



## Research Article

# Health-care use and cost in dementia caregivers: Longitudinal results from the Predictors Caregiver Study

Carolyn W. Zhu<sup>a,\*</sup>, Nikolaos Scarmeas<sup>b,c,d</sup>, Katherine Ornstein<sup>a,e</sup>, Marilyn Albert<sup>f</sup>, Jason Brandt<sup>f,g</sup>, Deborah Blacker<sup>h</sup>, Mary Sano<sup>i,j</sup>, Yaakov Stern<sup>b,c,d</sup>

<sup>a</sup>Department of Geriatrics and Palliative Medicine, Mount Sinai School of Medicine, New York, NY, USA

<sup>b</sup>Cognitive Neuroscience Division of the Taub Institute for Research on Alzheimer's Disease and the Aging Brain

<sup>c</sup>Gertrude H. Sergievsky Center, Columbia University Medical Center, New York, NY, USA

<sup>d</sup>Department of Neurology, Columbia University Medical Center, New York, NY, USA

<sup>e</sup>Division of General Internal Medicine, Department of Medicine, Mount Sinai School of Medicine, New York, NY, USA

<sup>f</sup>Department of Psychiatry and Behavioral Sciences, Johns Hopkins University, Baltimore, MD, USA

<sup>g</sup>The Copper Ridge Institute, Sykesville, MD, USA

<sup>h</sup>Department of Psychiatry, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

<sup>i</sup>Department of Psychiatry, Mount Sinai School of Medicine, New York, NY, USA

<sup>j</sup>James J. Peters VA Medical Center, Bronx, NY, USA

**Abstract**

**Objective:** To examine the effects of caregiver and patient characteristics on caregivers' medical care use and cost.

**Methods:** One hundred forty-seven caregiver/patient dyads were followed annually for 6 years in three academic Alzheimer's disease centers in the United States. Logistic, negative binomial, and generalized linear mixed models were used to examine overall effects of caregiver/patient characteristics on caregivers' hospitalizations, doctor visits, outpatient tests and procedures, and prescription and over-the-counter medications.

**Results:** Patients' comorbid conditions and dependence were associated with increased health-care use and costs of caregivers. Increases in caregiver depressive symptoms are associated with increases in multiple domains of caregivers' health-care use and costs.

**Discussion:** Findings suggest expanding our focus on dementia patients to include family caregivers to obtain a fuller picture of effects of caregiving. Primary care providers should integrate caregivers' needs in health-care planning and delivery. Clinical interventions that treat patients and caregivers as a whole will likely achieve the greatest beneficial effects.

© 2014 The Alzheimer's Association. All rights reserved.

**Keywords:**

Caregiving; Medical care; Cost; Dementia; Alzheimer's disease; Longitudinal study

**1. Introduction**

In 2012, more than 5.4 million older adults in the United States have dementia, two-thirds of whom live in the community and are cared for by family and friends [1]. A recent report estimated the annual cost per person attributable to dementia, including medical care, nursing home care, and

in-home formal and informal care, between \$41,689 and \$56,290 [2]. If the proportion of individuals with dementia living in the community remains stable, the burden of caregiving on family and friends will increase exponentially.

The mental and physical health effects of caregiving on family caregivers have been well documented. Compared with noncaregivers, caregivers have higher rates of depression, stress, and other psychological problems [3–7]. They also experience more physical problems, including lower self-rated health, weakened immune system, and increased cardiovascular problems [8–11]. Within the caregiver

\*Corresponding author. Tel.: 718-584-9000x6146; Fax: 718-741-4211.  
E-mail address: carolyn.zhu@mssm.edu

community, effects of caregiving are particularly strong for dementia caregivers as they face unique challenges in providing care because of the cognitive and physical disability experienced by patients and long duration of care [3–7].

Because of these negative health effects of caregiving, economic and health consequences to dementia caregivers can be substantial. A large and growing body of literature has examined health and community services used by caregivers of individuals with cognitively impairment [12–15]. However, the focus of the research has been on services that are potentially helpful for the caregivers in their role as caregivers. Results show that there is high need but often low use of these services. Main barriers to use include not knowing where to obtain services and that many caregivers wait too long to use services, by which time care recipients are often too frail to benefit. With few exceptions, caregivers' own health-care utilization has received little attention [16]. An early study examined a comprehensive set of health services use, including outpatient, inpatient, and home health care, but did not separate utilization by care recipient or caregiver [12,13]. Another study reported slightly higher cost from hospitalizations but lower cost from doctor visits in a sample of dementia caregivers compared with noncaregivers with similar socioeconomic characteristics, but the differences in magnitude were small [17]. Similarly small but statistically significant increases in caregivers' medication cost as caregiving hours increased have also been reported [18]. Caregivers' acute care utilization has been shown to increase as patients' behavioral and psychological symptoms and functional status worsened [19]. More recent analyses from the Resources for Enhancing Alzheimer's Caregiver Health study showed that caregivers' hospitalization rates and probability of multiple doctors' visit increased significantly during an 18-month study period, but the use of primary care and mental health service and select medication use (antidepressant and antianxiety medications) did not significantly increase [20]. It is unclear, however, whether patients' clinical characteristics were included or how they might have affected caregivers' medical care use in that study.

The relationship between caregiving and caregivers' health is typically described by the model of caregiver stress by Pearlin et al. in a process in which both care recipient and caregiver characteristics change over time but are important determinants of caregiver outcomes [21]. In this model, objective stressors are measured by the progression of care recipients' chronic illness and its decline. Typical outcomes include type and quantity of caregiving, caregivers' psychological stress, burden, and psychiatric and physical health. Early models of the caregiving process emphasized increased burden and stress over time, but longitudinal studies suggested adaptations over time and stable caregiver burden and depression [22,23]. In this study, we take advantage of a rare opportunity of having both caregiver and care recipient data in a longitudinal setting and extend

this model to examine caregivers' medical care use and related costs as outcomes. Because of the modest sample size of our study, we estimated a set of reduced form equations to examine the overall effects of patient and caregiver characteristics on caregivers' own medical care use and related costs.

