Predictors of Family Caregiver Ratings of Patient Quality of Life in Alzheimer's Disease: Cross-Sectional Results from the Canadian Alzheimer's Disease Quality of Life (CADQOL) Study

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Abstract

Objectives—To assess whether the core symptoms of Alzheimer's disease (AD) and caregiver factors consistently predict family caregiver ratings of patient quality of life (QOL) as assessed by a variety of QOL measures in a large national sample.

Design—Cross-sectional.

Setting—Fifteen dementia and geriatric clinics across Canada.

Participants—Family caregivers (n = 412) of community-living patients with AD of all severities.

Measurements—Caregiver ratings of patient QOL using three utility indexes, the EQ-5D, Quality of Well-Being Scale and Health Utilities Index, a global QOL visual analogue scale, a disease-specific measure, the QOL-AD, and a generic health status measure, the Short Form-36. Patient cognition was assessed with the AD Assessment Scale-Cognitive Subscale and Mini-Mental State Examination, function with the Disability Assessment for Dementia, and behavioral and psychological symptoms with the Neuropsychiatric Inventory and the Geriatric Depression

Scale. Caregiver burden was assessed with the Zarit Burden Interview and caregiver depression with the Center for Epidemiologic Studies-Depression scale. One-way analysis of variance and fully adjusted multiple linear regression were used to assess the relationship between patient dementia symptom and caregiver variables with QOL ratings.

Results—In multivariable analyses, caregiver ratings of patient function and depressive symptoms were the only consistent independent predictors of caregiver-rated QOL across the QOL measures.

Conclusions—Caregiver ratings of patient function and depression were consistent independent predictors of caregiver-rated QOL using a spectrum of QOL measures, while measures of patient cognition and caregiver burden and depression were not. These findings support the continued use of caregiver ratings as an important source of information about patient QOL and endorse the inclusion in AD clinical trials of caregiver-rated measures of patient function, depression and QOL.

Keywords

Alzheimer's disease; dementia; quality of life; utility; family caregiver; depression; function

In keeping with the increasing recognition of the importance of health-related quality of life (QOL) in Alzheimer's disease (AD), the International Working Group for the Harmonization of Dementia Guidelines has recommended that QOL be included as an outcome measure in all dementia trials.[1] There are two basic types of QOL measures: generic instruments, including health profile and utility measures, and disease-specific instruments.[2] Disease-specific measures are considered to be more sensitive at detecting disease-related changes, while generic measures facilitate comparisons across different diseases, as is often required in policy decision making. Utility measures, which can be used in cost-effectiveness analyses, include utility indexes and direct elicitation methods.[2]

Patient and caregiver reports of patient QOL provide unique and independent perspectives on QOL in AD.[3, 4] Patients with AD may have limited insight into their symptoms and the validity of their QOL ratings, especially in the more severe stages of dementia, has been questioned. Family caregivers can provide QOL information about the patient from the standpoint of persons without dementia who have an intimate experience of the disease coupled with prior knowledge of the values and goals of the individual. These ratings provide a viewpoint that is more representative of society as a whole, which is sometimes the preferred perspective, such as for health economic evaluations. However, caregiver ratings of patient QOL may bring their own biases, perhaps informed by their own burden of caring for the patient.

Several previous studies have assessed the predictors of caregiver ratings of the QOL of community-living patients with AD using multiple regression.[5–13] They have generally found that patient depression and function were significant independent predictors of QOL, while patient cognitive status assessed with the Mini-Mental State Examination (MMSE) was not. Results for patient behavioural disturbances, as measured by the total NPI score, have been conflicting. Some studies have noted that caregiver burden can influence

caregiver-rated patient QOL,[8, 12, 13] while results for caregiver depression have been inconsistent.[6, 10, 12] The majority of these studies have included only a single measure of QOL,[5–12] most commonly the disease-specific QOL-AD.[5–9] Only a few of these studies included generic QOL measures.[12, 13]

Given that different types of QOL measures assess different dimensions of QOL and that utility scores for the same disease can vary substantially depending on the utility measure used,[14] the objective of this study was to evaluate whether there are consistent predictors of caregiver-rated patient QOL across a spectrum of QOL measures or whether predictors of caregiver-rated patient QOL vary with different QOL measures in a large national sample of community-living patients with AD. In addition, we wanted to address some gaps in the literature on predictors of caregiver ratings of patient QOL in AD: conflicting data on the impact of caregiver factors on caregiver ratings; little information on the predictive ability of patients' cognitive performance as measured by the Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog), which is a more sensitive measure of cognitive impairment in AD than the MMSE;[15] lack of data on the predictors of caregiver ratings as measured by the Quality of Well Being (QWB) index and Short-Form 36;[16] and little available research incorporating comprehensive multiple regression models that include a full spectrum of patient factors (core dementia symptoms, demographics and comorbidity) and caregiver factors (demographics, comorbidity, burden and depression).

