HHS Public Access

Author manuscript

Am J Geriatr Psychiatry. Author manuscript; available in PMC 2018 March 01.

Published in final edited form as:

Am J Geriatr Psychiatry. 2017 March ; 25(3): 297–307. doi:10.1016/j.jagp.2016.10.007.

Participant-informant relationships affect quality of life ratings in incipient and clinical Alzheimer's disease

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Abstract

Objective—Clinical trials in incipient and clinical Alzheimer's disease (AD) often include informant-reported outcomes. While informant reports in AD dementia may be modulated by the nature of participant-informant relationships, whether informant type affects reporting at earlier disease stages is less certain. We sought to determine the effects of participant-informant relationships on informant assessments of quality of life (QOL), functional abilities, and behavioral symptoms in individuals with normal cognition (NC), mild cognitive impairment (MCI), and mild-to-moderate AD dementia.

Design—Cross-sectional.

Setting—Easton Center for Alzheimer's Disease Research at the University of California, Los Angeles.

Participants—A total of 399 individuals who met criteria for NC (n=100), MCI [amnestic (n=125) and nonamnestic (n=61)], and AD (n=113). Participants were subdivided into groups based on informant/participant relationships (spouse versus other).

Measurements—We examined informant effects on the Quality of Life-Alzheimer's Disease (QOL-AD) scale, Functional Activities Questionnaire (FAQ), and Neuropsychiatric Inventory (NPI).

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Disclosures: No disclosures to report.

Previous Presentations: American Academy of Neurology Annual Meeting, Vancouver, BC, Canada, April 15-21, 2016; American Geriatrics Society Annual Meeting, Long Beach, CA, May 19-21, 2016.

Results—After adjustments for demographic and cognitive factors, spouse informants reported higher participant QOL in the amnestic MCI and AD groups than did other informants. No informant effects were seen on QOL-AD ratings in the nonamnestic MCI or NC groups or on the FAQ or NPI in the MCI and AD groups.

Conclusions—Participant-informant relationships may modulate informant responses on subjective measures such as the QOL-AD in both incipient and clinical AD. Clinical trials that use informant measures may need to address these effects.

Keywords

informant; study partner; quality of life; mild cognitive impairment; Alzheimer's disease

Introduction

Alzheimer's disease (AD) is a neurodegenerative condition characterized by progressive cognitive deficits, behavioral abnormalities and functional disabilities. Since cognitive impairment may distort insight and limit the reliability of self-report by persons with mild-to-moderate AD dementia or earlier stages of the disease such as mild cognitive impairment (MCI), most diagnostic guidelines recommend that informant measures be included in evaluations (1, 2). Therefore, informant-based tools have been developed to measure behavioral symptoms (3), functional abilities (4), and quality of life (QOL) (5). These scales are frequently included in the assessment batteries used in clinical trials of potential AD therapeutics.

While informant reports represent an important source of information regarding disease progression (6), they also have limitations due to their subjective nature. Informant factors, such as age, education level, living situation, caregiver burden, and mental health may affect informant reports (7-10). Additionally, the nature of the relationship between the participant and informant may modulate informant assessments. Spouse informants view QOL of participants with AD dementia more favorably than do adult child informants (9-11). Likewise, differences in spouse versus non-spouse informant reports of cognition, behavior, function, and disease progression have also been reported (8, 12-14). However, other studies have failed to find evidence for effects of the relationship between the informant and participant on the discrepancy between patient and caregiver reported QOL (15) or rates of disease progression (16).

Current clinical trials of potential AD therapeutics are increasingly focused on individuals at earlier stages of disease progression such as MCI (17). Interventions initiated in the MCI stage of AD progression may be more effective than those initiated after the onset of dementia. However, the impact of the participant-informant relationship on informant measures in MCI is less well understood.

In this study, we examined the effects of spouse versus other informant types on informant reports for research participants with normal cognition, MCI, and mild-to-moderate AD dementia on assessments of behavioral symptoms, instrumental activities of daily living, and QOL. Based on prior work, primarily in AD dementia, we hypothesized that spouse

informants would report less severe behavioral symptoms and functional impairments (14) and better QOL (9-11). We also sought to determine whether different patterns of informant effects would emerge amongst different cognitive subtypes of MCI.

