewed by a consensus diagnosis panel, which included a psychologist, a neuropsychologist, a geriatrician, and a geriatric psychiatrist. Individuals were eligible for the clinical trial if they met criteria for possible or probable Alzheimer disease based on *Diagnostic and Statistical Manual of Mental Disorders, Third Edition,*[27] criteria.

All potential participants and their caregivers (both intervention and augmented usual care patients) were provided written materials and face-to-face counseling by a geriatric nurse practitioner, who had received specific training in communicating the diagnosis of Alzheimer disease to patients and families. This private meeting lasted between 40 and 90 minutes and was conducted at the primary care clinic. All participants also were provided with written materials describing local community resources, including access to the local chapter of the Alzheimer's Association. Primary care physicians provided permission for the meeting with the geriatric nurse practitioner and for approaching the patient for participation in the study. In addition, the primary care physicians for both augmented usual care and intervention participants received a written consultation note communicating the results of the diagnostic assessment. Because these interventions are not typical of usual care, we refer to the control group as "augmented usual care."

Randomization

To minimize the potential for contamination across groups, physicians were the unit of randomization. Thus, physician randomization status determined the patient's randomization status. Prior to initiating the study, we obtained a list of all primary care physicians at all participating clinics from the practice leadership. Physicians were randomized in blocks of 2 stratified by teaching status (faculty or resident) and the clinic site. A random number table was used to classify the first physician as usual care if the table generated an even number or intervention if the table yielded an odd number. The second physician was then assigned the opposite status and the process was repeated until all physicians were randomized. Physicians were not informed of their randomization status and control physicians did not have access to the intervention. Members of the diagnostic team, the geriatric nurse practitioner, and patients and caregivers were blinded to the physician's randomization status until the counseling session described above was completed and the patient consented to participate in the clinical trial and completed the baseline assessment.

Intervention

Primary care physicians of augmented usual care patients could pursue any evaluation or treatment they deemed appropriate. Intervention patients and their caregivers received collaborative care management for a maximum of 12 months by a team led by their primary care physician and a geriatric nurse practitioner who served as the care manager. All intervention patients were recommended for treatment with cholinesterase inhibitors (or memantine) unless contraindicated. The minimum intervention that all treatment group caregivers and patients received included education on communication skills; caregiver coping skills; legal and financial advice; patient exercise guidelines with a guidebook and videotape; and a caregiver guide provided by the local chapter of the Alzheimer's Association. All of the components of this minimum intervention as well as the behavioral interventions described below were provided by a geriatric nurse practitioner, who served as the care manager.

There were 2 care managers, each of whom was an advanced practice nurse, with 1 based at each of the 2 large primary care practices. Caregivers and patients were seen by the care manager in the primary care clinic bimonthly initially and then contacts were lengthened to monthly for a period of 1 year. At each contact with the care manager, caregivers completed the Memory and Behavior Problems Checklist[28] to assess current symptoms and stressors. Based on the caregiver's responses, individualized recommendations were made regarding how to manage a patient's behavioral symptoms. Items checked on a subscale of the Memory and Behavior Problems

Checklist activated a specific behavioral intervention protocol that had been developed for this study. These 8 protocols included personal care, repetitive behavior, mobility, sleep disturbances, depression, agitation or aggression, delusions or hallucinations, and the caregiver's physical health. Each of these protocols focused first on nonpharmacological interventions. A description of these nonpharmacological interventions has been previously published[29] and the protocols are available at http://iucar.iu.edu/research/behavioralprotocols.html. If the nonpharmacological approach failed, the care manager then collaborated with the primary care physician to institute drug therapy for depression, agitation, sleep disturbance, or delusions.

The primary care physician and the care manager were supported through 2 additional mechanisms. First, the care manager had weekly meetings with a support team comprised of a geriatrician, geriatric psychiatrist, and a psychologist who reviewed the care of new and active patients and monitored adherence to the standard protocols. Second, the care manager was supported by a Web-based longitudinal tracking system that managed the schedule for patient contacts, tracked the patient's progress and current treatments, and provided an instrument for communicating the patient's and caregiver's current clinical status to the entire care team. All intervention patients and their caregivers also were invited to participate in voluntary group sessions. During these sessions, caregivers were taken to a support session led by a social psychologist that focused on caregiver stress. Patients were taken to a nearby room for a group chair-based exercise class led by a health psychologist and the care manager.[30] The study protocol did not mandate additional visits to the primary care physician.

