The Effects of Patient Function and Dependence on Costs of Care in Alzheimer's Disease

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OBJECTIVES: To estimate incremental effects of patients' dependence and function on costs of care during the early stages of Alzheimer's disease (AD) and to compare strengths of their relationships with different cost components.

DESIGN: Multicenter, cross-sectional, observational study.

SETTING: Three university hospitals in the United States.

PARTICIPANTS: One hundred seventy-nine community-living patients with probable AD, with modified Mini-Mental State Examination scores of 30 or higher.

MEASUREMENTS: Patients' dependence was measured using the Dependence Scale (DS). Functional capacity was measured using the Blessed Dementia Rating Scale (BDRS). Total cost was measured by summing direct medical costs and informal costs. Direct medical costs included costs of hospitalization, outpatient treatment and procedures, assistive devices, and medications. Informal costs were estimated from time spent helping with basic and instrumental activities of daily living for up to three caregivers per patient using national average hourly earnings as wage rate.

RESULTS: DS and BDRS were associated with higher total cost; a 1-point increase in DS was associated with a \$1,832 increase in total cost, and a 1-point increase in BDRS was associated with a \$3,333 increase. Examining component costs separately identified potential differences between DS and BDRS. A 1-point increase in BDRS was associated with a \$1,406 increase in direct medical cost. A 1-point increase in DS was associated with a \$1,690 increase in informal cost.

CONCLUSION: Patients' dependence and function related differently to direct medical and informal cost, suggesting that measures of function and dependence provided unique information for explaining variations in cost of care for patients with AD, highlighting the value in measuring both constructs. **J Am Geriatr Soc 56:1497–1503, 2008.**

Key words: Alzheimer's disease; cost; function; dependence

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A defining feature of Alzheimer's disease (AD) is patients' loss of function. Instruments used in rating functional deficits in AD typically focus on patients' ability to perform self-care tasks.[1–4] One of the most frequently used instruments is the Blessed Dementia Rating Scale (BDRS),[1] but the BDRS and other measures of functional deficits do not fully assess patients' dependence on other individuals due to deterioration in cognition and function. To address this, the Dependence Scale (DS) has been developed to directly measure the required amount of assistance patients with AD need.[5] Earlier studies have demonstrated that patients' dependence on others indicates aspects of disability in AD that are related to, but distinct from, aspects of disability indicated by functional deficit.[6–8]

The tremendous effect of loss of function on costs of caring for patients with AD has been clearly established.[9–14] In earlier works from the Predictors Study, a large, multicenter study of patients with probable AD followed from early stages of the disease, the association between costs of direct medical care and informal caregiving and patients' functional status, as measured using the BDRS, was examined.[13,14] Few studies have examined the effect of dependence on costs of care for patients with dementia.[15] Whether dependence has an incremental effect on costs of

care for patients with AD, beyond that from loss of function, is yet to be determined. Therefore, the goals of this study were to examine how patients' dependence on others relates to total costs of care and components of costs; to estimate the incremental effect of dependence on costs during early stages of AD, independent of loss of function; and to compare the strengths of the relationships between patients' function and dependence and the different components of costs of care.

METHODS

Sample

The sample was drawn from the Predictors 2 cohort and consisted of 204 patients with probable AD recruited between 1998 and 2004 from three sites: Columbia University Medical Center, Johns Hopkins School of Medicine, and Massachusetts General Hospital.[16,17] Specifically, at the Columbia site, patients were recruited from the Memory Disorder Center and from physician's private practices through the Alzheimer's Disease Research Center (ADRC). At the Johns Hopkins site, patients were recruited from the ADRC and from several university clinics treating elderly, cognitively impaired patients. At the Massachusetts General Hospital site, patients were recruited from the Geriatric Neurobehavioral Clinic. The inclusion and exclusion criteria are fully described elsewhere.[16,17] Briefly, subjects met *Diagnostic and Statistical Manual for Mental Disorders, Third Edition, Revised,* criteria for primary degenerative dementia of the Alzheimer type and National Institute of Neurological Disorders and Stroke–Alzheimer's Disease and Related Disorders Association criteria for probable AD. Enrollment required a modified Mini-Mental State Examination (MMSE) score of 30 or higher, equivalent to a score of approximately 16 or higher on the Folstein MMSE.[18,19] The appropriate local institutional review boards approved the study. Because patients were followed at academic AD centers, they were well characterized, with high degrees of certainty in their AD diagnosis. One hundred nine of the patients have had brain autopsies. Post mortem diagnoses have been completed for 96 patients, 96% of whom had AD-type pathological changes based on Consortium to Establish A Registry for Alzheimer's Disease and National Institute on Aging–Reagan Criteria.[20,21]