## 2. Methods

### 2.1. Sample

Subjects for this study were recruited from the Predictors 2 Study, a longitudinal study of individuals with probable Alzheimer's disease (AD) or dementia with Lewy bodies prospectively followed from early stages of illness in three sites: Columbia University College of Physicians and Surgeons, Johns Hopkins University School of Medicine, and Massachusetts General Hospital. Recruitment of subjects in the Predictors 2 Study began in 1998 and ended in 2012. Inclusion/exclusion criteria and evaluation procedures of the Predictors 2 Study have been fully described elsewhere [24,25]. Briefly, after an initial evaluation, all subjects were diagnosed in a consensus conference with at least two faculty neurologists or psychiatrists specializing in dementia and one faculty neuropsychologist. Subjects with AD met NINCDS-ADRDA criteria for probable AD [26], and those with dementia with Lewy bodies were diagnosed according to the 1996 consensus guidelines for the disease [27]. At study entry, all subjects were required to have a modified Mini-Mental State Examination (MMSE) score (21)  $\geq 30$ , equivalent to a score of  $\geq 16$  on the standard MMSE [28]. Subjects were also required to have at least one family member/informant available. Subjects with parkinsonism, stroke, alcoholism, schizophrenia, schizoaffective disorder, and electroconvulsive treatments were excluded. After the baseline evaluation, all subjects were followed in person semiannually until dropout or death, with annual assessments of resource utilization. If subjects were unable to travel to the clinic for evaluation, they were visited at their residence (e.g., home, nursing home, or health-care facility). There was 94% follow-up of subjects. The study was approved by each local institutional review board.

The Predictors Caregiver Study was initiated 6 years after launching the Predictors 2 Study. A total of 180 caregivers were active in the Predictors Study at the time of, or subsequent to, the launching of the Predictors Caregiver Study. Throughout the Caregiver study, these 180 caregivers provided care for 160 subjects (care recipients hereafter). Of these 180 caregivers, health-care use data were missing for 21 caregivers. Deleting these observations leaves us with 159 caregivers with valid cost data for 147 care recipients. Of these 147 care recipients, 12 (8.2%) had multiple caregivers who participated with the subject at different times. We identified the caregiver who participated most often during the study as the subject's main

caregiver. Data on other caregivers were dropped from the analysis. Thus, the longitudinal cohort used in this analysis included 147 caregiver/care recipient dyads (for a total of 394 observations). On average, each dyad completed three annual assessments.

## 2.2. Measures

### 2.2.1. Outcomes

At baseline and annually thereafter, caregivers reported their own use of the following domains of medical care: overnight hospitalizations, doctor visits, outpatient tests and procedures (e.g., blood test, mammogram, urinalysis), and assistive devices (e.g., walkers, grab bars). For those who reported using a particular item, data on the intensity of use (e.g., number of hospitalizations, number of doctor visits) were also collected. Detailed information on prescription and over-the-counter (OTC) medications the caregiver took during the past 6 months including the name of the drug, number of days taking the drug, and number of pills per day were recorded on a concurrent medication form. We annualized utilization rates when domains were reported for less than a year (e.g., 3 months for outpatient medical tests and procedures and 6 months for medications). We converted physical quantities for each domain of care into monetary values using costing methods reported in earlier studies [29]. We then summed across all domains to obtain a total annual medical care cost for each caregiver. All cost values were adjusted to constant 2010 US dollars using the medical care component of the consumer price index [30]. Detailed descriptions on data collection and price conversion were reported earlier [31].

### 2.2.2. Caregiver characteristics

Caregiver age, gender, ethnicity, highest level of education, and relationship to care recipient were recorded at the start of the Caregiver Study. Whether the caregiver lived with the care recipient, frequency of contact with the care recipient, and length of time caregiver had known the care recipient were recorded at each annual visit. Whether caregiver assisted with basic activities of daily living (BADL), including eating, dressing, bathing, and using toilet, instrumental activities of daily living (IADL), including shopping, household chores, personal business, transportation, and social activities, average amount of hours the caregiver spent per day on providing care, whether a paid attendant assisted with care, and caregiver's employment status were reported annually. Caregiver comorbidities at baseline were computed using a modified Charlson scale and included items for myocardial infarction, congestive heart failure, peripheral vascular disease, hypertension, chronic obstructive pulmonary disease (COPD), arthritis, gastrointestinal diseases, liver disease, diabetes, chronic renal disease, and systemic malignancy

[32]. Caregiver depressive symptoms were measured by the six-item depression subsection of the Brief Symptom Inventory (BSI) [33]. The instrument asked the caregivers to rate on a five-point Likert scale how much during the past week they were bothered by the following: feeling lonely, feeling blue, feeling no interest in things, feeling hopeless about the future, feelings of worthlessness, and thoughts of ending his/her life. Response for each item ranged from "not at all" to "extremely," with higher scores indicating higher depressive symptoms.

### 2.2.3. Care recipient characteristics

At the baseline visit, demographic characteristics (e.g., age, gender, ethnicity, highest level of education) were recorded. Because care recipients' living arrangement may change over time and patterns of health service utilization and costs may differ substantially between individuals in different living arrangements [34], information on care recipients' living arrangements (living at home, in retirement homes, in assisted living facilities, or in nursing homes) was collected at each visit.

Data on several clinical characteristics of the patient that can be assessed reliably by a clinician were recorded at each visit. Disease progression was characterized by transition from milder stages of dementia to more severe stages, measured by MMSE [28]. Care recipients' dependence on others was measured by the Dependence Scale (DS) [35], a continuous index measuring the progressively greater dependence on others. Columbia University Scale for Psychopathology in Alzheimer's Disease (CUSPAD), a semi-structured interview administered by a physician or a trained research technician, was used to measure the presence or absence of psychotic symptoms, behavior problems, and depressive symptoms [36]. From the CUSPAD, we constructed a dichotomous variable to indicate the presence of psychotic symptoms if the patient had any delusions, hallucinations, or illusions [37,38]. We constructed a dichotomous variable to indicate the presence of behavioral problems if the patient had any of the following five symptoms: wandering away from home or caregiver, verbal outbursts, physical threats or violence, agitation or restlessness, or sundowning (more confusion at night or during evening compared with the day). We also constructed a dichotomous variable to indicate the presence of depressive symptoms if the patient had any depressed mood (i.e., sad, depressed, blue, down in the dumps) and either had difficulty sleeping or had a change in appetite. Comorbidities included items for myocardial infarction, congestive heart failure, peripheral vascular disease, hypertension, COPD, arthritis, gastrointestinal diseases, liver disease, diabetes, chronic renal disease, and systemic malignancy from the baseline visit.

### 2.2.4. Analysis

We estimated a set of reduced form equations to provide estimates of the overall effects of patient and caregiver

characteristics on caregivers' health-care use and costs. We examined three sets of outcomes: any medical care use, intensity of use, and costs.

For any medical care use, estimations were performed using random-effects logistic regressions. Dependent variables included any hospitalizations, any doctor visits, any prescription medication, any outpatient treatment/procedures, and any OTC medication. Because more than 93% of the caregivers reported using some medical care, we did not estimate an overall model for any medical care use. Estimates for any use models are exponentiated and represent adjusted odds ratios (ORs).