Methods

Research Participants

Participants were part of an ongoing study at the Mary S. Easton Center for Alzheimer's Disease Research at the University of California, Los Angeles (UCLA). We analyzed data from participants' first study visit. Volunteers and patients were recruited from the community and through the Memory Disorders Clinics at UCLA Medical Center, Olive View-UCLA Medical Center, and the Marina Campus of the Centinela-Freeman Medical Center. Inclusion criteria included: 1) participant age ≥ 50 years old, 2) diagnosis of normal cognition (NC), MCI, or mild-to-moderate AD dementia [AD group; Mini-Mental Status Exam (MMSE) scores ≥ 10], and 3) consistent participation of a single reliable informant. Diagnoses were determined via multidisciplinary consensus conference, and were based on physician interviews, neuropsychological testing, and neurological examinations. Participants in the AD group met criteria for AD dementia as defined by *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV) (18) and National Institute of Neurological and Communicative Disorders and Stroke/Alzheimer's Disease and Related Disorders Association (NINCDS/ADRDA) criteria (19). Participants in the MCI group met modified Petersen criteria: 1) subjective cognitive complaints, 2) essentially intact activities of daily living, 3) objective cognitive impairment, and 4) absence of dementia (17). The neuropsychological testing battery included assessments of memory, attention, language, visuospatial, and executive function as previously described (20). Participants were considered cognitively impaired if their score on at least one test in any domain was ≥ 1.5 standard deviations below published normative means. MCI participants were categorized as amnestic (AMN) or non-amnestic (NON) based on the presence or absence of memory impairment. Global cognitive functioning was assessed using the MMSE (21).

Informant Assessments

The spouse informant group included informants identified as a spouse or domestic partner. All other informants (adult children, grandchildren, nieces/nephews, cousins, siblings, friends, paid caregivers) were included in the other informant group.

Informants were queried with the Quality of Life-Alzheimer's Disease Scale (QOL-AD) (22) to separately evaluate the QOL of both the participant (p-QOL) and themselves (i-QOL) in 13 domains: physical health, energy, mood, living situation, memory, family, marriage (or a close relationship), friends, self as a whole, ability to do chores, ability to have fun, financial capabilities, and life as a whole (range 1-4 for each domain). Participants were also asked to evaluate their own QOL (s-QOL) using these same metrics. Average QOL scores were calculated using valid responses, and participants missing scores for more than 2 domains were excluded from subsequent analyses. Higher average QOL scores indicate better QOL.

Behavioral symptoms were assessed with the Neuropsychiatric Inventory (NPI) (23), for which informants report the presence, frequency (range 1-4), and severity (range 1-3) of 12 categories of behavioral symptoms: delusions, hallucinations, agitation/aggression, depression/dysphoria, anxiety, elation/euphoria, apathy/indifference, disinhibition, irritability/lability, aberrant motor behavior, sleep and nighttime behavior disorders, appetite/eating changes. If symptoms in a particular category were reported, frequency and severity scores were multiplied to generate a composite score for that category. Composite scores from each symptom category were summed to generate a total NPI score (range 0-144). Higher scores total NPI scores indicate greater behavioral symptomatology.

Functional abilities were assessed with the Functional Activities Questionnaire (FAQ) (24), in which informants report participants' abilities to perform 10 categories of instrumental activities of daily living (writing checks, paying bills, keeping financial records; assembling tax or business records; shopping alone; playing a game of skill; making coffee or tea; preparing a balanced meal; keeping track of current events; attending to and understanding a television program, book, or magazine; remembering appointments, family occasions, medications; and traveling out of the neighborhood; score range 0-3 for each category). Higher FAQ scores in each category indicate greater dependence. Activities that had never been performed prior to the onset of cognitive decline, or for which the informant had insufficient information were not scored. Participants were excluded from subsequent analyses if values were missing for more than 2 categories. Mean FAQ item scores were calculated from all category scores with valid responses as previously described (25).

Data Analysis

Statistical analyses were performed using SPSS Statistics 23.0 for Mac (IBM, Armonk NY). Demographic variables within each diagnostic group were compared between informant types using unpaired t-tests for continuous variables and chi-square tests for categorical variables. MMSE and informant indices were initially compared within each diagnostic group between informant types using unpaired t-tests. Multiple linear regression was subsequently used to determine the contributions of demographic, cognitive, and informant variables to the informant assessments on the NPI, FAQ, and QOL-AD. Reference conditions for categorical variables used in the regression analyses were as follows: sex-male; ethnicity- non-Hispanic White; informant- spouse. Separate paired t-tests were used to compare s-QOL and p-QOL scores within each diagnostic group.