Following earlier work,[13,14] 15 patients (7.3%) living in nursing homes were excluded, because patterns of care use and costs differ substantially for nursing home patients.[22] Nine patients (4.4%) with missing cost data and one patient with missing Dependence Scale data were also excluded from the analysis sample. The final analysis sample consisted of baseline data from 179 patients.

Measures

Patient characteristics and cost outcomes used in this study are briefly described below. Details of the measures and the costing methods used were reported in earlier studies.[13,14]

Cost Outcomes

Patients and informants reported use of four domains of medical care in the previous year, including hospitalizations, outpatient treatment and procedures, assistive devices, and medications. Prices were obtained using public databases, as described in detail in earlier reports. All cost values were adjusted to constant 2005 dollars using the medical care component of the Consumer Price Index. Information about informal caregiving time for activities of daily living (ADLs) and instrumental activities of daily living (IADLs) and for supervision was obtained from up to three caregivers (primary and two secondary caregivers) for each patient. ADLs included eating, dressing, and personal care. IADLs included shopping, chores, personal business, and transportation. Hours of informal care provided per day for each caregiving task were asked about in the following categories: 0, up to 3 hours, 3 to 6 hours, 6 to 9 hours, 9 to 12 hours, and more than 12 hours. The categories were transformed into continuous values using the mean of each category as the estimated hours of care provided. For subjects who reported more than 12 hours per day for a particular type of task, the values were top-coded to 12 hours. Total hours of care provision for IADL and ADL tasks were top-coded at 16 hours to provide 8 hours of sleep for the caregivers.[23] No caregiver provided more than 16 hours of care per day at baseline. The hours reported for each task were summed to obtain an estimate of total caregiving hours each patient received. The national average hourly earning for all private industries for each year was used as the hourly wage rate to estimate unpaid caregiving costs.[24] Total cost of care was estimated by summing costs of direct medical care and informal caregiving costs.

Dependence Scale

The DS consists of 13 items representing a wide range of levels of care required by a patient, from subtle items such as needing reminders or advice to more gross forms such as needing to be fed.[5] All items address patients' needs. In some cases, the need is only for supervision, without any specific tasks linked to the need. The instrument is designed to be administered to a reliable informant who lives with the patient or one who is well informed about the patient's daily activities and needs. With the exception of the first two items (needs reminders to manage chores, needs help to remember important things such as appointments), which are coded as 0 (no), 1 (occasionally, at least once a month), and 2 (frequently, at least once a week), responses to the rest of the items are coded dichotomously and indicate whether the patient requires assistance in a particular item (0 = no, 1 = yes). The total DS score is the sum of scores on all 13 items (range 0–15) and provides a continuous index of progressively greater dependence on others. Reliability and validity of the scale have been established in earlier studies, with reliability coefficients ranging between 0.66 and 0.93.[5] For ease of presenting descriptive results, the sample was stratified into quartiles based on the total DS score, with the first quartile representing the lowest level of dependence and the highest quartile the most severe level of dependence.