Methods

Design

This report is based on cross-sectional analyses of baseline data derived from the Canadian Alzheimer's Disease Quality of Life (CADQOL) study.

Participants

Community-living patients with probable AD[17] of any severity, who had a family caregiver with a minimum of two contacts with them per week, were recruited from 11 memory clinics and 4 geriatric assessment clinics across Canada that provide diagnostic services and ongoing care for patients with dementia. This paper describes the results for caregiver ratings of the QOL of patients with AD, which for the remainder of this paper will be denoted as caregiver-rated QOL.

Demographic and Medical Data

The caregiver provided demographic and medical information about the patient and themselves.

Measures of Caregiver Burden and Depression

Caregiver burden was measured using the Zarit Burden Interview (ZBI), a 22-item self-administered questionnaire with scores ranging from 0–88.[18] Caregiver depression was assessed with the Center for Epidemiologic Studies-Depression scale (CES-D) with scores ranging from 0–63.[19] Higher scores indicate greater burden and depressive symptoms, respectively.

Measures of Patient Cognition, Function and Behavioral and Psychological Symptoms of Dementia

Cognition of the person with AD was measured using the Mini-Mental State Examination (MMSE)[20] and the ADAS-Cog.[15] Functional assessment of the AD patients was measured using the caregiver-rated Disability Assessment for Dementia (DAD).[21] Behavioral and psychological symptoms of the AD patient were measured using the caregiver-rated Neuropsychiatric Inventory (NPI).[22] Caregiver ratings of patients' depressive symptoms were made using the 30-item Geriatric Depression Scale (GDS), where they responded to questions based on their perception of how the patient was feeling. [23]

Measures of Quality of Life

Table 1 lists the domains included in the QOL measures used in this study.

Disease-Specific QOL Measure—The QOL in AD (QOL-AD) is a 13-item instrument developed to evaluate QOL in persons with AD. Scores range from 13–52. It has been shown to be reliable and valid for ratings by family caregivers.[5, 24]

Generic Health Utility Indexes—The EQ-5D, Quality of Well-Being Scale (QWB) and Health Utilities Index (HUI) are each composed of a health state classification system and an algorithm to convert ratings into utility scores based on community-derived health preferences. These utility indexes, which are scored on 0–1 scales, differ in terms of content, structure and scoring function.[14, 16] They have been shown to be reliable and valid for caregiver ratings of AD patients.[13, 16] We used version 2/3 of the HUI, which allows for the derivation of HUI2 and HUI3 scores, [25] but report here only HUI3 ratings as the HUI2 and HUI3 scores were highly correlated and yielded equivalent results.

Global QOL Rating Scale—We used a directly elicited visual analogue scale (VAS) in the form of a vertical “feeling thermometer” labelled from 0 (death) to 100 (full health).

Generic Health Profile Measure—The Short Form-36 (SF-36) is a widely used QOL measure that generates summary scales for physical components (PCS) and for mental health components (MCS) .[26] The SF-36 has been shown to be a reliable and valid measure for caregiver ratings of AD patients.[27] The scores for the PCS and MCS have been norm-based to a mean of 50 and a standard deviation of 10.

The assessment involved two sessions. In the first session, the demographic and medical data were collected and the caregiver completed the DAD, the NPI and the caregiver GDS ratings of the patient. In the second session, the caregiver completed the QOL measures on their own, with the exception of the VAS, which was administered by a research assistant. The order of the QOL measures was randomly assigned. Caregivers provided QOL ratings using the EQ-5D, QWB, VAS and QOL-AD, which have been validated for use by both patients and caregivers, as well as using the HUI and SF-36, which have demonstrated validity for caregiver-rated QOL in AD, but questionable validity for patient self-ratings.[13, 16, 27, 28]

Excluded and Missing Data

The validity of the data at one site could not be established by audit, so these data were excluded. All other data were entered in duplicate and compared to minimize entry errors. Caregivers with complete scores on a QOL measure were retained for the analyses pertaining to that measure. Five caregivers who were missing scores on all of the QOL measures and one caregiver who was missing all demographic information were excluded from the analyses. For the remaining sample of 412 caregivers, when 20% or less of the total items was missing from a measure, QOL scores were derived in accordance with scoring practices for the specific measure (e.g. prorated scores). Multiple imputation with the R package *mi* was used for any predictor variables missing more than 20% of their total items. [29] This affected only 27 observations; 6.6% of our analytic sample.