Ethics

Both participants and their informants provided written consent, as approved by the Institutional Review Boards at UCLA and each individual site.

Results

Demographics

Demographic data for NC, MCI, and AD participants with spouse versus other informants are shown in Table 1. Participants with spouse informants were generally younger, more likely to be male and non-Hispanic White, and had more years of formal education than

those with other informants, though not all comparisons were significant for each diagnostic group. These demographic disparities were most pronounced in the AD group. By definition, all participants with spouse informants were either married or living as married. Lower proportions of participants with other informants were married (NC: 19.6%, MCI: 20.8%, AD: 22.2%). Demographic data for spouse versus other informants are shown in Table 2. Compared to other informants, spouse informants were generally older, more likely to be male and non-Hispanic White, and had more years of formal education, though again, not all comparisons were significant for each diagnostic group. Across diagnostic groups, virtually all of the spouse informants lived with their respective participants. Significantly lower rates of co-residence were seen with other informants. Collectively, adult children were the most common other informants, and their proportion of the other informant group increased across diagnostic groups from NC (32.6%) to MCI (42.9%) to AD (74.6%).

Informant effects on the NPI, FAQ, and QOL-AD

Unadjusted spouse- and other informant-reported NPI, FAQ, and p-QOL scores for each diagnostic group are shown in Figure 1. Unpaired t-tests revealed higher total NPI scores for NC participants with spouse versus other informants [Figure 1A; $t(98)=2.32$, $p=0.022$]. There were no differences on mean FAQ item scores between informant types for any of the three groups (Figure 1B). Unpaired t-tests indicated that p-QOL ratings (Figure 1C) for participants with spouse informants were significantly higher in AD [$t(111)=3.29$, $p=0.001$], but this difference fell just short of significance in MCI [$t(184)=1.95$, $p=0.053$].

Because participants in the spouse and non-spouse informant groups varied across a number of factors, separate multiple linear regression analyses were used to identify which cognitive, demographic, and informant variables influenced NPI, FAQ, and QOL-AD ratings. In these adjusted analyses, NC participants with spouse informants continued to have higher NPI scores than those with other informants (Supplementary Table 1). There were no effects of informant type on global NPI in the MCI or AD groups or the FAQ for any of the diagnostic groups (data not shown). For the QOL-AD analyses, i-QOL was included as a covariate to address the possibility that informants' views of their own QOL could modulate their assessments of their participants' QOL (26). As expected, i-QOL and p-QOL scores were positively correlated in the NC, MCI, and AD groups [NC: $r(98)=0.647$, $p<0.001$; MCI: $r(184)=0.542$, $p<0.001$; AD: $r(111)=0.508$, $p<0.001$]. After adjusting for MMSE, participant demographics, and informant factors, spouse informants reported higher p-QOL than other informants in the MCI and AD groups, but not in the NC group (Table 3). Within the other informant groups, comparisons between informants who co-resided with their participants versus those who did not co-reside failed to demonstrate any effects of co-residence on p-QOL in any of the three diagnostic groups either before or after adjustments for demographic and cognitive factors (data not shown).

We also sought to determine whether s-QOL ratings differed between participants with spouse versus other informants. Overall, paired t-tests indicated that s-QOL and p-QOL scores were similar in the NC [$t(99)=1.02$, $p=0.31$] and MCI [$t(185)=-1.81$), $p=0.071$] groups and that s-QOL scores were significantly higher than p-QOL scores in the AD group [$t(111)=-6.73$, $p<0.001$]. Unpaired t-tests revealed significantly higher s-QOL ratings from

participants with spouse informants in the MCI [$t(184)=2.655$, $p=0.009$] and AD groups [$t(110)=3.306$, $p=0.001$], but not in the NC group [$t(98)=0.412$, $p=0.682$]. These informant-related differences in s-QOL within the MCI and AD groups persisted after adjusting for MMSE and demographic variables via multiple regression analyses (Table 4). There were no informant-related differences in i-QOL in any of the three diagnostic groups, either before (Table 2) or after (data not shown) adjustments for demographic differences.