Functional Assessment

Functional capacity was measured using the BDRS Part I (IADLs) and Part II (ADLs).[1] The following IADL items are included in the BDRS: difficulty performing chores around the house (e.g., cleaning), handling money, remembering

short lists (e.g., shopping), walking across a room, walking several blocks, recognizing one's whereabouts, and remembering things that happened recently. The response options for these items were none (0), some difficulty (0.5), and a lot of difficulty (1). The following three ADL items are included: eating, dressing, and bladder and bowel control. The response options for these items ranged from 0 to 3, with higher score indicating more difficulty. For example, for the item on eating, the response options were eat cleanly (0), messily or only with a spoon (1), only able to eat simple solids such as pudding (2), and need to be fed (3). The total BDRS score is the sum of scores on all 10 items (range 0–17), with higher scores indicating worse functional status. Reliability and validity of the scale have been established in earlier studies, with reliability coefficients between 0.60 and 0.80.[1]

Other Clinical and Demographic Characteristics

In addition to measures of dependence and function, several other clinical and demographic characteristics were obtained in the study. Disease progression was characterized according to transition from milder stages of dementia to more-severe stages, measured according to the MMSE.[18] Lower MMSE scores indicate worse cognitive status. Columbia University Scale for Psychopathology in Alzheimer's Disease, a semistructured interview administered by a physician or a trained research technician, was used to measure patients' psychotic, behavioral, and depressive symptoms.[25,26] The Unified Parkinson's Disease Rating Scale was used to measure extrapyramidal signs (EPSs).[26–28] Patients' medical histories were used to construct a modified version of the Charlson Comorbidity Index.[29] Comorbid conditions included myocardial infarct, congestive heart failure, peripheral vascular disease, hypertension, chronic obstructive pulmonary disease, arthritis, gastrointestinal diseases, mild liver disease, diabetes mellitus, chronic renal disease, and systemic malignancy. No patients reported clinical strokes, metastatic tumors, or acquired immunodeficiency syndrome at baseline. Patients' age, ethnicity, sex, highest level of education, and marital status were also recorded.

Analysis

Patient characteristics were compared across the DS score quartiles. Comparisons of categorical variables were performed using chi-square tests, and comparisons of continuous variables were performed using analyses of variance. Following previous work, separate equations were estimated for total costs, direct medical costs, and informal caregiving costs using generalized linear models.[13,14]

The independent variables fell into three groups: main independent variables (DS and BDRS scores), other clinical variables (e.g., MMSE), and demographic variables. Because there was concern about possible collinearity between the main independent variables and other clinical variables, two sets of models were estimated for each equation: a full model, which controlled for all clinical and demographic variables in addition to the main independent variables, and a trimmed model, which controlled only for the demographic variables in addition to the main independent variables. It was decided to present results from the trimmed models rather than the full models for the following

reasons. Aside from depressive symptoms and comorbidity index, the excluded clinical variables were highly correlated with DS and BDRS. (Correlations between the excluded clinical variables with DS ranged from -0.28 for the MMSE to 0.20 for EPSs, and with BDRS ranged from 0.15 for behavioral problems to 0.25 for EPS.) The individual clinical variables were not statistically significant in the estimating models, and coefficient estimates for DS and BDRS in the full models were not substantially different from those in the trimmed models. Comparison of the Akaike Information Criterion and the Bayesian Information Criterion suggests that the trimmed models performed as well as the full models. Results of the full models are available upon request. The effect of an interaction term for DS and BDRS was also examined. Results showed that the interaction term was not statistically significant in any of the models, so it was dropped from the final specification. All analyses were performed using Stata 9.0 (Stata Corp., College Station, TX).