Data Analysis

We computed Pearson correlations between patient QOL ratings using the different QOL measures. We calculated mean caregiver QOL ratings for each severity level for the patient core dementia symptom measures. The DAD and ADAS-Cog scores were divided into quartiles. Many patients scored zero for the NPI, so we treated that as a separate category and divided the remaining scores into tertiles. For the GDS, we used groupings based on the literature: 0–10, 11–13, 14–20 and > 20.[23, 30] We conducted unadjusted analyses using an F-test from a one-way analysis of variance to compare the mean QOL across the levels of the symptom severity scores.

We used multiple linear regression to examine the relationships between each of the proxy QOL outcomes and the patients' core dementia symptom predictor variables. These adjusted models included patient and caregiver age, sex (male vs. female), education (grade 9–13 or > grade 13 vs. < grade 9), comorbidity measured by the Charlson score (2 or 3 vs. 1 for patients, as all patients receive 1 point for dementia; 1 or 2 vs. 0 for caregivers), [31] and study center (5 centres each with less than 25 participants were grouped as a single center). The models were also adjusted for the first language spoken by the patient (English vs. other), caregiver burden (ZBI) and depression (CES-D), caregiver employment status and the caregiver's relationship to the patient (spouse vs. other). Regression coefficients for the patients' core dementia symptom variables and for the caregivers' burden and depression variables are expressed as the estimated mean difference in the QOL outcome per standard deviation of the predictor variable. Regression coefficients for age are expressed per 5 year increase in age. Parameter estimates were averaged across 10 imputed datasets and p-values were computed using a t-test for a single parameter and an F-test for group variables, using an estimated degrees of freedom that accounts for the imputation process.[32, 33] The relative importance of each variable to the QOL outcomes was summarized with the Lindeman, Merenda and Gold (LMG) R^2 , which is an average of the R^2 increments from adding the variable of interest to all possible models without the variable.[34] Because this relative importance measure is an average across all of the possible models, it is independent of the order of entry of the variable.

Data were analyzed using R, version 2.7.0 (April 22, 2008).[35] Since we carried out many hypothesis tests, statistical significance was set at $p < 0.01$. Estimates of minimal clinically

important differences for the QOL measures are .06–.07 for the EQ-5D, .03 for the QWB, .03–.04 for the HUI, .07–.10 for the VAS, 3–5 units for the SF-36 and one standard deviation for the QOL-AD.[25, 36–38]

Results

We carried out assessments on 418 patient-caregiver dyads. We excluded six assessments because of excessive missing data, leaving an analytic sample of 412. Tables 2 and 3 summarize the characteristics of the caregivers and the patients, respectively. The caregiver analytic sample had a mean age of 72.2 (standard deviation [SD]: 12.3), 62.6% were female and 74.8% were spouses of the patient. Ninety-nine caregivers (24.0%) scored 16 or higher on the CES-D, suggestive of clinical depression,[19] and 98 (23.8%) had ZBI scores > 38. The patient sample had a mean age of 80.7 (SD: 7.9), a mean MMSE of 20.8 (SD: 6.2) (64.1% with scores > 20, 17.7% with scores 16–20, 10.0% with scores 11–15 and 8.2% with scores < 11), and 50.5% were female. A total of 103 patients (25.0%) had DAD scores less than 50, 257 (62.4%) had caregiver-rated GDS scores over 10, suggestive of clinical depression, and NPI ratings were skewed to lower scores, with 62 (15.0%) having a score of 0.

Table 4 displays the correlations between QOL ratings using the different measures. The correlations were only moderate (0.31–0.65).

Table 5 summarizes analyses exploring the relationship between dementia symptom severity scores and caregiver-rated QOL. Mean QOL ratings were consistently lower for all the QOL measures with more severe cognitive impairment (ADAS-Cog and MMSE [results not shown]), functional impairment (DAD), behavioral disturbance (NPI) and depressive symptoms (GDS). Analyses for caregiver burden (ZBI) and caregiver depressive symptoms (CES-D) (results not shown) showed that mean caregiver ratings of patient QOL were consistently lower for all the QOL measures with more severe caregiver burden and depressive symptoms.

Table 6 displays the results from fully-adjusted linear regression analyses exploring the predictors of caregiver-rated QOL for all the QOL measures. Of the measures of core dementia symptoms, the DAD (function) and GDS (depressive symptoms) were the only consistent statistically significant independent predictors of caregiver-rated QOL across the QOL measures, and they had the largest beta coefficients and made the largest LMG R^2 contributions for the three utility indexes, the QOL-AD and the SF-36 PCS. For the global VAS, the DAD, GDS and NPI (behavioral symptoms) had similar beta coefficients and made similar LMG R^2 contributions. Caregiver depressive symptoms (CES-D) were not a significant independent predictor of any of the caregiver-rated QOL measures. Caregiver burden (ZBI) was a significant independent predictor only of the SF-36 MCS. For all the QOL measures, compared with the patient variables, the caregiver variables made relatively small LMG R^2 contributions to the caregiver ratings of patient QOL.