For intensity of use, dependent variables included number of doctor visits, number of prescription medications, number of outpatient treatment/procedures, and number of OTC medications. We did not estimate a model for number of hospitalizations because only 46 hospitalizations were reported throughout the study. Intensity of use was examined using negative binomial regressions. We chose negative binomial over Poisson regressions because with count data, it is more robust when the variance is not equivalent to the mean of the distribution and it models between-subject heterogeneity [39]. It is unclear whether different processes govern zero and nonzero counts. We compared our results from our models, which assume the same processes for zero and nonzero counts, with those obtained from zero-inflated negative binomial models, which assume different processes for zero and nonzero counts. Results were substantively similar, and we therefore chose the simpler and more familiar negative binomial models. Estimates for intensity of use models are exponentiated and represent incidence rate ratios (IRRs).

For caregivers who used a particular domain of medical care, we then estimated a generalized linear mixed regression model for its related cost. Similar to models on intensity of use, we did not estimate models for hospitalizations because of its low use rates. In addition to the four models of medical care use, a model estimating total cost of medical care was also estimated. Because the distributions of the cost variables were highly positively skewed, we constructed log-transformed costs as dependent variables. Estimates for the cost models are interpreted as semielasticities, that is, percentage change in cost from a unit change in the independent variable.

For all three sets of models, we first examined bivariate association between caregivers' medical care use and each caregiver/care recipient characteristic. Variables that were not significantly associated with caregivers' medical care use in bivariate analyses were dropped from our final models. We tested several interaction terms between care recipient characteristics (dependence and chronic conditions) and caregiver characteristics (chronic conditions and depressive symptoms). They were statistically insignificant and were dropped from the analyses. Our final model therefore included the following independent variables for the caregiver: baseline age, gender, education, comorbid

conditions, depressive symptoms (measured by the depression subsection of the BSI), and an indicator for a spouse caregiver. Care recipient characteristics included in the final models were baseline comorbid conditions, DS, indicator for whether the care recipient was depressed, and indicator for the presence of psychiatric problems. All caregiver and care recipient clinical characteristics, except baseline comorbid conditions, were time-varying current values.

Because of the longitudinal nature of the study, caregivers could contribute multiple observations in the study. We included a random intercept term to allow between-person variations and a random slope term to allow within-person variations over time [40]. Fixed effects of time were estimated by including indicators for assessment intervals [41]. All models controlled for indicators for site as fixed effects. All analyses were performed using Stata 9.0 [42].

### 3. Results

#### 3.1. Caregiver and care recipient characteristics at baseline

The typical caregiver in this sample was 65 years old (standard deviation [SD], 13.4), female (76%), white (84%), and a college graduate with 16 years of schooling (SD, 3.3; Table 1). Slightly more than half of the caregivers were spouses (55%) and a third were adult children (35%). The caregivers were relatively healthy, reporting fewer than one chronic condition at baseline. The most prevalent chronic conditions reported were hypertension (24%), depression (10%), diabetes (6%), and cancer (6%). Other chronic conditions were reported by less than 5% of the caregivers. The most commonly reported medications included antihypertensive agents (26%), medications for dyslipidemia (18%), and psychotropic medications (12%). Other medications were reported by less than 10% of the caregivers. Slightly more than a third of the caregivers reported being employed at the time (37%). Those who were working reported an average of 32 work hours/wk (SD, 18). Three-fourths of the caregivers helped with IADLs (78%) and about half with BADLs (47%). Among those who provided help, caregivers reported spending an average of 3 h/d helping with IADLs (SD, 2.6) and 2 hours on activities of daily living (ADLs) (SD, 1.9). A small fraction of caregivers also reported having other helpers who provided IADL (18%) or ADL help (14%). Among those with other helpers, caregivers reported that other helpers spent an average of 3 h/d helping with either ADLs or IADLs.

The typical care recipient in this sample was 76 years old (SD, 7.3), female (55%), white (90%), had an average of 15 years of schooling (SD, 3.2), and had fewer than one chronic condition at baseline (mean, 0.8; SD, 1.1) other than dementia. The most prevalent chronic conditions for the care recipients included hypertension (34%), depression



Table 1  
Baseline demographic characteristics of caregiver/care recipient dyads  
(n = 147)

Variables	Mean ± SD
Caregiver characteristics	
Age (y)	65.2 ± 13.4
Younger than 65 (%)	47.6
65–74 (%)	24.5
75 or older (%)	27.9
Female (%)	75.5
Race (%)	
White	83.7
Black	7.5
Years of schooling	15.9 ± 3.3
Relationship to care recipient (%)	
Spouse	55.1
Child	35.4
Other	9.5
Number of comorbid conditions	0.5 ± 0.9
Hypertension (%)	23.8
Depression (%)	9.5
Diabetes (%)	5.7
Cancer (%)	5.7
Medication use (%)	
Antihypertensive	26.0
For dyslipidemia	17.9
Antidepressant	8.9
Other psychotropic medications	12.2
Vitamins	8.1
Depressive symptoms*	8.1 ± 3.1
Employment status (%)	
Currently working	37.4
Hours of work per week <sup>†</sup>	31.9 ± 18.2
Provided help with IADL/BADLs (%)	
IADL	78.2
ADL	46.9
Other helpers helped with IADL	17.7
Other helpers helped with ADL	13.6
Hours of help per day <sup>†</sup>	
IADL	3.1 ± 2.6
ADL	2.4 ± 1.9
Other helpers helped with IADL	0.6 ± 1.6
Other helpers helped with ADL	0.5 ± 1.7
Total hours from all helpers <sup>†</sup>	5.4 ± 6.2
Care recipient characteristics	
Age (y)	75.6 ± 7.3
Female (%)	55.1
Race (%)	
White	89.8
Black	8.2
Years of schooling	14.7 ± 3.2
Living arrangement (%)	
Home	68.7
Retirement home	15.6
Nursing home	15.0
Number of comorbid conditions <sup>‡</sup>	0.8 ± 1.1
Hypertension (%)	34.0
Depression (%)	13.2
Diabetes (%)	7.6
Angina (%)	7.0
COPD (%)	7.0
MMSE (range, 0–30)	17.4 ± 7.7
Mild AD: MMSE ≥21 (%)	42.9
Moderate AD, MMSE 10–20 (%)	38.4
Severe AD, MMSE <10 (%)	18.8

(Continued)

Table 1  
Baseline demographic characteristics of caregiver/care recipient dyads  
(n = 147) (Continued)

Variables	Mean ± SD
Dependence Scale (range, 0–15)	6.7 ± 3.1
Presence of psychotic symptoms (%)	44.2

Abbreviations: SD, standard deviation; IADL, instrumental activities of daily living; BADL, basic activities of daily living; ADL, activities of daily living; COPD, chronic obstructive pulmonary disease; MMSE, Mini-Mental State Examination; AD, Alzheimer's disease.