RESULTS

Baseline demographic and clinical characteristics of the patients are summarized in Table 1 and compared across DS quartiles. Because of the study inclusion criteria, patients were at early stages of AD. The typical patient was female (58%), aged 76, white, and had more than 14 years of education. The average DS score $\pm$ standard deviation was 5.2 ± 2.2, indicating a mild level of dependence. Almost one-quarter of the patients (23.5%) had DS scores of 3 or lower; another 31.2% had DS scores between 4 and 5; the modal DS score was 6 (24.0%), and the rest had DS scores between 7 and 12 (21.2%). At baseline, no patient had a DS score above 12. The average MMSE score in this sample was 22.1 ± 3.6, and the average BDRS score was 3.5 ± 2.1. Although almost all patients had some IADL limitations (98.8%), 64.0% were not limited in ADLs. Behavioral problems were common (41.6%). Approximately one-third (30.2%) had psychotic symptoms, 20.5% had depressive symptoms, and 14.5% had EPSs. On average, patients had less than one comorbid condition (mean 0.8 ± 0.9); 47.8% did not have any comorbid conditions. The most prevalent comorbid conditions included hypertension (36.9%), diabetes mellitus (9.6%), and myocardial infarction (6.2%). During the previous year, patients averaged less than one hospitalization (mean 0.3 ± 0.6), two outpatient treatments or procedures (mean 2.0 ± 2.1), one assistive device (mean 1.2 ± 1.1), and four medications (mean 3.8 ± 1.5). Although patients were at early stages of AD, they received an average of 20.7 ± 24.0 hours of informal care a week.

Data in Table 1 show that DS was related to other clinical characteristics in expected ways and suggest that DS captures global severity and various aspects of the disease. Aside from depressive symptoms, DS was strongly associated with all other clinical characteristics included in the analysis. Specifically, patients with more-severe levels of dependence were older ($P = .001$); had more functional limitations ($P < .001$), worse MMSE scores ($P < .001$), and more comorbidities ($P = .006$); and were more likely to exhibit behavioral problems ($P = .02$), EPSs ($P = .005$), and psychotic symptoms ($P = .007$). In addition, patients with more-severe levels of dependence had more outpatient

Table 1. Demographic and Clinical Characteristics According to Quartile of Dependence Scale (DS)

		Quartile of DS Score (Range)			
Characteristic	All (Range 0–15) (N = 179)	1 (0–3) (n = 42)	2 (4–5) (n = 56)	3 (6) (n = 43)	4 (7–15) (n = 38)
Female, n (%)	104 (58.1)	28 (66.7)	30 (53.6)	23 (53.5)	23 (60.5)
Age					
Mean ± SD***	76.03 ± 8.0	72.83 ± 7.7	75.41 ± 7.3	76.77 ± 8.8	79.63 ± 7.1
<65, n (%)***	16 (8.9)	6 (14.3)	4 (7.1)	5 (11.6)	1 (2.6)
65–74, n (%)	51 (28.5)	18 (42.9)	21 (37.5)	6 (14.0)	6 (15.8)
75–84, n (%)	88 (49.2)	17 (40.5)	25 (44.6)	24 (55.8)	22 (57.9)
≥85, n (%)	24 (13.4)	1 (2.4)	6 (10.7)	8 (18.6)	9 (23.7)
Race, n (%)					
White	171 (95.5)	40 (95.2)	54 (96.4)	40 (93.0)	37 (97.4)
Other	8 (4.5)	2 (4.8)	2 (3.6)	3 (7.0)	1 (2.6)
Years of schooling completed					
Mean ± SD	14.37 ± 3.1	14.83 ± 3.5	14.64 ± 3.3	14.40 ± 2.8	13.42 ± 2.7
<12, n (%)	17 (9.5)	4 (9.5)	7 (12.5)	3 (7.0)	3 (7.9)
12, n (%)	60 (33.5)	13 (31.0)	15 (26.8)	14 (32.6)	18 (47.4)
13–15, n (%)	28 (15.6)	4 (9.5)	8 (14.3)	10 (23.3)	6 (15.8)
≥16, n (%)	74 (41.3)	21 (50.0)	26 (46.4)	16 (37.2)	11 (28.9)
Blessed Dementia Rating Scale score (range 0–17), mean ± SD***	3.50 ± 2.1	1.69 ± 1.1	2.91 ± 1.1	4.05 ± 1.5	5.75 ± 2.3
Mini-Mental State Examination score (range 0–30), mean ± SD***	22.12 ± 3.6	23.55 ± 3.2	22.64 ± 4.0	21.33 ± 3.6	20.68 ± 2.6
Behavioral problems, n (%)**	74 (41.6)	21.4 ((9)	24 (43.6)	21 (48.8)	20 (52.6)
Extrapyramidal signs, n (%)***	25 (14.5)	4 (10.0)	2 (3.6)	4 (9.8)	15 (40.5)
Depressive symptoms, n (%)	36 (20.5)	5 (11.9)	15 (27.8)	7 (16.3)	9 (24.3)
Psychotic symptoms, n (%)**	54 (30.2)	5 (11.9)	17 (30.4)	14 (32.6)	18 (47.4)
Number of comorbidities					
Mean ± SD**	0.78 ± 0.9	0.48 ± 0.8	0.71 ± 0.9	0.95 ± 1.0	1.03 ± 0.9
0, n (%)***	85 (47.8)	29 (69.0)	30 (53.6)	15 (34.9)	11 (29.7)
1, n (%)	61 (34.3)	8 (19.0)	15 (26.8)	21 (48.8)	17 (45.9)
≥2, n (%)	32 (18.0)	5 (11.9)	11 (19.6)	7 (16.3)	9 (24.3)
Use of direct medical care					
Number of hospitalizations, mean ± SD	0.32 ± 0.6	0.19 ± 0.5	0.32 ± 0.6	0.42 ± 0.5	0.34 ± 0.6
Number of outpatient treatments and procedures, mean ± SD**	2.02 ± 2.1	1.31 ± 1.4	1.88 ± 2.0	2.40 ± 2.2	2.61 ± 2.4
Number of assistive devices, mean ± SD***	1.19 ± 1.1	0.93 ± 0.7	0.86 ± 0.6	1.51 ± 1.3	1.61 ± 1.4
Number of medications, mean ± SD	3.79 ± 1.5	3.50 ± 1.5	3.98 ± 1.3	3.70 ± 1.4	3.92 ± 1.9
Informal caregiving hours per week, mean ± SD**	20.70 ± 24.0	14.09 ± 25.6	17.11 ± 21.6	27.75 ± 24.2	25.38 ± 23.3