Informant effects on MCI subtypes

MCI has been subdivided into cognitive subtypes (17). Although prior work from our group did not reveal significant differences in p-QOL between amnestic and non-amnestic MCI (27), potential informant effects were not examined in that study. We addressed this question by performing a two-way analysis of variance, which showed no overall effect of MCI subtype [$F(1,182)=0.62$, $p=0.43$] or informant type [$F(1,182)=0.49$, $p=0.48$] on p-QOL scores. However, there was a significant interaction between these variables [$F(1,182)=13.00$, $p<0.001$], prompting additional analyses of informant effects on p-QOL within the AMN and NON subgroups. Demographic data for the MCI subgroups are shown in Table 5. In the AMN subgroup, participants with spouse informants were significantly more likely to be non-Hispanic White [$\chi^2(125)=11.88$, $p=0.001$]. In the NON subgroup, participants with spouse informants were more likely to be male [$\chi^2(61)=14.59$, $p<0.001$].

In the AMN group, unpaired t-tests indicated that participants with spouse informants had higher p-QOL [$t(123)=3.88$, $p<0.001$] and s-QOL [$t(123)=3.93$, $p<0.001$] scores than those with other informants. These differences persisted after adjusting for MMSE, demographic, and informant (for p-QOL) variables via multiple linear regression analyses (Table 6). In contrast, in the NON group, similar p-QOL and s-QOL scores were seen in spouse versus other informants with both unpaired t-tests [p-QOL: $t(59)=1.65$, $p=0.11$; s-QOL: $t(59)=0.66$, $p=0.51$] and multiple linear regression analyses (data not shown).

QOL-AD item analyses for AMN and AD groups

We then investigated which specific p-QOL items showed the most pronounced informant-related differences in the AMN (Figure 2A) and AD (Figure 2B) groups. Unpaired t-tests in the AMN group revealed significantly higher scores amongst participants with spouse informants on the physical health [$t(123)=-4.37$, $p<0.001$], energy [$t(123)=-3.57$, $p<0.001$], and life as a whole [$t(123)=-3.56$, $p=0.001$] items after Bonferroni correction for multiple comparisons (critical $p<0.004$). When separate multiple linear regression analyses adjusting for MMSE, demographic factors, and i-QOL were performed for each item, participants with spouse informants had higher scores on the physical health, energy, friends, and life as a whole items after Bonferroni correction (Supplemental Table 2).

Unpaired t-tests in the AD group revealed significantly higher scores amongst participants with spouse informants on the mood [$t(111)=-3.10$, $p=0.002$], living situation [$t(111)=-3.07$, $p=0.003$], family [$t(111)=-3.21$, $p=0.002$], and marriage [$t(100)=-5.15$, $p<0.001$] items after Bonferroni correction. Subsequent multiple linear regression analyses indicated that participants with spouse informants had higher scores on the family and marriage items after Bonferroni correction (Supplemental Table 2).

Discussion

The purpose of this study was to examine whether spouse and other informants differentially evaluate people with NC, MCI, and mild-to-moderate AD dementia using three informant measures (QOL-AD, NPI, and FAQ). Compared to other informants, spouse informants reported better p-QOL for MCI and AD participants, but not for NC participants (after adjustments for demographic, cognitive, and informant factors). In contrast, no consistent informant effects were seen on the NPI or FAQ in the MCI or AD groups. These findings suggest that participant-informant relationships can modulate some informant measures collected in studies of cognitively impaired participants.

Informant effects on p-QOL ratings in MCI and AD

The tendency of spouse informants to report higher p-QOL relative to adult child caregivers has been previously reported for people with dementia (9, 10). Our results extend these findings to informants for participants meeting diagnostic criteria for MCI. This trend may be due to systematic differences in the way informants assess p-QOL. Increased burden amongst adult child caregivers has been associated with lower p-QOL ratings (9), suggesting that caregiver burden and depression influence p-QOL ratings (28, 29). However, it remains uncertain whether adult children actually experience greater caregiver burden than spouses (9, 13, 30). QOL assessments may also be impacted by the informant's interpretation of the QOL-AD questions (i.e. ability to assume the participant's perspective as opposed to their own) (5, 31, 32). Spouses may be more likely to assess QOL from the participant's perspective, because of their shared life experiences and the more interdependent and emotionally connected nature of their relationship (13).