Discussion

We conducted a comprehensive study of the predictors of family caregiver ratings of the QOL of patients with AD using a broad spectrum of patient and caregiver predictor variables and QOL measures. Although there is some overlap in the domains included in the different QOL measures (Table 1), each instrument uses different operational definitions for the domains and has unique structures and scoring rules. We found only moderate correlations between them (Table 4). Despite the differences between the QOL measures, we noted several consistent findings. Caregiver assessments of patient function and depression were the strongest independent predictors of caregiver-rated QOL across the measures. Performance-based cognition, as measured by the ADAS-Cog and MMSE (results not shown), was not a significant independent predictor of any of the QOL measures. The SF-36 is unique compared to the other QOL measures in that it offers a separate physical and mental health component summary score. This distinct element of the SF-36 is reflected in the different predictors of the MCS (patient depressive and behavioral symptoms and caregiver burden) versus the PCS (patient age, comorbidity, function and depressive symptoms).

These results cannot be explained simply on the basis of the content of the QOL measures (i.e. the inclusion or exclusion of domains that relate to the predictor variables). This is shown by the following observations. Patient function was a significant independent predictor of ratings on the HUI3, which lacks a specific functional status domain. Patient depressive symptoms and function were significant and borderline significant predictors, respectively, of global ratings of QOL on the visual analogue scale, which has no domains. Patient depressive symptoms were an independent predictor of ratings on the SF-36 PCS, which does not include a depression domain. Finally, cognitive performance was not a significant independent predictor of ratings on the QWB, HUI3 and QOL-AD, which have a cognitive/memory domain. However, differences in the methods of elicitation of the core dementia symptoms may have influenced the results in that the only dementia symptom that was not an independent predictor of any of the QOL measures, cognitive status, was derived using performance-based measures while all others were derived by caregiver report.

Our findings confirm previous reports in the literature that patient function and patient depressive symptoms are independent predictors of caregiver-rated QOL-AD scores,[5, 8, 39] although Fuh et al. found patient depression, but not function, to be an independent predictor of QOL-AD scores.[7] Karlawish et al. reported that patient self-care activities were an independent predictor of caregiver-rated HUI2 and EQ-5D scores.[13] Banerjee et al. did not find patient function to predict caregiver-rated scores on the dementia-specific DEMQOL.[10] The discrepancies in the findings about function may relate, at least partly, to differences in the functional measures used.

Our results also confirm previous findings that cognition measured by the MMSE is not an independent predictor of caregiver-rated scores on the QOL-AD[5, 7, 39] and the EQ-5D and HUI2.[13] Hurt et al. recently reported that in a population with mild to moderate dementia, the ADAS-Cog, a more sensitive performance-based measure of cognition in AD than the MMSE, was not associated with caregiver-rated DEMQOL scores.[11] Our study

adds to this literature by showing that the ADAS-Cog was not a significant independent predictor of QOL across six different QOL measures. This finding does not negate the importance of cognitive impairment as a contributing factor to the functional impairment and behavioural and psychological symptoms of dementia. However, in terms of the influence on caregiver ratings of patient QOL, caregiver measures of patients' functional impairment and depressive symptoms have considerably greater impact.

Given that the ADAS-Cog does not appear to be an important independent predictor of caregiver-rated QOL, the use of this measure as a primary outcome in clinical trials may not be measuring what is of most importance from the perspective of family caregivers. If the focus of AD clinical trials is to improve or preserve the QOL of persons with AD, primary outcomes of studies should include measures that have the greatest impact on patient QOL, such as caregiver ratings of patient function and depression symptoms. In addition, given our finding that a considerable amount of the variance (44–75%) of the QOL ratings is not explained by commonly measured patient and caregiver factors, direct measures of QOL should be included in dementia intervention trials.

Previous studies had inconsistent results regarding patient behavioral and psychological symptoms as measured by the NPI total score. The NPI total score was a significant independent predictor of caregiver-rated DEMQOL scores,[10] but not QOL-AD scores.[7, 39] We also found conflicting results, with the NPI total score being a significant independent predictor of caregiver-rated HUI3, VAS and SF-36 MCS scores, but not EQ-5D, QWB, QOL-AD and SF-36 PCS scores. Thus, it appears that different QOL measures are more sensitive than others to patients' behavioral and psychological symptoms.