Differences between quartiles of Dependence Scale significant at $P <$ ** .05; *** .01.
SD = standard deviation.

treatments and procedures ($P = .02$) and more assistive devices ($P < .001$) and received more informal caregiving time ($P = .02$).

Unadjusted Costs

At baseline, almost all patients used some medical care (98.3%, n = 176) and informal care (93.9%, n = 168). Average annual direct medical costs were estimated at $8,675 and informal costs at $18,440 ($\sim$ 19 h/wk). Figure 1 plots reported average annual direct medical costs and informal costs according to DS score quartiles. Total costs and informal costs were significantly higher in patients in higher DS score quartiles ($P = .03$ and .04).

Adjusted Costs

Table 2 presents multivariate regression results of patient characteristics on total costs, direct medical costs, and informal costs. The DS and BDRS were entered into the model as continuous variables and were significantly associated with higher total costs: A 1-point increase on the DS was associated with a $1,832 increase in total costs, and a 1-point increase on the BDRS was associated with a $3,333 increase in total costs. Examining direct medical costs and informal costs separately identified potential differences between the DS and BDRS. Direct medical costs were significantly associated with BDRS: a 1-point increase on the BDRS was associated with a $1,406 increase in direct medical costs. However, informal costs were significantly
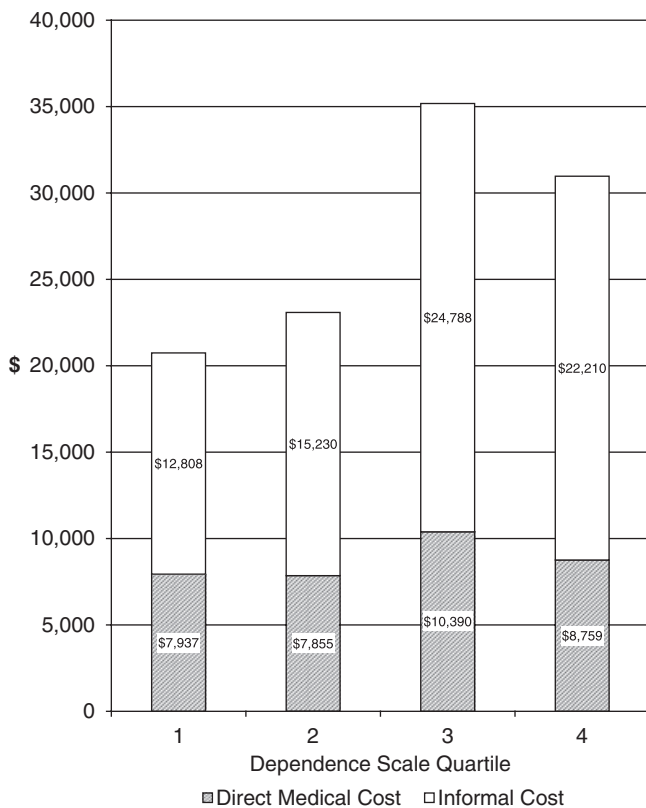
Figure 1. Direct medical costs included costs of hospitalization, outpatient treatment and procedures, assistive devices, and medications, with prices obtained from public databases. Informal costs were estimated by costs of informal caregiving time for activities of daily living and instrumental activities of daily living obtained from up to three caregivers for each patient. National average hourly earning for all private industries was used as the hourly wage rate to estimate informal caregiving costs.