Outcome Measures

The caregivers of patients in both treatment groups completed a baseline assessment by telephone with interviewers who were blinded to the patient's randomization status. This telephone interview was repeated at 6, 12, and 18 months. The interview included 3 standardized instruments developed by the Alzheimer's Disease Cooperative Study investigators[31]: the Neuropsychiatric Inventory (NPI),[32,33] activities of daily living,[34] and health care resource use.[31] Caregivers also provided the data to complete the Cornell Scale for Depression in Dementia[35,36] for the patient. Caregivers completed the caregiver portion of the NPI and the Patient Health Questionnaire-9 to assess the caregiver's mood.[37] Patients completed the Telephone Interview for Cognitive Status, a telephone version of the Mini-Mental State Examination (MMSE).[38] Using each patient's list of prescribed medications, we calculated a chronic disease score as a measure of medical comorbidity.[39,40] The patient's race was identified by the caregiver and race was considered an important patient characteristic to measure because prior work in this patient population demonstrated that race was associated with the prevalence of cognitive impairment.[4] Caregiver's satisfaction with the patient's care was assessed with the question: "Over the last 3 months, how would you rate the quality of care [the patient] has received overall from the primary care clinic?"

Process of care measures included the frequency of initiation for any of the 8 protocols for caregiver education and nonpharmacological management of behavioral symptoms. We report these educational processes of care measures only for the intervention group for 3 reasons. First, the protocols were only available through the study for intervention patients and were not otherwise available in the primary care clinics. Second, primary care physicians infrequently record the provision or content of counseling in the medical record even when it occurs. Third, telephone interviewers were not allowed to query respondents about these interventions because this would have provided a mechanism for the telephone interviewer to learn the patient's randomization status. Process of care measures for pharmacotherapy were collected for both treatment groups using the pharmacy database from each study site.

At each follow-up interview, caregivers completed the Alzheimer's Disease Cooperative Study health resource use questionnaire.[31] Specific questions included "In the last 6 months, how many times was [the patient] examined by a doctor or nurse? In the last 6 months, how many times was she [or he] admitted to the hospital and how many nights for each hospital stay?" The caregiver also provided information on whether the patient had been placed in a nursing home for long-term care.

Statistical Analysis

The primary hypothesis was that older adults in the intervention group would have lower total NPI scores compared with augmented usual care patients at 12 months. We specifically hypothesized that the intervention would not result in significant differences in cognition between groups because we anticipated frequent ambient use of cholinesterase inhibitors among the augmented usual care group. In addition, we suspected lower effectiveness of cholinesterase inhibitors among primary care patients with a high burden of medical and social comorbidity. These patients are underrepresented in efficacy studies of pharmacotherapy. We chose the NPI as the outcome measure most likely to be sensitive to change in this heterogeneous patient population. We did not exclude patients without behavioral and psychological symptoms of dementia at baseline because most patients with Alzheimer disease will develop behavioral and psychological symptoms of dementia and because the process of care changes we hoped to facilitate are broader than behavioral and psychological symptoms of dementia interventions alone. Consistent with the current geriatric health services literature, cognition, activities of daily living, and resource use are included as secondary outcome measures because it is possible to improve behavioral and psychological symptoms of dementia at the expense of overall functioning.

Table 1. Baseline Comparison of Demographic Characteristics*

	Augmented Usual Care (n = 69)	Intervention (n = 84)	*P* Value
Patient Characteristics			
Female	27 (39.1)	39 (46.4)	.41
Black	40 (58.0)	35 (41.7)	.05
Married	33 (47.8)	41 (48.8)	>.99
Medicaid recipient	46 (70.8)	57 (76.0)	.56
Age, mean (SD), y	77.7 (5.7)	77.4 (5.9)	.79
Annual income, mean (SD), $	14 113 (12 190)	15 750 (14 215)	.48
Education, mean (SD), y	8.6 (3.8)	9.6 (4.5)	.15
Mini-Mental State Examination score, mean (SD)	17.5 (5.2)	18.6 (5.9)	.24
No. of medications taking, mean (SD)	5.8 (2.8)	5.8 (3.2)	.98
Chronic disease score, mean (SD)	8.0 (3.9)	7.6 (4.0)	.63
Caregiver Characteristics			
Age, mean (SD), y	61.7 (14.4)	60.3 (15.5)	.56
Female	66 (95.7)	70 (83.3)	.02
Live with patient	50 (72.5)	56 (66.7)	.48
Relationship of caregiver to patient			
Spouse	32 (46.4)	36 (42.9)	.81
Child	25 (36.2)	30 (35.7)	
Other	12 (17.4)	18 (21.4)	

*Values are expressed as number (percentage) unless otherwise indicated.