Findings in the literature are also inconsistent regarding the impact of caregiver factors such as burden and depression on caregiver ratings of patient QOL. Studies have found that caregiver burden may impact caregiver-rated QOL using the QOL-AD[8, 24] and the EQ-5D,[13] while others found that burden was not an independent predictor of caregiver ratings using the HUI2 or DEMQOL.[10, 13] Reports on the influence of caregiver depression on caregiver-rated QOL-AD scores have also been contradictory.[5, 6] We found that caregiver depression was not a significant independent predictor of any of the QOL measures while burden was a significant independent predictor only of the SF-36 MCS. Our results show that although there is some variability among QOL measures, patient factors have a much greater impact on caregiver ratings of patient QOL than caregiver factors do. This supports the continued use of caregiver ratings as an important source of information about patient QOL from the perspective of someone with direct experience of the disease and prior knowledge of the patient's values and goals. This can be particularly helpful in instances when patients cannot provide valid ratings of their own QOL and when a viewpoint that is more representative of a societal perspective is preferred, such as for health policy decision making.

Our study has several strengths. It is the largest study of its kind, included a comprehensive spectrum of QOL measures and patient and caregiver predictor variables, and used fully adjusted regression analyses. There are a number of limitations. Our sample was community-living and skewed to patients with milder dementia, so the results may not

accurately reflect predictors for those who are institutionalized and/or have severe dementia, but they are likely germane to AD clinical trial populations with mild-to-moderate dementia. The study caregivers and patients were highly educated. Therefore, the results may not be generalizable to caregivers and patients with limited formal education. Our total NPI scores were skewed to lower scores, so our results may not be representative of populations with more severe behavioural disturbances. This limitation is common to most dementia studies, since patients with more severe behavioural disturbances are less likely to volunteer or to meet inclusion criteria.

In conclusion, in a large national study of patients with AD, we showed that predictors of caregiver ratings of patient QOL are quite consistent across diverse QOL measures that differ in methodological approach and content. We confirmed that caregiver ratings of patient function and depression were the most important independent predictors of caregiver-rated QOL and showed that patient cognitive performance, as measured by the ADAS-Cog, and caregiver measures of burden and depression were not important independent predictor of caregiver-rated QOL. Our findings support the continued use of caregiver ratings as an important, unique source of information about patient QOL and endorse the inclusion of caregiver-rated measures of patient function, depression and QOL in AD clinical trials.

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Table 1

Quality of Life Domains Included in the EQ-5D, QWB, HUI3, QOL-AD and SF-36

EQ-5D	QWB	HUI3	QOL-AD	SF-36
Self-care	Self-care	Dexterity	Usual/meaningful activities	Physical functioning
Usual activities	Usual/social activities	Ambulation	Physical health	Social functioning
Mobility	Mobility	Emotion	Social relationships	Role limitations (physical)
Anxiety/depression	Physical activities	Cognition	Mood	Role limitations (emotional)
Pain	21 symptom/problem complexes	Vision	Energy	Mental health
		Hearing	Memory	Vitality
		Speech	Living situation	Bodily pain
		Pain	Financial situation	General health perceptions
			Global rating of life	

EQ-5D = European Quality of Life-5 Dimensions; QWB = Quality of Well-Being Index; HUI3 = Health Utilities Index, version 3; QOL-AD = Quality of Life-Alzheimer's Disease; SF-36 = Short Form-36.

Each EQ-5D item is rated on 3 levels. Each HUI3 item is rated on 5-6 levels. The QWB functional scales (self-care, usual/social activities, mobility and physical activities) include 2-8 items per scale. The QWB symptom/problem complexes include physical and emotional health, cognitive and sensory function, speech, general weakness and limb function, and pain.

Table 2

Caregiver Characteristics

Characteristic	Analytic Sample (n = 412)		
	N	Mean (SD)/%	Median (IQR)
Age	408	72.2 (12.3)	74.6 (65.2–81.6)
Female	258/412	62.6%	
First Language English	353/412	85.7%	
Education	410		
<9 Grades	17	4.1%	
9–13 Grades	120	29.3%	
College or University	273	66.6%	
Employed	89/412	21.6%	
Relationship to Patient	412		
Spouse	308	74.8%	
Child	85	20.6%	
Live with Patient	352/412	85.4%	
Live with Child	73/412	17.7%	
Live with Other Dependents	81/412	19.7%	
Comorbidity	411		
Charlson = 0	217	52.8%	
Charlson = 1	110	26.8%	
Charlson = 2	84	20.4%	
Zarit (Burden)	409	28.8 (14.0)	28.0 (17.0 – 38.0)
CES-D (Depression)	408	10.7 (7.9)	9.0 (5.0 – 15.0)

SD = Standard Deviation; IQR = Interquartile Range; Charlson = Charlson Comorbidity score; Zarit Burden Interview is a measure of caregiver burden; CES-D = Center for Epidemiologic Studies-Depression scale.