It is also possible that participants with spouse informants actually have better QOL. Both p-QOL and s-QOL ratings were higher in the AMN and AD participants with spouse informants than those with other informants. If p-QOL differences were primarily driven by informants' perception of QOL, one might expect similar s-QOL ratings and divergent p-QOL ratings. Instead, the parallel nature of p-QOL and s-QOL ratings in the AMN and AD groups suggests that participants with spouse informants may indeed have better underlying QOL. In general, social relationships enhance the QOL of people with dementia (33-35). However, adult children may have a more distant relationship with their cognitive impaired parent, and their caregiving roles may conflict with their other responsibilities (11). In contrast, spouses, particularly those who participate as informants in research studies, may be more committed to and capable of nurturing a cognitively impaired partner (11, 13).

Informant effects in MCI subtypes

Within the MCI group, informant effects for p-QOL ratings were seen with participants in the AMN subgroup, but not in the NON subgroup. Spouses may be more accurate than adult children in assessing the memory function of patients with MCI and AD (8, 12). While such findings might suggest that the discrepancy between informant effects in the AMN and NON subgroups could be driven by the memory p-QOL item (i.e. other informants might overestimate the degree of memory deficits in the AMN group), this item was rated similarly by spouse and other informants in the AMN subgroup. Nevertheless, memory impairment

may be more salient than other cognitive deficits, particularly for non-spouse informants. As such, the presence of memory symptoms could result in broader reductions in perceived participant QOL amongst non-spouse informants, particularly since no informant effects were seen in the NC or NON groups.

Informant effects on specific QOL-AD domains

Item level analyses of informant effects in the AMN and AD groups revealed partially overlapping patterns of QOL-AD items affected by participant-informant relationships. In the AMN group, participants with spouse informants had higher p-QOL scores on items contributing to the previously identified physical well-being/health and social/environment factors on the QOL-AD (36, 37). In the AD group, spouse informants only reported higher p-QOL scores on items contributing to the social/environment factor, suggesting that the breadth of these informant effects narrows with disease progression. Our analyses of informant effects in AD dementia only included participants with mild-to-moderate disease severity. Accordingly, it remains possible that different patterns of informant effects on the QOL-AD may emerge in severe AD dementia.

Co-residence and p-QOL ratings

The difference in p-QOL ratings between spouse and other informants did not appear to be attributable to participants' living arrangements, as similar p-QOL scores were reported by other informants regardless of whether or not they lived with the participant. Co-residence alone does not necessarily increase informants' awareness of participants' well being. Indeed, dementia patients who live with their spouses are diagnosed at earlier stages of disease progression than those who live with someone other than their spouse (38), reinforcing the suggestion that spouses may be more closely attuned to cognitive and functional decline (8, 12). Both the informant's relationship to the cognitively impaired person and whether or not they live together may affect their awareness and/or actions regarding such impairments. Unfortunately, we were unable to more rigorously investigate potential interactions between living situation and type of informant with this data set, since almost all of the participants in the spouse informant group lived with their informant.

Absence of informant effects on the NPI and FAQ

In our cohort, no informant effects were seen on adjusted analyses of the NPI or FAQ in the MCI and AD groups. This result is consistent with a recent study of these instruments in an MCI population (39), though a prior report did show informant effects on similar behavioral and functional assessments in a mixed population of participants with MCI and dementia (14). Our findings suggest that behavioral and functional assessments may be relatively more objective than QOL ratings, and therefore less likely to be modulated by participant-informant relationships.

Limitations and future directions

There are a few factors that may limit the interpretation of our results. Caregiver burden and depression indices for informants, which may affect QOL-AD ratings (7, 9, 10, 28, 29), were not collected. However, we indirectly adjusted for these variables by including informants'

self-rated QOL in our regression analyses. While informant demographics may also modulate QOL assessments (10, 11), they are closely correlated with the participant-informant relationship, and thus were not further included in the regression analyses. The effects of living situation and participant-informant relationship are also closely intertwined, and we were unable to fully disentangle these variables, since almost all of spouse informants lived with their respective participants. Future studies with similar numbers of spouse and non-spouse informants in similar living situations may be needed to address this question. Finally, our analyses were relatively underpowered for determining whether QOL differences between participants with spouse versus other informants were due to actual underlying differences in participants' QOL or systematic differences in informants' impression of participants' QOL. Additional investigations with participants who have both spouse and non-spouse informants would address this issue more directly.