Nursing home placement or death was considered an end point for the study. Patients or their caregivers were not contacted further after these end points were reached. In our original power calculations, we determined that a sample size of 225 participants would result in 80% power to detect a difference of 4.2 points on total NPI scores between groups using a 2-tailed α level of .05. We did not reach this sample size because we exhausted the available pool of potential participants across all participating clinics after nearly 3 years of recruitment. Although we did not reach targeted enrollment, the effect size of the intervention on the NPI exceeded the posited difference of 4.2 thus eliminating concern for type I error on the primary outcome measure. The sample size does limit the power to detect smaller differences in cognition, activities of daily living, or nursing home placement.

Two-sample *t* tests and χ^2 tests were used to compare the demographic and clinical characteristics of intervention and augmented usual care patients at baseline. For each dependent variable, mixed-effects regression models were used including 6-, 12-, and 18-month follow-up data in an intention-to-treat analyses using last observation carried forward for patients who were lost to follow-up before reaching a study end point. Baseline values were adjusted for in the model. Because NPI scores are highly skewed, we analyzed the log (total NPI + 1). In the mixed-effects models, time was treated as a categorical variable, with time, intervention status, and their interaction being included as fixed effects. A random effect for physician and patient nested within physician was included to account for within-patient and within-physician correlation. If the time × intervention interaction was significant, the difference at each time point was tested to determine when the intervention took effect. For time to death and nursing home placement, Kaplan-Meier estimation was used to obtain the survival curves. The Wilcoxon test was used to test for differences between the intervention and augmented usual care groups. We used SAS software version 9.1 (SAS Institute Inc, Cary, NC). All tests were considered significant at $P<.05$.

RESULTS

Sample Characteristics

Baseline characteristics of the 153 individuals randomized to intervention or augmented usual care appear in TABLE 1. These patients were cared for by 74 different primary care physicians (37 in each treatment group). The mean number of enrolled patients per augmented usual care physician was 1.9 (range, 1-6 patients) and per intervention physician was 2.3 (range, 1-8 patients). Approximately 80% of usual care patients were seen by faculty physicians while 71% of intervention patients were seen by faculty ($P=.26$). Half of the study patients were black and most patients had multiple comorbid chronic conditions and were socioeconomically disadvantaged. Augmented usual care patients were significantly more likely to be black and have a female caregiver. Approximately 1 in 5 of the caregivers was neither a spouse nor a child of the patient. Patients had moderate dementia as demonstrated by the group mean MMSE score of 18. The mean MMSE score of our sample is comparable with the weighted mean MMSE score of 17.9 among studies of cholinesterase inhibitors, which was identified in a recent systematic review.[15]

Process of Care

The mean (SD) number of contacts with the care manager was 14.4 (8.9) and the median was 13 (range, 0-51) over 12 months. Approximately half of these contacts (mean [SD], 7.7 [5.8]; median, 7 [range, 0-28]) were face-to-face and half were telephone contacts (mean [SD], 6.7 [5.8]; median, 5 [range, 0-35]). During these visits, the care manager initiated treatment protocols based on responses to the Memory and Behavior Problems Checklist. TABLE 2 shows the frequency of use of these protocols. Demonstrating the level of symptoms and distress among this population, 89% of intervention patients triggered at least 1 protocol for behavioral and psychological symptoms of dementia with a mean of 4 per patient from a total of 8 possible pro-

tocols. Although support group counseling was offered only as an option, 56% of patients and their caregivers attended at least 1 session. Intervention group patients were more likely to be treated with cholinesterase inhibitors and antidepressants (TABLE 3). However, 55% of the augmented usual care group also received cholinesterase inhibitors, underscoring the fact that the control group in this study is not a placebo control. In addition, the intervention did not result in an increased use of antipsychotics or sedative-hypnotics compared with augmented usual care. At 12 months, 82.8% of intervention caregivers rated the patient's primary care as very good or excellent compared with 55.9% of those in augmented usual care ($P=.002$). At 18 months (6 months after the intervention ended), only 70% of intervention caregivers rated the patient's primary care as very good or excellent compared with 62% of those in augmented usual care ($P=.27$).