The excluded caregivers (n = 6) were more likely to be female (83.3%) than those in the analytic sample. Data on the remaining characteristics were only available for 1–3 of the 6 excluded caregivers, so no further meaningful comparisons could be made with the analytic sample.

Table 3**Patient Characteristics**

Characteristic	Analytic Sample (n = 412)		
	N	Mean (SD)/%	Median (IQR)
Age	412	80.7 (7.9)	81.1 (75.8 – 86.4)
Female	208/412	50.5%	
First Language English	336/412	81.6%	
Education	407		
<9 Grades	38	9.3%	
9–13 Grades	147	36.1%	
College or University	222	54.5%	
Married	329/412	79.9%	
Live Alone	43/411	10.5%	
* Private Home	375/412	91.0%	
Comorbidity	412		
Charlson = 1	233	56.6	
Charlson = 2	92	22.3%	
Charlson = 3	87	21.1%	
MMSE (Cognition)	412	20.8 (6.2)	23.0 (18.0 – 25.0)
ADAS-Cog (Cognition)	411	29.1 (12.1)	25.3 (21.0 – 34.3)
DAD (Function)	412	66.0 (25.0)	68.4 (49.7 – 88.9)
NPI (Behavior)	411	11.1 (12.4)	7.0 (2.0 – 15.5)
GDS (Depression)	396	13.4 (6.7)	12.0 (8.0 – 18.0)

SD = Standard Deviation; IQR = Interquartile Range; MMSE = Mini-Mental State Examination; ADAS-Cog = Alzheimer's Disease Assessment Scale-Cognitive Subscale; DAD = Disability Assessment for Dementia; NPI = Neuropsychiatric Inventory; GDS = Geriatric Depression Scale (caregiver proxy rated)

* Private home represents a house, condominium or apartment that the patient owns or rents. Most patients not living in a private home lived in a retirement home or a relative's home.

The excluded patients (n = 6) were older (mean age 84.2 (5.2)) and were more likely to be female (83.3%) than those in the analytic sample. Data on the remaining characteristics were only available for 2–4 of the 6 excluded patients, so no further meaningful comparisons could be made with the analytic sample.

Table 4

Correlations* (95% Confidence Intervals) Between Quality of Life Measures

	EQ-5D	QWB	HUI3	VAS	QOL-AD	SF-36 MCS
EQ5D						
QWB	0.48 (0.41–0.56)					
HUI3	0.60 (0.53–0.66)	0.58 (0.51–0.64)				
VAS	0.32 (0.23–0.40)	0.32 (0.23–0.41)	0.46 (0.37–0.53)			
QOL-AD	0.56 (0.49–0.63)	0.50 (0.42–0.57)	0.65 (0.59–0.71)	0.47 (0.39–0.54)		
SF-36 MCS	0.39 (0.30–0.47)	0.38 (0.29–0.46)	0.46 (0.38–0.53)	0.34 (0.26–0.43)	0.60 (0.54–0.66)	
SF-36 PCS	0.52 (0.44–0.59)	0.37 (0.28–0.45)	0.40 (0.31–0.48)	0.31 (0.22–0.39)	0.36 (0.28–0.45)	–0.06 (–0.15–0.04)

* The correlation values are Pearson's correlation coefficients.

EQ-5D = European Quality of Life-5 Dimensions; QWB = Quality of Well-Being Index; HUI3 = Health Utilities Index; VAS = Visual Analog Scale; QOL-AD = Quality of Life- Alzheimer's Disease; SF-36 MCS and PCS = Short Form-36 Mental Component and Physical Component Scales, respectively

Table 5
Mean Caregiver Patient QOL Scores for Different Severity Levels of Patient Core Symptom Variables