\*Depressive symptoms are measured by the six-item depression subsection of the Brief Symptom Inventory (range, 0–30).

<sup>†</sup>Hours of work and hours of help are computed among those who were employed and provided help only.

<sup>‡</sup>Prevalence of other comorbid conditions were all <5%.

(13%), diabetes (8%), angina (7%), and COPD (7%). Rates of other chronic conditions were low: myocardial infarction, congestive heart failure, and cancer were present in 4% of the sample, and chronic liver disease and renal disease were present in 2% of the sample. At baseline, most of the care recipients were living at home (69%), and the rest was evenly split between living in retirement homes (16%) or in nursing homes (15%). Average MMSE score at baseline was 17.4 (SD, 7.7) and DS score was 6.7 (SD, 3.1).

### 3.2. Caregiver baseline and overall medical care use and cost

At baseline, 93% of the caregivers reported using some type of medical care; 10 (6.8%) reported not using any medical care (Table 2). During the entire study period, 4 of the 147 caregivers reported not using any medical care at all. Across all assessments (n = 401), no medical care use was reported only 6.6% of the time (n = 26).

At baseline, 10% of caregivers reported being hospitalized at least once during the previous assessment interval, three-fourths (74%) had a doctor visit, and 65% received outpatient tests and procedures. A quarter of caregivers (26%) used assistive devices. Prescription (76%) and OTC (58%) medications were common. Average annual medical care cost was estimated at \$2585 (SD, 6386) in the year before baseline assessment, with the most expensive components being hospitalizations (mean, \$1122; 43.4% of total cost) and prescription medications (\$798; 30.9%).

Table 2 also presents data on overall use and cost throughout the study period. Time trend in caregiver medical care use and costs was statistically insignificant for all domains except for prescription and OTC medication use, where they both decreased slightly (both  $P < .05$ ).

### 3.3. Multivariate results on utilization

Not surprisingly, caregivers' own chronic conditions were associated with increased likelihood of having any doctor visits (OR, 2.493;  $P < .01$ ) and hospitalization (OR, 1.67;  $P < .10$ ), although the association with hospitalization was

Table 2  
Caregivers' baseline and overall medical care utilization

Variables	Baseline (n = 147)	Across all assessments (n = 394)
Utilization rate (%)		
Any use	93.2	93.4
Hospitalizations	10.2	11.7
Prescription medications	75.5	70.1
Doctor visits	74.1	75.4
Over-the-counter (OTC) medications	57.8	48.2
Outpatient tests/procedures	64.6	67.0
Assistive devices	25.9	24.1
Intensity of use among users, mean $\pm$ SD		
Number of hospital admissions	1.1 $\pm$ 0.5	1.2 $\pm$ 0.6
Number of nights at hospital	3.9 $\pm$ 5.1	4.8 $\pm$ 4.7
Number of doctor visits	2.8 $\pm$ 4.6	2.7 $\pm$ 4.4
Number of assistive devices	1.4 $\pm$ 1.0	1.5 $\pm$ 1.0
Number of outpatient tests/procedures	2.8 $\pm$ 2.3	2.7 $\pm$ 2.2
Number of prescription medications	3.2 $\pm$ 2.4	3.3 $\pm$ 2.6
Number of OTC medications	3.3 $\pm$ 2.5	3.2 $\pm$ 2.4
Cost per person, mean \$ $\pm$ SD		
Total	2585 $\pm$ 6386	3068 $\pm$ 6993
Hospitalizations	1122 $\pm$ 5754	1503 $\pm$ 6088
Prescription medications	798 $\pm$ 994	868 $\pm$ 1253
Outpatient tests/procedures	412 $\pm$ 851	448 $\pm$ 903
Doctor visits	154 $\pm$ 301	160 $\pm$ 298
Assistive devices	53 $\pm$ 178	54 $\pm$ 204
OTC medications	46 $\pm$ 110	34 $\pm$ 85

Abbreviation: SD, standard deviation.

marginally significant (Table 3). Each point increase in caregivers' BSI depression subsection score was associated with increased likelihood of prescription (OR, 1.112;  $P < .05$ ) and OTC (OR, 1.117;  $P < .05$ ) medication use. After controlling for caregiver health, demographic characteristics were largely not associated with medical care use, except that older caregivers were more likely to use outpatient tests (OR, 1.192;  $P < .01$ ).

Several care recipient characteristics were associated with caregiver medical care use. In particular, care recipi-

ents' chronic conditions were associated with caregivers' increased likelihood of doctor visits (OR, 1.557;  $P < .05$ ) and use of outpatient tests and procedures (OR, 1.319;  $P < .05$ ). Care recipients' DS score was also associated with caregivers' increased likelihood of doctor visits (OR, 1.116;  $P < .05$ ) and use of outpatient tests and procedures (OR, 1.106;  $P < .05$ ). Care recipients' psychiatric problems were associated with caregivers' increased likelihood of prescription medication use (OR, 1.801;  $P < .05$ ) and hospitalization (OR, 2.083;  $P < .10$ ), although the association with hospitalization was marginally significant. Compared with adult children and other caregivers, spouse caregivers were more likely to use prescription (OR, 1.841;  $P < .10$ ) and OTC (OR, 2.043;  $P < .10$ ) medications, although the effects were only marginally significant.

### 3.4. Multivariate results on intensity of use

Among caregivers who reported using medical care, caregivers' own chronic conditions were associated with increases in the number of doctor visits (IRR, 1.271;  $P < .01$ ), number of prescription medications (IRR, 1.432;  $P < .01$ ), and, to a lesser extent, number of outpatient tests and procedures (IRR, 1.073;  $P < .10$ ) (Table 4). Caregivers' BSI depression subsection score was significantly associated with all four domains of medical care: number of doctor visits (IRR, 1.036;  $P < .01$ ), number of outpatient tests and procedures (IRR, 1.044;  $P < .01$ ), number of OTC medications (IRR, 1.038;  $P < .05$ ), and, to a lesser extent, prescription medications (IRR, 1.023;  $P < .10$ ). As expected, caregivers who were older had more doctor visits (IRR, 1.068;  $P < .10$ ), outpatient tests and procedures (IRR, 1.100;  $P < .05$ ), and prescription (IRR, 1.061;  $P < .10$ ) and OTC (IRR, 1.102;  $P < .05$ ) medications. In addition, female caregivers and caregivers with more schooling also had more doctor visits and OTC medications, although their effects were only marginally significant (Table 4).