associated with the DS; a 1-point increase on the DS was associated with a $1,690 increase in informal costs.

DISCUSSION

In this study, the incremental effect of patients' dependence on total costs of care and on two main component costs (direct medical care costs and informal caregiving costs) were estimated in a sample of patients in early stages of AD, controlling for patient's function. Patients' dependence on others was measured using the DS and patients' function using the BDRS. As expected, as patients' dependence increased, all aspects of costs increased substantially. Similar to previous studies, patients' function was independently associated with costs. It was found that function and dependence were both significantly associated with total costs yet related differently to direct medical care costs and informal caregiving costs. Poorer function was associated with higher direct medical care costs, whereas more-severe levels of dependence were associated with higher informal caregiving costs. These results confirm that BDRS and DS represent distinct components of disability in AD, suggest that measures of patients' function and dependence provide unique information for explaining variations in costs of care for patients with AD, and highlight the value of measuring both constructs in economics and outcomes research.

Table 2. Generalized Linear Models of Direct Medical Costs and Informal Costs at Baseline

Variable	Total Costs	Medical Costs[†]	Informal Costs[‡]
	Coefficient (Standard Error)		
Dependence Scale	1,832 (916)**	298 (408)	1,690 (749)**
Blessed Dementia Rating Scale	3,333 (1,698)**	1,406 (712)**	1,941 (1,458)
Aged <65 (1 = yes, 0 = no)	− 5,751 (6,055)	− 5,323 (2,641)**	− 1,322 (5,058)
Women (1 = yes, 0 = no)	887 (3,794)	− 1,214 (1,613)	1,965 (3,197)
Site (reference = Columbia)			
Johns Hopkins	− 3,611 (4,551)	− 2,276 (1,927)	− 1,784 (3,835)
Massachusetts General	− 12,902 (4,471)**	− 1,316 (1,959)	− 12,074 (3,754)***
Constant	50,305 (5,457)***	8,942 (2,368)***	23,515 (4,519)***
Log likelihood	− 2118.66	− 1907.99	− 2038.94
Akaike Information Criterion	22.38	20.19	21.54
Bayesian Information Criterion	− 809.44	− 795.75	− 870.14

$P <$ ** .05; *** .01.

[†] Direct medical costs included costs of hospitalization, outpatient treatments and procedures, assistive devices, and medications, with prices obtained from public databases.

[‡] Informal costs were estimated by costs of informal caregiving time for activities of daily living and instrumental activities of daily living obtained from up to three caregivers for each patient. National average hourly earning for all private industries was used as the hourly wage rate to estimate informal caregiving costs.