Conclusions

While the significance of the participant-informant relationship in QOL-AD assessments has previously been reported in AD populations, the analyses presented here extend this finding to amnestic MCI. Clinical trials and other research studies in MCI and AD that use the QOL-AD as an outcome measure should address the potential confounds introduced by differences in participant-informant relationships, by enrolling equivalent numbers of participants with spouse and non-spouse informants, stratifying randomization by informant type, and/or including other analytic adjustments for this important factor.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This research was supported by the National Institute on Aging (T35 AG026736 [UCLA Medical Student Training in Aging Research Program] and P50 AG16570 [UCLA Alzheimer's Disease Research Center]), the California Alzheimer's Disease Centers, and the Sidell-Kagan Foundation.

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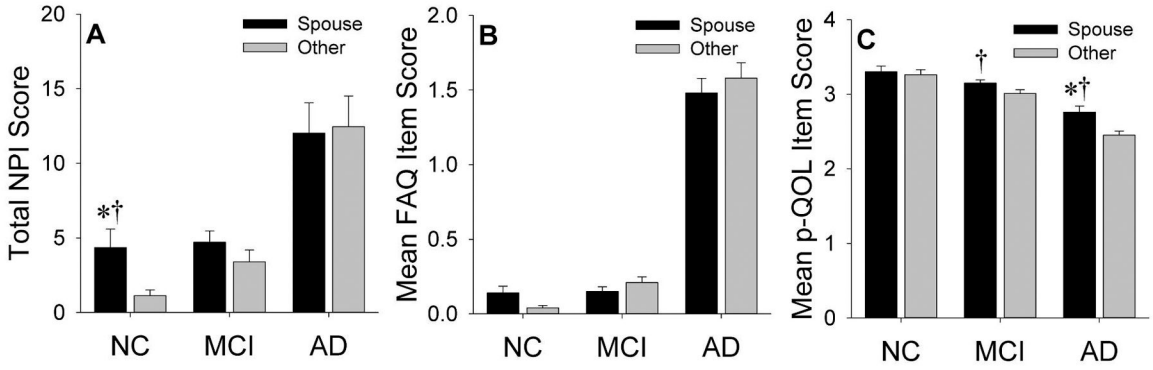

Figure 1.

Unadjusted scores for spouse versus other informants on A) total NPI, B) mean FAQ item, and C) mean p-QOL item indices in the NC, MCI, and AD groups. Error bars represent standard error of the mean. *p<0.05 versus other informant group in unadjusted analyses; †p<0.05 versus other informant group after adjustment for demographic, cognitive, and informant factors. See text for details regarding specific statistical tests and degrees of freedom.

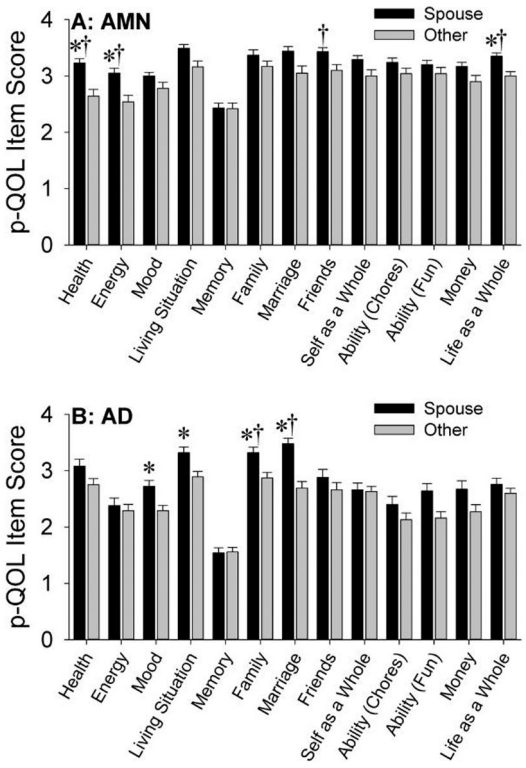

Figure 2.