Table 3  
Random-effects logistic regression results on caregivers' medical care use over time (n = 394)

Variable	Any hospitalizations, OR (SE)	Any doctor visits, OR (SE)	Any outpatient treatment, OR (SE)	Any prescription medications, OR (SE)	Any over-the-counter (OTC) medications, OR (SE)
Caregiver					
Age in 5-y increments	1.099 (0.140)	1.145 (0.101)	1.192 (0.074)***	1.145 (0.079)	1.127 (0.087)
Female	1.131 (0.651)	1.831 (0.815)	1.486 (0.440)	1.850 (0.609)*	1.640 (0.622)
Year of schooling	0.967 (0.068)	1.069 (0.068)	1.000 (0.041)	0.929 (0.046)	1.061 (0.054)
Baseline comorbid conditions	1.670 (0.454)*	2.493 (0.870)***	1.102 (0.203)	1.171 (0.259)	1.380 (0.296)
Brief Symptom Inventory (BSI)	1.025 (0.056)	1.079 (0.064)	1.052 (0.042)	1.112 (0.053)**	1.117 (0.050)**
Care recipient					
Baseline comorbid conditions	1.185 (0.244)	1.557 (0.328)**	1.319 (0.171)**	1.014 (0.125)	0.961 (0.135)
Dependence Scale (DS)	0.962 (0.074)	1.160 (0.071)**	1.106 (0.046)**	1.040 (0.048)	0.958 (0.048)
Depressed	0.533 (0.407)	1.495 (0.839)	0.860 (0.304)	0.636 (0.248)	0.525 (0.245)
Presence of psychiatric problems	2.083 (0.914)*	0.892 (0.299)	1.244 (0.308)	1.801 (0.493)**	0.788 (0.227)
Spouse caregiver	2.247 (1.507)	1.758 (0.844)	1.428 (0.464)	1.841 (0.681)*	2.043 (0.842)*

Abbreviations: OR, odds ratio; SE, standard error.

NOTE. \* $P < .10$ ; \*\* $P < .05$ ; \*\*\* $P < .01$ .

Table 4

Random-effects negative binomial regression results on caregivers' intensity of medical care use over time (n = 394)

Variable	Number of doctor visits, IRR (SE)	Number of outpatient treatment, IRR (SE)	Number of prescription medications, IRR (SE)	Number of over-the-counter (OTC) medications, IRR (SE)
Caregiver				
Age in 5-y increments	1.068 (0.038)*	1.100 (0.033)**	1.061 (0.036)*	1.102 (0.050)**
Female	1.378 (0.239)*	1.154 (0.174)	0.948 (0.159)	1.538 (0.345)*
Year of schooling	1.048 (0.024)**	0.992 (0.018)	0.971 (0.020)	1.054 (0.029)*
Baseline comorbid conditions	1.271 (0.110)***	1.073 (0.079)*	1.432 (0.121)***	1.121 (0.128)
Brief Symptom Inventory (BSI)	1.036 (0.016)**	1.044 (0.015)***	1.023 (0.014)*	1.038 (0.020)**
Care recipient				
Baseline comorbid conditions	1.076 (0.065)	1.094 (0.055)*	1.034 (0.063)	0.970 (0.080)
Dependence Scale (DS)	1.026 (0.023)	1.046 (0.021)**	1.017 (0.020)	0.995 (0.028)
Depressed	0.999 (0.205)	0.938 (0.174)	0.864 (0.178)	0.699 (0.199)
Presence of psychiatric problems	1.010 (0.123)	1.154 (0.130)	1.169 (0.118)	0.899 (0.142)
Spouse caregiver	1.072 (0.203)	1.150 (0.184)	1.398 (0.244)**	1.862 (0.436)***

Abbreviations: IRR, incidence rate ratio; SE, standard error.

NOTE. \* $P < .10$ ; \*\* $P < .05$ ; \*\*\* $P < .01$ .

Care recipients' characteristics were largely not associated with the intensity of caregivers' medical care use, except for care recipients' chronic conditions (IRR, 1.094;  $P < .10$ ) and DS score (IRR, 1.046;  $P < .05$ ), which increased the number of outpatient tests and procedures the caregivers had.

### 3.5. Multivariate results on costs

By far the most influential variable that affects caregivers' total medical care is caregivers' own chronic conditions (Table 5). Each additional chronic condition was associated with a 33.2% increase in total medical care cost. Caregivers' chronic conditions were also associated with a 13.4% increase in the cost of doctor visits and 33.3% increase in the cost of prescription medications (both  $P < .05$ ). Increases in caregivers' depressive symptoms, as measured by the BSI depression subsection score, were also associated with increases in caregivers' medical care cost. Each point increase in caregivers' BSI score was

associated with a 3.6% increase in the cost of doctor visits, a 10% increase in the cost of outpatient treatment/procedures (both  $P < .01$ ), and a 4% increase in total medical care cost ( $P < .10$ ).

Care recipients' characteristics were largely not associated with caregivers' medical care cost, except for care recipients' chronic conditions and DS score, which were marginally associated with higher cost of outpatient tests and procedures ( $P < .10$ ).

## 4. Discussion

Providing care to individuals with dementia often has negative health consequences for caregivers. In this study, we extend Pearlin model to examine caregivers' own health-care use in a longitudinal setting. We followed a sample of dementia caregivers who participated along with their care recipients in a natural history study of dementia and estimated in a set of reduced form models overall effects of caregivers' own sociodemographic and health

Table 5

Generalized linear mixed regression results on caregivers' medical care costs (dependent variable = log cost)