	N [†] (%)	EQ-5D (n=410) Mean (SD)	QWB (n=410) Mean (SD)	HUI3 (n=411) Mean (SD)	VAS (n=407) Mean (SD)	QOL-AD (n=409) Mean (SD)	SF-36 PCS (n=408) Mean (SD)	SF-36 MCS (n=408) Mean (SD)
ADAS (Cognition)								
8-21	110 (26.7)	0.82 (0.16)	0.56 (0.17)	0.48 (0.27)	0.70 (0.17)	36.0 (6.2)	46.3 (11.6)	50.5 (11.5)
22-25	98 (23.8)	0.80 (0.16)	0.50 (0.15)	0.36 (0.27)	0.67 (0.16)	34.8 (6.3)	44.0 (9.5)	46.7 (12.7)
26-34	101 (24.5)	0.76 (0.17)	0.46 (0.17)	0.31 (0.26)	0.64 (0.18)	33.0 (5.7)	42.4 (11.5)	46.3 (11.8)
35-70	103 (25.0)	0.68 (0.22)***	0.39 (0.17)***	0.16 (0.24)***	0.61 (0.21)*	31.2 (6.0)***	42.5 (11.5)	45.5 (13.7)
DAD (Function)								
0-49	103 (25.0)	0.65 (0.20)	0.37 (0.16)	0.10 (0.22)	0.59 (0.20)	30.3 (5.7)	40.1 (12.4)	45.8 (13.7)
50-68	105 (25.5)	0.76 (0.15)	0.45 (0.16)	0.28 (0.23)	0.63 (0.20)	32.3 (6.0)	43.3 (11.3)	45.1 (13.7)
69-88	103 (25.0)	0.79 (0.18)	0.50 (0.16)	0.37 (0.24)	0.68 (0.16)	34.8 (5.4)	44.5 (9.4)	46.7 (11.1)
89-100	101 (24.5)	0.85 (0.17)***	0.60 (0.15)***	0.58 (0.23)***	0.73 (0.15)***	37.9 (5.5)***	47.6 (10.2)***	52.0 (10.3)**
NPI (Behavior)								
0	62 (15.0)	0.84 (0.16)	0.59 (0.16)	0.55 (0.24)	0.76 (0.14)	37.8 (5.2)	46.5 (10.0)	55.0 (7.6)
1-6	133 (32.3)	0.81 (0.15)	0.51 (0.18)	0.41 (0.25)	0.69 (0.17)	35.4 (5.9)	45.4 (10.6)	50.6 (10.3)
7-14	104 (25.2)	0.75 (0.17)	0.45 (0.17)	0.28 (0.25)	0.63 (0.16)	33.4 (5.6)	41.9 (10.8)	46.6 (11.8)
15-73	113 (27.4)	0.68 (0.22)***	0.41 (0.16)***	0.16 (0.25)***	0.58 (0.21)***	29.9 (5.8)***	42.3 (12.3)	39.8 (13.8)***
GDS (Depression)								
0-10	155 (37.6)	0.84 (0.16)	0.55 (0.18)	0.45 (0.27)	0.71 (0.16)	37.5 (5.1)	46.2 (9.6)	54.7 (8.2)
11-13	86 (20.9)	0.77 (0.16)	0.48 (0.17)	0.37 (0.26)	0.70 (0.15)	33.9 (5.4)	43.5 (10.2)	49.6 (9.3)
14-20	95 (23.1)	0.72 (0.19)	0.43 (0.16)	0.26 (0.25)	0.61 (0.18)	31.9 (5.3)	40.7 (12.7)	44.8 (10.5)
21-30	76 (18.4)	0.65 (0.21)***	0.40 (0.14)***	0.13 (0.25)***	0.56 (0.22)***	28.3 (5.8)***	43.4 (12.2)*	32.8 (12.2)***

EQ-5D = European Quality of Life-5 Dimensions; QWB = Quality of Well-Being Index; HUI3 = Health Utilities Index, version 3; VAS = global quality of life Visual Analog Scale; QOL-AD = Quality of Life-Alzheimer's Disease; SF-36 MCS and PCS = Short Form-36 Mental Component and Physical Component Scales, respectively; ADAS = Alzheimer's Disease Assessment Scale-Cognitive sub-scale; DAD = Disability Assessment for Dementia; NPI = Neuropsychiatric Inventory; GDS = Geriatric Depression Scale.

The EQ-5D, QWB, HUI3 and VAS are rated on 0-1 scales; The QOL-AD is rated on a 13-52 scale; the SF-36 MCS and PCS are norm based to a mean score of 50 and standard deviation of 10.

* p<0.01;

** p<0.001;

*** p 0.0001;

the p-values comparing the mean quality of life scores across the levels of the symptom severity scores were derived from the overall F-test in a one-way analysis of variance. All tests had numerator degrees of freedom (df) of 3 and denominator df of 407, 408, 404, 406 and 405 for the EQ-5D, QWB, HUI3, VAS, QOL-AD and SF-36, respectively.

[†]N = the number of participants from the full analytic cohort (n=412) in each severity level for each of the core dementia symptom measures. Because not all cohort participants completed each quality of life measure, the number of participants in each core symptom severity level varied slightly among the quality of life measures compared with the total cohort. These differences were 2 or less participants per severity level except for the following core symptom severity levels for the VAS: ADAS 8-21 (n=107, 26.3%) and GDS 0-10 (n=151, 37.1%).