Overall attrition for any reason was relatively low for this frail patient population (17% at 12 months and 25% at 18 months). Attrition due to death (7 augmented usual care patients vs 8 intervention patients; $P>.99$), nursing home placement (5 vs 7 patients; $P>.99$), or dropping out of the study or unable to contact (8 vs 4 patients; $P=.14$) were not significantly different between the 2 groups at 18 months. Time to death and time to nursing home placement also did not differ between groups. In comparing those lost to follow-up for any reason between intervention and augmented usual care patients, there were no group differences in baseline total NPI score, MMSE score, or chronic disease score.

Main Outcomes

The patient and caregiver outcomes at all time points for both groups appear in TABLE 4. Intervention patients experienced significant improvements in total NPI scores compared with patients who received augmented usual care. Lower NPI scores reflect fewer behavioral symptoms. Although the intervention was discontinued at 12 months, significant improvements in NPI scores continued at the 18-month assessment. The intervention had no significant impact on patient depression scores as measured by the Cornell Scale for Depression in Dementia, cognition as measured by the Telephone Interview for Cognitive Status, or function as measured by the Alzheimer's Disease Cooperative Study's activities of daily living compared with augmented usual care. Caregivers experienced significant improvements in caregiver stress at 12 months but not at 18 months as measured by the caregiver NPI. Lower scores on the caregiver NPI reflect fewer symptoms of stress related to the patient's behavioral and psychological symptoms of dementia. These improvements in caregiver stress were reflected in improved caregivers' Patient Health Questionnaire-9 scores at the 18-month assessment.

Health Care Use

Augmented usual care patients reported fewer cumulative physician or nurse visits (mean [SD], 5.6 [5.1]; median, 4 [range, 0-27]) than intervention patients (mean [SD], 9.3 [13.4]; median, 5 [range, 0-67]) over the 12 months of the intervention ($P=.03$) and these differences persisted at 18 months (7.5 [median, 5.5; range, 0-36] vs 12.9 [median, 9.0; range, 0-127]; $P=.02$). There was no difference in cumulative hospitalization rates between augmented usual care and intervention patients at 12 months (18.8% vs 22.6%, respectively; $P=.69$) or at 18 months (24.6% vs 29.8%; $P=.59$) or in mean hospital days at 12 months (1.0 vs 1.7; $P=.34$) or at 18 months (1.5 vs 2.6; $P=.28$). Rates of nursing home placement did not differ significantly between augmented usual care and intervention patients at 12 months (1.5% vs 6.0%; $P=.22$) or at 18 months (2.9% vs 8.3%; $P=.19$).

COMMENT

To our knowledge, this is the first randomized clinical trial testing the effectiveness of treatment guidelines for Alzheimer disease as delivered through a collaborative care model. We believe this is the first trial in this area that integrates these recommendations within primary care. This setting is important because it represents the care site in which most older adults receive their medical care, including those with

Table 2. Intervention Patients Receiving Nonpharmacological Protocols

	No. (%) of Intervention Patients Receiving Nonpharmacological Protocol (n = 84)
Offered to all intervention patients	
Stress/coping	76 (90.5)
Exercise	76 (90.5)
Communication	74 (88.1)
Legal and financial	72 (85.7)
Offered based on reported symptoms	
Caregiver's physical health	75 (89.3)
Depression	69 (82.1)
Repetitive behavior	62 (73.8)
Aggression	60 (71.4)
Mobility	52 (61.9)
Personal care	35 (41.7)
Sleep disturbances	31 (36.9)
Delusions	26 (31.0)
Optional participation	
Support group attendance	47 (56.0)