Variable	Total costs, Coeff. (SE)	Doctor visits, Coeff. (SE)	Outpatient treatments, Coeff. (SE)	Prescription medications, Coeff. (SE)	Over-the-counter (OTC) medications, Coeff. (SE)
Caregiver					
Age in 5-y increments	0.078 (0.057)	0.041 (0.025)*	0.074 (0.056)	0.044 (0.057)	0.082 (0.068)
Female	−0.141 (0.284)	0.252 (0.122)**	0.407 (0.270)	−0.251 (0.283)	0.521 (0.339)
Year of schooling	−0.032 (0.038)	0.022 (0.016)	0.003 (0.034)	−0.008 (0.038)	0.061 (0.043)
Baseline comorbid conditions	0.332 (0.158)**	0.134 (0.062)**	−0.038 (0.141)	0.333 (0.159)**	−0.067 (0.173)
Brief Symptom Inventory (BSI)	0.042 (0.024)*	0.036 (0.013)***	0.101 (0.028)***	0.021 (0.019)	0.017 (0.029)
Spouse caregiver	0.444 (0.299)	0.007 (0.135)	−0.096 (0.283)	−0.106 (0.296)	0.444 (0.380)
Care recipient					
Baseline comorbid conditions	0.057 (0.106)	0.000 (0.041)	0.150 (0.093)*	−0.033 (0.110)	−0.104 (0.127)
Dependence Scale (DS)	−0.003 (0.033)	−0.007 (0.017)	0.063 (0.036)**	−0.013 (0.029)	0.016 (0.042)
Depressed	0.121 (0.345)	−0.205 (0.139)	0.342 (0.321)	0.403 (0.366)	−0.422 (0.449)
Presence of psychiatric problems	0.267 (0.171)	0.064 (0.092)	0.277 (0.208)	−0.065 (0.141)	−0.030 (0.215)
Number of observations	368	296	264	276	190

Abbreviations: Coeff., coefficient; SE, standard error.

NOTE. \* $P < .10$ ; \*\* $P < .05$ ; \*\*\* $P < .01$ .

characteristics and care recipients' clinical characteristics on caregivers' medical care use and costs. Not surprisingly, the most consistent predictors of caregivers' medical care use and costs were caregivers' own physical and mental health. Higher comorbid conditions were associated with caregivers' increased likelihood of hospitalizations and doctor visits and also with increases in the number of doctor visits and prescription medications and their related costs. Each additional comorbid condition was associated with a 33% increase in the caregivers' total medical care cost. Consistent with existing literature [43], we found that caregivers' depressive symptoms were independently associated with caregivers' likelihood of using prescription and OTC medications, number of doctor visits, and outpatient tests and procedures as well as related costs.

The relationship between caregivers' depressive symptoms and health-care cost is of note. Improvements on caregiver depression have been consistently reported in dementia caregiver intervention programs [44,45]. However, little is known of the effects of reduced depressive symptoms on caregiver health-care costs. This lack of information has impeded widespread adoption of successful interventions. Although the Predictors Study is a natural history study of dementia, our results suggest that improvements in caregiver depressive symptoms are associated with modest reductions in multiple domains of caregivers' medical care use and costs and fill an important gap toward understanding intervention's full benefit.

In addition to caregivers' own characteristics, our results showed an independent effect of caregiving on caregivers' health-care use. After controlling for caregivers' own socio-demographic and health characteristics, objective stressors of care recipients' disease severity and clinical characteristics remain important predictors of caregivers' medical care utilization. In particular, care recipients' comorbidities and dependence on others were associated with increases in caregivers' likelihood of doctor visits and outpatient tests and procedures. Presence of psychiatric symptoms in the care recipient was associated with an almost two-fold increase in caregivers' likelihood of using prescription medications. These results are consistent with an earlier study that showed dementia patients' behavioral and psychological problems and functional status were associated with caregivers' emergency care and hospitalizations [19]. Interestingly, both studies also reported that cognitive impairment itself was not associated with caregiver's medical care use. These results are consistent with the literature that behavioral symptoms in dementia patients are important predictors of caregiving time, caregiver burden, quality of life, and other negative outcomes [22,46–48]. In other studies, however, behavioral problems have been shown to be unrelated to caregiver service use, and the effects of care recipient behavioral problems were small compared with the effects of ADL problems [14]. Together, these results highlight the difficulties of managing behavioral symptoms of dementia and suggest that behavioral symptoms

have differential effects on different dimensions of caregiver health and health-care use.

Our study did not, however, find strong associations between care recipient characteristics and caregivers' intensity of medical care use and costs. Care recipients' dependence on others had a small significant effect on the number and costs of outpatient tests and procedures caregivers had. Care recipients' comorbidities were also only marginally associated with the number and costs of outpatient tests and procedures caregivers had. It is unclear why care recipient characteristics were not more strongly associated with caregivers' intensity of medical use [49]. As a secondary analysis, we examined high-intensity use using several different cutoff points (e.g.,  $\geq 3$ ,  $\geq 5$  prescription medications) and found substantively similar results. These results are consistent with an earlier report comparing costs of hospitalization and doctor visits using data from a sample of caregivers of veterans with dementia with those from non-caregivers with similar socioeconomic characteristics [17]. In the present sample of caregivers whose provision of caregiving hours was relatively low, perhaps, the burden of caregiving has not led the caregivers to neglect their own medical care needs. Perhaps, this sample of well-educated caregivers has more resources available to them, limiting our ability to detect differences in their health-care use and expenditures. It is worth noting that these data are based on caregiver self-report of utilization and are subject to recall bias. Such non-differential misclassification is likely to result in reducing estimated effect. It may also be possible that the overall burden of caregiving is more likely to impact overall utilization patterns than the intensity of use. It is also possible that instead of caregiver and patient characteristics independently affecting caregiver health-care utilization as modeled in this study, caregiver health (e.g., chronic conditions) is a consequence of patients' dementia. More research in this area is clearly needed.

There are several limitations to our study. First, patients were selected from tertiary care university hospitals and specialized AD centers and are a nonrandom sample of individuals affected by the disease in the general population. Patients in our sample were predominantly white, highly educated, and healthier than community-based samples. Caution is needed in generalizing the results of this study to patients of other ethnicities, patients at lower education and income levels, and to community AD patients. Second, it should be noted that for analysis of health-care use and costs, our sample may be somewhat underpowered. With this in mind, we attempted to include a parsimonious set of independent variables in our estimation models. Third, because the Predictors Study is a natural history study of dementia, no interventions were conducted, and comparison data on individuals without dementia or their caregivers were not available. Therefore, we chose to estimate a set of reduced form equations, providing estimates of total effects of exogenous patient and caregiver variables on caregiver health-care use. Several hypotheses



have been generated from Pearlin model. On the one hand, increasing caregiving demands, measured by care recipients' clinical characteristics, could negatively affect caregiver health through wear and tear, thereby increase caregivers' health-care use. On the other hand, if caregivers adapt to their caregiving role, care recipients' clinical characteristics may not strongly affect caregivers' health or health-care use. It is also possible that caregivers may ignore their own health and health-care use because of high cost of care and the tremendous amount of time devoted to care provision. Testing these structural mechanisms of caregiving is beyond the scope of the present study. It is worth noting that in this cohort of caregivers, health-care utilization remained stable over time, suggesting adaptation in caregiving, or more complex mechanisms that affect caregiving health-care use are present. Important next steps include examining the structural mechanisms of caregiving, examination of caregiver health-care use outcomes through intervention studies, and including comparison groups to estimate the effects of caregiving on caregiver health-care use due to dementia.