Unadjusted p-QOL item scores in A) AMN and B) AD participants with spouse versus other informants. *p<0.004 versus other informant group in unadjusted analyses; †p<0.004 versus other informant group after adjustment for demographic, cognitive, and informant factors. See text for details regarding specific statistical tests and degrees of freedom.

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Table 1

Participant demographics

	NC			MCI			AD		
	Spouse	**Other**		**Spouse**	**Other**		**Spouse**	**Other**	
N	54	46		109	77		50	63	
	Frequency		$\chi^2(1)$	Frequency		$\chi^2(1)$	Frequency		$\chi^2(1)$
% Male	72.2%	28.3%	19.23*	52.3%	24.7%	14.24*	64.0%	15.9%	27.65*
% Non-Hispanic White	85.2%	58.7%	8.84*	79.8%	58.4%	10.01*	68.0%	36.5%	11.06*
	Mean (SD)		*t*(98)	Mean (SD)		*t*(184)	Mean (SD)		*t*(111)
Age	70.0 (9.4)	70.8 (9.2)	-0.43	68.9 (7.9)	71.5 (10.1)	-1.87	70.7 (10.1)	75.8 (10.8)	-2.58*
Education	17.2 (2.5)	16.5 (3.1)	1.12	16.1 (2.8)	15.2 (3.1)	2.00*	14.9 (3.7)	9.4 (6.0)	5.89*
MMSE	28.5 (1.5)	29.1 (0.9)	-2.41*	27.2 (2.9)	27.2 (2.4)	0.07	20.7 (4.6)	18.6 (4.8)	2.37*
s-QOL	3.26 (0.51)	3.22 (0.44)	0.41	3.21 (0.38)	3.05 (0.44)	2.66*	3.12 (0.49)	2.80 (0.54)	3.31*[a]
p-QOL	3.30 (0.57)	3.26 (0.46)	0.35	3.15 (0.45)	3.01 (10.46)	1.95	2.76 (0.58)	2.44 (0.44)	3.29*

s-QOL: participant's rating of own QOL. p-QOL: informant's rating of participant's QOL.

* $p<0.05$;

[a] df=110 due to missing data from one participant.

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Table 2

Informant demographics

	NC			MCI			AD		
	Spouse	**Other**		**Spouse**	**Other**		**Spouse**	**Other**	
N	54	46		108	77		50	63	
	Frequency		$\chi^2(1)$	Frequency		$\chi^2(1)$	Frequency		$\chi^2(1)$
% Male	27.8%	23.9%	0.19	47.2%	31.2%	4.81*	40.0%	25.4%	2.74
% Non-Hispanic White	79.2%	56.5%	5.91*	75.0%	53.9%	8.85*	72.0%	34.9%	15.34*
% Co-residence	100.0%	13.0%	78.26*	100.0%	18.2%	133.99*	98.0%	38.1%	43.75*
	Mean (SD)		$t(98)$	Mean (SD)		$t(184)$	Mean (SD)		$t(115)$
Age	67.1 (10.2)	57.8 (13.5)	3.83*	67.1 (8.8)	56.9 (15.0)	5.35*	67.5 (12.2)	50.3 (11.6)	7.59*
Education	15.8 (2.6)	15.8 (2.8)	0.09	16.5 (2.6)	15.6 (2.4)	2.29*	14.9 (3.4)	14.2 (4.4)	0.90
i-QOL	3.35 (0.41)	3.27 (0.41)	1.00	3.25 (0.48)	3.25 (0.37)	0.10	3.25 (0.45)	3.13 (0.45)	1.38

i-QOL: informant's rating of own QOL.

*$p<0.05$.

Table 3

Multiple regression analyses for p-QOL

	NC			MCI			AD		
	β	***t*(99)**	***p***	**β**	***t*(185)**	***p***	**β**	***t*(112)**	***p***
Informant	0.090	0.973	0.333	-0.200	-3.046	*0.003*	-0.219	-2.084	*0.040*
i-QOL	0.593	7.393	*<0.001*	0.522	8.555	*<0.001*	0.446	5.295	*<0.001*
Age	-0.089	-1.017	0.312	0.069	1.058	0.291	0.064	0.760	0.449
Sex	-0.063	-0.718	0.475	0.166	2.503	*0.013*	0.053	0.584	0.561
Ethnicity	-0.154	-1.801	0.075	0.066	1.034	0.303	-0.104	-1.087	0.279
Education	0.125	1.522	0.131	0.062	0.933	0.352	0.084	0.773	0.441
MMSE	0.109	1.294	0.199	0.075	1.155	0.250	-0.042	-0.512	0.610
Overall Model	Adj r^2 = 0.434			Adj r^2 = 0.325			Adj r^2 = 0.300		

p-QOL: informant's rating of participant's QOL. i-QOL: informant's rating of own QOL. β: Standardized β estimate. Reference conditions: Informant- spouse; Sex- male; Ethnicity- non-Hispanic White.