Table 3. Group Comparison of Pharmacological Management

	Augmented Usual Care (n = 69)	Intervention (n = 84)	*P* Value
Prescribed medication			
Cholinesterase inhibitors	38 (55.1)	67 (79.8)	.002
Memantine*	6 (8.7)	7 (8.3)	>.99
Antidepressants	19 (27.5)	38 (45.2)	.03
Antipsychotics	5 (7.3)	11 (13.1)	.29
Sedative-hypnotics	7 (10.1)	8 (9.5)	>.99
No prescribed medications	1 (1.5)	1 (1.2)	>.99

*All 13 patients prescribed memantine also received a cholinesterase inhibitor.

dementia, and primary care physicians frequently prescribe psychoactive medications to these older adults. This setting is also important because it represents the logical target for any initiatives to improve the early identification and treatment of dementia or precursor conditions. The primary care practices targeted in the current study serve a medically-indigent, mixed-race population with multiple comorbid conditions. These patient groups have been understudied in previous treatment trials[15] of Alzheimer disease and these patients have fewer personal resources, including family caregivers. The enrolled patients were, however, similar to previous clinical trials in terms of severity of dementia and severity of neuropsychiatric symptoms.

Table 4. Clinical Outcomes*

Instrument	Mean (SD) Score: Augmented Usual Care	Mean (SD) Score: Intervention	Between-Group Difference (95% CI)	*P* Value
Total Patient Neuropsychiatric Inventory (range, 0-144)†				
Baseline	13.4 (21.2)	10.5 (15.3)	−2.8 (−8.3 to 2.6)	.33
6 mo	11.1 (16.4)	9.4 (12.9)	−1.1 (−5.4 to 3.1)	.61
12 mo	16.1 (19.4)	8.0 (12.0)	−5.6 (−9.9 to −1.3)	.01
18 mo	16.2 (18.7)	8.4 (10.2)	−5.4 (−9.9 to −1.2)	.01
No. of Neuropsychiatric Inventory modules ≥1 (range, 0-12)†				
Baseline	3.2 (2.8)	3.0 (2.7)	−0.2 (−1.0 to 0.7)	.68
6 mo	2.9 (2.4)	2.7 (2.6)	−0.1 (−0.9 to 0.6)	.75
12 mo	3.5 (2.7)	2.5 (2.5)	−0.7 (−1.5 to 0.01)	.05
18 mo	3.6 (2.8)	2.3 (2.4)	−0.9 (−1.7 to −0.2)	.02
Cornell Scale for Depression in Dementia (range, 0-38)†				
Baseline	5.4 (5.9)	4.4 (4.9)	−1.1 (−2.8 to 0.6)	.22
6 mo	5.2 (5.4)	4.3 (6.0)	−0.3 (−1.8 to 1.1)	.65
12 mo	5.8 (5.9)	3.5 (3.9)	−1.0 (−2.6 to 0.5)	.17
18 mo	5.4 (4.4)	4.2 (3.9)	−0.1 (−1.6 to 1.5)	.94
Telephone Interview for Cognition (range, 0-41)‡				
Baseline	17.1 (6.8)	17.9 (8.3)	0.8 (−2.0 to 3.6)	.52
6 mo	16.0 (7.1)	16.9 (8.8)	−0.6 (−2.1 to 0.9)	.46
12 mo	14.6 (8.2)	16.7 (8.9)	0.9 (−0.6 to 2.6)	.22
18 mo	15.3 (9.0)	16.0 (9.5)	0.1 (−1.5 to 1.7)	.93
Alzheimer Disease Cooperative Study Group ADLs (range, 0-78)‡				
Baseline	49.3 (15.9)	50.6 (15.8)	1.3 (−4.4 to 7.1)	.62
6 mo	47.0 (16.7)	49.3 (8.8)	0.6 (−3.0 to 4.3)	.73
12 mo	44.6 (17.0)	48.6 (17.7)	1.4 (−2.3 to 5.1)	.44
18 mo	42.1 (16.8)	45.7 (20.1)	2.5 (−1.2 to 6.2)	.18
Total Caregiver Neuropsychiatric Inventory (range, 0-60)†				
Baseline	6.5 (10.4)	4.2 (5.6)	−2.4 (−4.9 to 0.2)	.08
6 mo	5.7 (7.2)	4.4 (6.4)	−0.1 (−2.0 to 1.8)	.92
12 mo	7.7 (8.7)	3.5 (5.8)	−2.2 (−4.2 to −0.2)	.03
18 mo	7.4 (9.7)	4.6 (6.3)	−1.0 (−3.0 to 1.0)	.33
Caregiver Patient Health Questionnaire-9 (range, 0-27)†				
Baseline	4.4 (5.6)	3.8 (5.1)	−0.6 (−2.3 to 1.1)	.49
6 mo	4.3 (5.1)	3.6 (5.0)	−0.5 (−1.8 to 0.9)	.50
12 mo	4.6 (5.6)	3.1 (3.9)	−0.9 (−2.2 to 0.5)	.21
18 mo	5.2 (5.3)	3.1 (4.5)	−1.6 (−3.0 to −0.2)	.02