The ultimate goal of health services research is to improve health outcomes of care recipients and caregivers. With the aging of the population and increases in the size of population with dementia, the effects of caregiving on caregiver health and health-care use will continue to be important at both the individual and societal level. Beyond the direct measures and costs of dementia patients' health-care utilization, results from this study suggest that there is a direct effect of dementia on caregivers' health-care use. It is imperative that we expand our focus on dementia patients to include family caregivers. In terms of community services provided to the caregivers, access to and involvement of a social worker has been shown to be important in linking caregivers to available support. Primary care providers, although central to coordinating health-care delivery to the care recipients, could be an important link in integrating caregivers' needs while planning and delivering health-care services to patients. Clinical interventions that treat the patients and their caregivers as a whole will most likely achieve the greatest beneficial effects.

### Acknowledgments

The Predictors Study is supported by federal grants AG07370, RR00645, and U01AG010483. The authors have reported no conflicts of interest.

Author contributions are as follows: study concept and design, C. Zhu and Y. Stern; acquisition of data, N. Scarmeas, M. Albert, J. Brandt, D. Blacker, M. Sano, and Y. Stern; analysis and interpretation of data, C. Zhu, N. Scarmeas, K. Ornstein, and Y. Stern; drafting of manuscript, C. Zhu; critical revision of manuscript for important intellectual content, C. Zhu, N. Scarmeas, K. Ornstein, J. Brandt, D. Blacker, M. Sano, Y. Stern; and statistical analysis, C. Zhu.

### RESEARCH IN CONTEXT

- 1 Systematic review: Providing care to individuals with dementia can often have negative health consequences. As a result, economic and health consequences to dementia caregivers can be substantial. However, most studies have focused on the patient. With few exceptions, caregiver health-care utilization has received little attention. The goal of this study was to examine the effects of caregiver and patient characteristics on caregivers' medical care use and cost.
- 2 Interpretation: In this present study, we take advantage of a rare opportunity of having both caregiver and care recipient data in a longitudinal setting and examine whether, and how, caregivers' medical care use and related costs are associated with their own health and sociodemographic characteristics as well as care recipients' increasing dementia severity and clinical characteristics. We hypothesize that caregivers' medical care use and costs will increase as care recipients' health declines, and the effects on caregivers' health-care use will vary by objective stressors and by domain of care. Our results show that patients' comorbid conditions and dependence were associated with increased health-care use and costs of caregivers. Improvements in caregiver depressive symptoms are associated with modest reductions in multiple domains of caregivers' medical care use and costs.
- 3 Future directions: Findings suggest that we should expand our focus on dementia patients to include family caregivers to obtain a fuller picture of effects of caregiving. For example, although improvements on caregiver depression have been consistently reported in dementia caregiver intervention programs, little is known of the effects of reduced depressive symptoms on caregiver health-care costs. This lack of information has impeded widespread adoption of successful interventions. However, because the Predictors Study is a natural history study of dementia, no interventions were conducted, and comparison data on individuals without dementia or their caregivers were not available. Therefore, we chose to estimate a set of reduced form equations, providing estimates of total effects of exogenous patient and caregiver variables on caregiver health-care use. Important next steps include examination of caregiver health-care use outcomes through intervention studies and including comparison groups to estimate the effects of caregiving on caregiver health-care use due to dementia.