Table 4

Multiple regression analyses for s-QOL

	NC			MCI			AD		
	β	***t*(99)**	***p***	**β**	***t*(185)**	***p***	**β**	***t*(111)**	***p***
Informant	-0.001	-0.012	0.990	-0.214	-2.710	*0.007*	-0.270	-2.411	*0.018*
Age	-0.121	-1.160	0.249	0.019	0.244	0.808	0.155	1.723	0.088
Sex	0.160	1.516	0.133	0.101	1.279	0.203	0.165	1.695	0.093
Ethnicity	-0.315	-3.095	*0.003*	-0.052	-0.677	0.499	-0.092	-0.913	0.364
Education	0.306	3.138	*0.002*	-0.026	-0.322	0.748	0.306	2.804	*0.006*
MMSE	0.097	0.987	0.326	0.042	0.537	0.592	-0.108	-1.227	0.223
Overall Model	Adj r^2 = 0.189			Adj r^2 = 0.019			Adj r^2 = 0.210		

s-QOL: participant's rating of own QOL. β: Standardized β estimate. Reference conditions: Informant-spouse; Sex- male; Ethnicity- non-Hispanic White.

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Table 5

Participant demographics for MCI subtypes

	AMN			NON		
	Spouse	**Other**		**Spouse**	**Other**	
N	75	50		34	27	
	Frequency		$\chi^2(1)$	Frequency		$\chi^2(1)$
% Male	49.3%	32.0%	3.69	58.8%	11.1%	14.59*
% Non-Hispanic White	85.3%	58.0%	11.77*	67.6%	59.3%	0.46
	Mean (SD)		*t*(123)	Mean (SD)		*t*(59)
Age	69.2 (8.0)	71.4 (9.8)	-1.39	68.3 (7.8)	71.6 (11.0)	-1.39
Education	16.1 (2.8)	15.4 (3.3)	1.37	16.1 (2.6)	15.0 (2.6)	1.56
MMSE	26.8 (3.2)	26.7 (2.3)	0.17	28.0 (2.0)	27.9 (2.3)	0.08
i-QOL	3.32 (0.48)	3.2 (0.36)	1.21	3.11 (0.44)	3.28 (0.39)	-1.59
p-QOL	3.21 (0.42)	2.9 (0.43)	3.88*	3.01 (0.50)	3.21 (0.44)	-1.65
s-QOL	3.24 (0.35)	2.96 (0.45)	3.93*	3.15 (0.44)	3.22 (0.38)	-0.66

s-QOL: participant's rating of own QOL. p-QOL: informant's rating of participant's QOL. i-QOL: informant's rating of own QOL.

* $p \leq 0.001$.

Table 6

Multiple regression analyses for p-QOL and s-QOL in amnestic MCI

	p-QOL			s-QOL		
	Standardized β Estimate	***t*(124)**	***p***	**Standardized β Estimate**	***t*(124)**	***p***
Informant	-0.338	-4.569	*<0.001*	-0.295	-3.188	*0.002*
i-QOL	0.571	8.213	*<0.001*	---	---	---
Age	0.112	1.522	0.131	0.010	0.103	0.918
Sex	0.050	0.683	0.496	-0.002	-0.025	0.980
Ethnicity	0.145	1.969	0.051	-0.155	-1.671	0.097
Education	0.004	0.054	0.957	-0.063	-0.666	0.507
MMSE	0.052	0.715	0.476	-0.006	0.069	0.945
Overall Model	Adj r^2 = 0.425			Adj r^2 = 0.009		

i-QOL: informant's rating of own QOL. Reference conditions: Informant- spouse; Sex- male; Ethnicity-non-Hispanic White.