Abbreviation: ADLs, activities of daily living.
*Intention-to-treat, mixed-effects regression models adjusted for baseline score and using last observation carried forward.
†Higher scores equate with worse symptoms.
‡Higher scores equate with better function.

Unlike previous trials[41-43] that have focused on medications alone or psychosocial interventions alone, the current study adopted a comprehensive set of guidelines and integrated these guidelines within the context of primary care. We have demonstrated that this comprehensive approach results in clinically significant improvements in behavioral and psychological symptoms of dementia. These improvements are accompanied by a reduction in caregiver stress. The control patients in this study received augmented usual care, which included counseling for the patient and his/her caregiver about the diagnosis of Alzheimer disease, written educational materials, and referral to community resources. Control physicians received notification of the patient's diagnosis and could choose to treat Alzheimer disease or the behavioral and psychological symptoms of dementia. Thus, our findings may underestimate the impact of the intervention compared with true usual care.

We found no evidence that the intervention improves or worsens cognition, activities of daily living, or rates of nursing home placement. Prior studies[44-46] of similar size have shown a decline in the rate of deterioration in cognition among older adults treated with cholinesterase inhibitors compared with adults treated with placebo. There are several reasons why we may not have found such differences. First, 55% of the patients in our augmented usual care group were treated with cholinesterase inhibitors. Second, unlike most efficacy studies, our patient population included a more heterogeneous group of older adults who had multiple competing morbidities; these comorbidities may limit the tolerability and effectiveness of these medications. Third, our assessment of cognition by telephone interview may be less sensitive to change over time than longer instruments administered in person.

Demonstrating differences in nursing home placement may require either a larger sample size or a longer follow-up period. Rates of nursing home placement were low for both groups during the observation period. In a study of support and counseling for spouse-caregivers of patients with Alzheimer disease that was specifically designed to forestall nursing home placement, Mittelman et al[41] reported a mean time of 2.7 and 4 years to nursing home placement among controls and intervention patients, respectively. The current study is limited to 18-month outcomes. In addition to the shorter follow-up period, the scope and complexity of the intervention studied in the current trial requires a substantial amount of time to implement, especially among this patient population. For many patients, the full implementation of the protocol required 3 to 6 months.

The clinical impact of the intervention tested in the current study, as measured by differences on the NPI, exceeds that of most previous studies reporting changes on the NPI. Looking at mean differences at 12 months, we found a group difference in NPI scores of 7.4 without adjusting for baseline differences and a group difference of 5.6 with this adjustment. In a recent comprehensive review of the impact of cholinesterase inhibitors on neuropsychiatric symptoms, Trinh et al[47] reported a mean NPI improvement of 1.72 (95% confidence interval, 0.87-2.57). In a similar review of pharmacological treatment of neuropsychiatric symptoms, Sink et al[15] reported that "pharmacologic therapies are not particularly effective for management of neuropsychiatric symptoms of dementia." These authors found only 1 clinical trial that reported group differences in total NPI scores as high as 8 points. In that study, 206 nursing home patients with severe Alzheimer disease (mean MMSE score of 6.9) were followed up for only 6 weeks.[48] In a randomized trial testing the combination of donepezil and memantine compared with donepezil alone among 404 patients with Alzheimer disease, Tariot et al[43] reported a 3.8-point difference in total NPI score between groups at 6 months. The group difference in NPI score in the current study of 5.6 points over 12 months was associated with a reduction in caregiver stress. Notably, these improvements were achieved without significantly increasing the use of antipsychotics or sedative-hypnotics. In addition, 6 months after the care management ended, the intervention group still had a 5.4-point difference in NPI scores compared with the augmented usual care group.