## References

- [1] Alzheimer's Association. 2012 Alzheimer's disease facts and figures. *Alzheimers Dement* 2012;8:131–68.
- [2] Hurd MD, Martorell P, Delavande A, Mullen KJ, Langa KM. Monetary costs of dementia in the United States. *N Engl J Med* 2013; 368:1326–34.
- [3] Schulz R, Sherwood PR. Physical and mental health effects of family caregiving. *Am J Nurs* 2008;108:23–7. quiz 27.
- [4] Covinsky KE, Newcomer R, Fox P, Wood J, Sands L, Dane K, et al. Patient and caregiver characteristics associated with depression in caregivers of patients with dementia. *J Gen Intern Med* 2003; 18:1006–14.
- [5] Schulz R, Beach SR. Caregiving as a risk factor for mortality: the Caregiver Health Effects Study. *JAMA* 1999;282:2215–9.
- [6] Schulz R, Martire LM. Family caregiving of persons with dementia: prevalence, health effects, and support strategies. *Am J Geriatr Psychiatry* 2004;12:240–9.
- [7] Schulz R, Mendelsohn AB, Haley WE, Mahoney D, Allen RS, Zhang S, et al. End-of-life care and the effects of bereavement on family caregivers of persons with dementia. *N Engl J Med* 2003; 349:1936–42.
- [8] Kiecolt-Glaser JK, Dura JR, Speicher CE, Trask OJ, Glaser R. Spousal caregivers of dementia victims: longitudinal changes in immunity and health. *Psychosom Med* 1991;53:345–62.
- [9] King AC, Oka RK, Young DR. Ambulatory blood pressure and heart rate responses to the stress of work and caregiving in older women. *J Gerontol* 1994;49:M239–45.
- [10] Navaie-Waliser M, Feldman PH, Gould DA, Levine C, Kuerbis AN, Donelan K. When the caregiver needs care: the plight of vulnerable caregivers. *Am J Public Health* 2002;92:409–13.
- [11] Vitaliano PP, Zhang J, Scanlan JM. Is caregiving hazardous to one's physical health? A meta-analysis. *Psychol Bull* 2003; 129:946–72.
- [12] Toseland RW, McCallion P, Gerber T, Banks S. Predictors of health and human services use by persons with dementia and their family caregivers. *Soc Sci Med* 2002;55:1255–66.
- [13] Toseland RW, McCallion P, Gerber T, Dawson C, Gieryc S, Guilamo-Ramos V. Use of health and human services by community-residing people with dementia. *Soc Work* 1999;44:535–48.
- [14] Robinson KM, Buckwalter KC, Reed D. Predictors of use of services among dementia caregivers. *West J Nurs Res* 2005;27:126–40. discussion 141–127.
- [15] Brodaty H, Thomson C, Thompson C, Fine M. Why caregivers of people with dementia and memory loss don't use services. *Int J Geriatr Psychiatry* 2005;20:537–46.
- [16] Haley WE, Gitlin LN, Wisniewski SR, Mahoney DF, Coon DW, Winter L, et al. Well-being, appraisal, and coping in African-American and Caucasian dementia caregivers: findings from the REACH study. *Aging Ment Health* 2004;8:316–29.
- [17] Moore MJ, Zhu CW, Clipp EC. Informal costs of dementia care: estimates from the National Longitudinal Caregiver Study. *J of Gerontol* 2001;56:S219–28.
- [18] Van Houtven CH, Wilson MR, Clipp EC. Informal care intensity and caregiver drug utilization. *Rev Econ Household* 2005;3:415–33.
- [19] Schubert CC, Boustani M, Callahan CM, Perkins AJ, Hui S, Hendrie HC. Acute care utilization by dementia caregivers within urban primary care practices. *J Gen Intern Med* 2008;23:1736–40.
- [20] National Alliance for Caregiving/Schulz R, Cook T. Caregiving costs: declining health in the Alzheimer's caregiver as dementia increases in the care recipient. Bethesda, Maryland: National Alliance for Caregiving; 2011.
- [21] Nichols LO, Chang C, Lummus A, Burns R, Martindale-Adams J, Graney MJ, et al. The cost-effectiveness of a behavior intervention with caregivers of patients with Alzheimer's disease. *J Am Geriatr Soc* 2008;56:413–20.
- [22] Pearlin LI, Mullan JT, Semple SJ, Skaff MM. Caregiving and the stress process: an overview of concepts and their measures. *Gerontologist* 1990;30:583–94.
- [23] Gaugler J, Davey A, Pearlin L, Zarit S. Modeling caregiver adaptation over time: the longitudinal impact of behavior problems. *Psychol Aging* 2000;15:437–50.
- [24] Gaugler JE, Kane RL, Kane RA, Newcomer R. The longitudinal effects of early behavior problems in the dementia caregiving career. *Psychol Aging* 2005;20:100–16.
- [25] Gaugler JE, Pot AM, Zarit SH. Long-term adaptation to institutionalization in dementia caregivers. *Gerontologist* 2007; 47:730–40.
- [26] Stern Y, Folstein M, Albert M, Richards M, Miller L, Bylsma F, et al. Multicenter study of predictors of disease course in Alzheimer disease (the "Predictors Study"). I. Study design, cohort description, and intersite comparisons. *Alzheimer Dis Assoc Disord* 1993;7:3–21.
- [27] Richards M, Folstein M, Albert M, Miller L, Bylsma F, Lafleche G, et al. Multicenter study of predictors of disease course in Alzheimer disease (the "Predictors Study"). II. Neurological, psychiatric, and demographic influences on baseline measures of disease severity. *Alzheimer Dis Assoc Disord* 1993;7:22–32.
- [28] McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology* 1984;34:939–44.
- [29] McKeith IG, Fairbairn AF, Bothwell RA, Moore PB, errier IN, Thompson P, et al. An evaluation of the predictive validity and inter-rater reliability of clinical diagnostic criteria for senile dementia of Lewy body type. *Neurology* 1994;44:872–7.
- [30] Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;12:189–98.
- [31] Zhu CW, Scarmeas N, Torgan R, Albert M, Brandt J, Blacker D, et al. Longitudinal study of effects of patient characteristics on direct costs in Alzheimer disease. *Neurology* 2006;67:998–1005.
- [32] Bureau of Labor Statistics. Consumer price index. Available at: <http://www.bls.gov/cpi/home.htm>; 2007; Accessed February 13, 2014.
- [33] Zhu CW, Scarmeas N, Torgan R, Albert M, Brandt J, Blacker D, et al. Clinical features associated with costs in early AD: baseline data from the Predictors Study. *Neurology* 2006;66:1021–8.
- [34] Charlson ME, Charlson RE, Peterson JC, Marinopoulos SS, Briggs WM, Hollenberg JP. The Charlson comorbidity index is adapted to predict costs of chronic disease in primary care patients. *J Clin Epidemiol* 2008;61:1234–40.
- [35] Derogatis LR, Melisaratos N. The Brief Symptom Inventory: an introductory report. *Psychol Med* 1983;13:595–605.
- [36] Menzin J, Lang K, Friedman M, Neumann P, Cummings JL. The economic cost of Alzheimer's disease and related dementias to the California Medicaid program ("Medi-Cal") in 1995. *Am J Geriatr Psychiatry* 1999;7:300–8.
- [37] Stern Y, Albert SM, Sano M, Richards M, Miller L, Folstein M, et al. Assessing patient dependence in Alzheimer's disease. *J Gerontol* 1994;49:M216–22.
- [38] Devanand DP, Miller L, Richards M, Marder K, Bell K, Mayeux R, et al. The Columbia University Scale for Psychopathology in Alzheimer's disease. *Arch Neurol* 1992;49:371–6.
- [39] Scarmeas N, Brandt J, Albert M, Hadjigeorgiou G, Papadimitriou A, Dubois B, et al. Delusions and hallucinations are associated with worse outcome in Alzheimer disease. *Arch Neurol* 2005;62:1601–8.
- [40] Scarmeas N, Brandt J, Blacker D, Albert M, Hadjigeorgiou G, Dubois B, et al. Disruptive behavior as a predictor in Alzheimer disease. *Arch Neurol* 2007;64:1755–61.

- [41] Long J, Freese J. Regression models for categorical and limited dependent variables. Thousand Oaks, CA: Sage; 1997.
- [42] Rabe-Hesketh S, Skrondal A. Multilevel and longitudinal modeling using Stata. College Station, TX: Stata Press; 2005.
- [43] Singer J, Willet J. Applied longitudinal data analysis: modeling change and event occurrence. New York: Oxford University Press; 2003.
- [44] Statacorp. Stata statistical software: release 11. College Station, Texas: StataCorp LP; 2010.
- [45] Katon WJ, Lin E, Russo J, Unutzer J. Increased medical costs of a population-based sample of depressed elderly patients. *Arch Gen Psychiatry* 2003;60:897–903.
- [46] Schulz R, O'Brien A, Czaja S, Ory M, Norris R, Martire LM, et al. Dementia caregiver intervention research: in search of clinical significance. *Gerontologist* 2002;42:589–602.
- [47] Pinquart M, Sorensen S. Associations of stressors and uplifts of caregiving with caregiver burden and depressive mood: a meta-analysis. *J Gerontol B Psychol Sci Soc Sci* 2003;58:P112–28.
- [48] Zhu C, Moore M, Clipp E. Informal costs of dementia care and patients' problem behavior. In: Andrieu S, Aquino J-P, eds. *Family and professional cares: findings lead to action*. Serdi: Fondation Médéric Alzheimer Paris; 2002.
- [49] Christakis NA, Allison PD. Mortality after the hospitalization of a spouse. *N Engl J Med* 2006;354:719–30.