Table 6
Predictors of Caregiver Rated Patient Quality of Life from Fully Adjusted Regression Analyses

Variables	EQ-5D (n=410) (Model R ² = 0.37)			QWB (n=410) (Model R ² = 0.38)			HUI3 (n=411) (Model R ² = 0.55)			VAS (n=407) (Model R ² = 0.25)			QOL-AD (n=409) (Model R ² = 0.56)			SF-36 MCS (n=408) (Model R ² = 0.54)			SF-36 PCS (n=408) (Model R ² = 0.24)		
	β	P	R ² *	β	P	R ² *	β	P	R ² *	β	P	R ² *	β	P	R ² *	β	P	R ² *	β	P	R ² *
<i>Patient</i>																					
Age	-0.013	0.108	0.01	0.001	0.911	0.00	-0.037	0.0001	0.03	-0.005	0.547	0.00	-0.123	0.582	0.00	0.751	0.100	0.00	-1.774	0.001	0.04
Sex (Male)	0.014	0.632	0.01	-0.001	0.964	0.00	0.040	0.271	0.00	0.004	0.897	0.00	-0.132	0.868	0.00	-2.925	0.070	0.00	2.832	0.124	0.00
Charlson Score		0.798	0.00		0.009	0.01		0.460	0.00		0.178	0.01		0.029	0.01		0.505	0.00		<0.001	0.04
ADAS-Cognition	-0.020	0.070	0.05	-0.017	0.096	0.04	-0.025	0.081	0.06	-0.007	0.527	0.01	0.253	0.418	0.03	0.340	0.590	0.00	0.423	0.556	0.01
DAD (Function)	0.051	<0.0001	0.09	0.054	<0.0001	0.11	0.116	<0.0001	0.18	0.030	0.015	0.04	2.213	<0.0001	0.10	-0.549	0.411	0.01	3.371	<0.0001	0.05
NPI (Behavior)	-0.004	0.705	0.03	-0.003	0.794	0.02	-0.035	0.009	0.06	-0.030	0.007	0.05	-0.026	0.930	0.05	-1.944	0.001	0.08	1.194	0.081	0.00
GDS (Depression)	-0.062	<0.0001	0.10	-0.040	<0.0001	0.06	-0.091	<0.0001	0.11	-0.032	0.003	0.05	-2.697	<0.0001	0.19	-6.208	<0.0001	0.25	-1.880	0.004	0.02
Other		0.317	0.00		0.036	0.02		0.818	0.00		0.725	0.00		0.437	0.00		0.408	0.00		0.639	0.00
<i>Caregiver</i>																					
Spouse	0.016	0.708	0.00	0.041	0.298	0.00	-0.049	0.361	0.00	-0.004	0.923	0.00	-0.490	0.681	0.00	4.034	0.096	0.00	-4.307	0.117	0.00
Zarit (Burden)	0.011	0.316	0.02	-0.026	0.016	0.05	-0.004	0.760	0.05	-0.000	0.976	0.02	-0.766	0.017	0.08	-2.067	0.002	0.09	1.213	0.102	0.00
CES-D (Depression)	-0.019	0.064	0.02	0.008	0.386	0.01	-0.006	0.619	0.02	-0.010	0.355	0.01	-0.384	0.169	0.04	-0.680	0.229	0.04	-0.585	0.360	0.00
Other		0.473	0.02		0.856	0.01		0.716	0.01		0.761	0.02		0.136	0.02		0.293	0.01		0.168	0.03
<i>Study Center</i>		0.449	0.02		0.008	0.04		0.635	0.01		0.115	0.03		0.039	0.03		0.098	0.03		0.299	0.03

EQ-5D = European Quality of Life-5 Dimensions; QWB = Quality of Well-Being Index; HUI3 = Health Utilities Index, version 3; VAS = global quality of life Visual Analog Scale; QOL-AD = Quality of Life-Alzheimer's Disease; SF-36 MCS and PCS = Short Form-36 Mental Component and Physical Component Scales, respectively; β = β -coefficient; P = P-value; R^2 = LMG R^2 , the average of R increments from adding the variable to models without the variable, across all of the possible models; Charlson score = measure of comorbidity; ADAS = Alzheimer's Disease Assessment Scale-Cognitive sub-scale; DAD = Disability Assessment for Dementia; NPI = Neuropsychiatric Inventory; GDS = Geriatric Depression Scale; Other Patient Variables = education and first language; Zarit = Zarit Burden Interview (a measure of caregiver burden); CES-D = Center for Epidemiologic Studies-Depression scale; Other Caregiver Variables = age, sex, education, employment status and comorbidity.

All tests were t-tests with estimated degrees of freedom (df) ranging between 282 and 377, except for the Charlson score (numerator df=2, denominator df > 300), 'other' patient variables (numerator df=3, denominator df > 300), 'other' caregiver variables (numerator df=7, denominator df > 300), and study center (numerator df=9, denominator df > 300), which used F-tests.