We were unable to identify any prior intervention studies that specifically targeted patients with Alzheimer disease cared for in primary care practices. Most previous studies enrolled patients from specialty clinics, Alzheimer disease centers, or nursing homes while others used volunteer samples from the community.[41,42] For example, Teri et al[42] enrolled 153 community-dwelling patients with Alzheimer disease and demonstrated significant improvement in function and depression scores among patients receiving an exercise plus behavioral management intervention. Mittelman et al[49] enrolled a volunteer sample of 206 spouse-caregivers for Alzheimer disease patients in a study testing the effectiveness of individual, family, and support group counseling. Mittelman et al demonstrated significant delays in nursing home placement among the intervention group after more than 3 years of follow-up. Global neuropsychiatric scores were not reported in these 2 studies and neither study was integrated with the primary care management of the patient's comorbid conditions.

Our study was specifically designed to apply the shared elements of current treatment guidelines for patients with Alzheimer disease. The study design does not allow us to identify subcomponents of the intervention that might represent the most important active ingredients. Consistent with chronic disease management models, the strength of the intervention is believed to be due to its comprehensive and integrated approach. Unfortunately, application of these treatment guidelines is beyond the resources of most primary care practices as currently structured. This is true both in terms of the practice design requirements and the costs.

Our study was not designed to complete a formal cost-effectiveness analysis. However, we can provide an estimate of the cost of the intervention. We estimate per patient annual costs of the care manager to be approximately $1000 per patient based on a case load of 75 patients per year. Establishing the computer-based tracking system, organizing access to consultants, and arranging for group sessions would represent additional costs per patient. The intervention group also reported more physician or nurse visits than the augmented usual care group. Medication costs for cholinesterase inhibitors are estimated at $1200 per year but these medication costs are not unique to this care management program. Costs of antipsychotic, antidepressant, and sedative-hypnotics used in the management of behavioral and psychological symptoms of dementia represent other current costly expenditures for patients with Alzheimer disease in primary care. Murman and Colenda[50] have estimated that a 1-point deterioration on the NPI is associated with an additional $250 to $400 per year in direct health care costs. Thus, future studies should address the potential for cost savings with this intervention.

Our study has important limitations. The sample size may not have provided sufficient power to detect smaller changes in cognition or nursing home placement and there were baseline differences in race of the patients and the sex of the caregivers between the 2 treatment groups. We repeated the mixed-effect regression models adjusting for these differences and these analyses and our results remained unchanged. Studies of Alzheimer disease among nonvolunteer samples present formidable recruitment challenges. These challenges include patient reluctance to be labeled with a diagnosis of dementia, the need for a consenting caregiver, regulatory requirements for study partici-

pants, the costs of standardized screening and diagnosis, resource limitations within primary care practices, barriers to tracking patients and caregivers over time, and the competing morbidity and mortality from the spectrum of chronic illnesses found among vulnerable older adults. Although the study design supports a high level of internal validity, the generalizability of the findings is limited to those patient-caregiver dyads that were willing to pursue both an evaluation of cognitive impairment and enroll in a clinical trial. The study design also may have biased against demonstrating a larger impact of the intervention because we did not document the caregiver's adherence to the nonpharmacological protocols and reductions in adherence would be expected to reduce the effectiveness of the intervention. In addition, the control patients in this study received a substantive intervention as part of the study protocol and some control patients received substantive additional treatments by their primary care physicians.

In summary, application of the current treatment guidelines for the care of older primary care patients with Alzheimer disease resulted in significant improvements in behavioral and psychological symptoms of dementia and significant improvement in caregiver stress. These improvements exceed those previously reported in studies focusing on pharmacological therapy alone. Achieving a guideline-level dose and duration of the intervention required a care manager who supported the patient's caregiver and physician and adhered to recommended treatment protocols. The intervention demonstrates that care for patients with Alzheimer disease can be improved in the primary care setting but not without substantial changes in the system of care.

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All great art is by its very essence in conflict with the society with which it coexists. It expresses the truth about existence regardless of whether this truth serves or hinders the survival purpose of a given society. All great art is revolutionary because it touches upon the reality of man and questions the reality of the various transitory forms of human society.
—Erich Fromm (1900-1980)