These results have substantial policy implications. They provide information for deriving estimates of potential cost savings if interventions are developed that aim to improve patients' function and lessen their dependence on others. Earlier studies have estimated that BDRS and DS scores worsen by 1.5 points and 1 point per year, respectively.[6,30] Results in this study suggest that small differences in patients' function and dependence may be associated with large differences in medical care costs and informal caregiving costs. For example, an intervention that delays the worsening of BDRS score by 1 point in patients with AD could be expected to yield average savings of $1,406 per year in direct medical costs. An intervention that delays the worsening of DS score by 1 point in patients with AD could be expected to yield average savings of $1,690 per year in informal caregiving costs. Thus, the choice of interventions that aim to delay a patient moving to higher levels of functional impairment or dependence on others have the potential to yield substantial economic benefit. Comparison of the strengths of the effects of BDRS and DS on different cost components suggests that success of the interventions to control costs and improve patient outcome depends on the cost component targeted.

The potential cost savings estimated are generated from a sample of mildly demented patients. Although most cost savings may not be realized immediately, a delay in disease progression for patients at early stages of the disease may yield greater cost savings than the same delay experienced by patients at later disease stages. Because subjects have been followed closely in this study, future work will address questions of lifetime cost savings more appropriately by using longitudinal analyses. Longitudinal analyses also will confirm whether the relationships between BDRS and DS and different cost components are consistent over time.

This study focused on direct medical costs and informal costs. An important component of costs that is not included in this analysis is nonmedical costs, which include, among others, costs for home health aides, respite care, and adult day care. Previous studies have shown that the proportion of total costs attributable to nonmedical costs is smaller than direct medical costs and informal costs.[31] Therefore, the effects of excluding nonmedical costs from the total cost estimations should be minimal. Results from secondary analyses, including use of nonmedical care as an explanatory variable, showed that it was not significantly associated with direct medical care costs or informal costs. Indeed, few patients in this sample (12.3%, n = 22) reported using nonmedical care, precluding detailed analysis of its relationship to patients' dependence. Bivariate analysis of the relationship between use (and costs) of nonmedical care and patients' dependence showed that there was minimal use (and costs) of nonmedical care for patients at mild levels of dependence and that costs did not begin to rise until moderate levels of dependence were reached. This suggests that, over time, as patients' dependence increases, it is likely that use and costs of nonmedical care will increase. Although the magnitude of these costs may continue to be smaller than direct medical care and informal care costs, they are nevertheless important for patients and families. Future longitudinal analyses will examine use and costs of nonmedical care in more detail.

Several limitations of this study should be noted. First, data reported here are cross-sectional; therefore results can be interpreted only as associations. Although poorer function and dependence may lead to higher costs, it also is possible that low spending on health care indicates insufficient medical care and results in poor health. In this sample of patients with relatively high education levels, however, the latter explanation is less likely. Second, aside from the patient characteristics included in the model, other variables may be associated with higher costs, although the focus of this study was to examine whether the dependence scale could explain variations in costs, and identifying predictors of informal care was beyond the scope of this article. Third, patients and informants, most of whom were the patients' primary caregivers reported data on patients' healthcare costs from this study. Studies have shown that caregivers are able to accurately report medical information of their care recipients.[32,33] There is no reason to believe that this sample was systematically different, although it is possible that there were additional costs important to patients and families beyond the resource items collected. The cost estimates were from society's perspective, because all costs, regardless of the payer, were collected. Fourth, patients were selected from tertiary care university hospitals and specialized diagnostic and treatment centers and thus represent a nonrandom sample of those affected by AD in the population. The patients in the sample were predominantly white and highly educated. Caution is needed in generalizing the results of this study to patients with lower levels of education and income and to nonwhite patients. Future research will need to examine the relationship between costs and the potential variables in samples that are more representative of the general population, but because patients were drawn from multiple locations, generalizability of the findings is enhanced. Substantial cost differences were found across sites. This result is consistent with regional differences in health services use and costs documented in the literature[34] and more specifically a recent study on service use and costs of patients with AD.[35] Because different sites were included in these studies, the results of the current study are not directly comparable with those of these studies. Further investigations are needed to examine whether variations in use and costs reflect differences in regional preferences, availability of or access to services, ethnic and cultural differences, or socioeconomic factors.

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