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QUALITY OF LIFE AND CAREGIVER BURDEN IN FAMILIAL FRONTOTEMPORAL LOBAR DEGENERATION: ANALYSES OF SYMPOMATIC AND ASYMPTOMATIC INDIVIDUALS WITHIN THE LEFFTDS COHORT

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Abstract

Objective: The Longitudinal Evaluation of Familial Frontotemporal Dementia Subjects evaluates familial frontotemporal lobar degeneration (FTLD) kindreds with MAPT, GRN, or C9orf72 mutations. Objectives were to examine whether health-related quality of life (HRQoL) correlates with clinical symptoms and caregiver burden, and whether self-rated and informant-rated HRQoL would correlate with each other.

Methods: ~~Individuals were classified using the CDR® plus NACC FTLD.~~ HRQoL was measured with DEMQOL and DEMQOL-proxy; caregiver burden with the Zarit Burden Interview (ZBI). For analysis, Pearson correlations and weighted kappa statistics were calculated.

Results: The cohort of 312 individuals included symptomatic and asymptomatic individuals. CDR® plus NACC FTLD was negatively correlated with DEMQOL ($r=-0.20$, $p=.001$), as were ZBI and DEMQOL ($r=-0.22$, $p=0.0009$). There was fair agreement between subject and informant DEMQOL ($\kappa=0.36$, $p<.0001$).

Conclusion: Lower HRQoL was associated with higher cognitive/behavior impairment and higher caregiver burden. These findings demonstrate the negative impact of FTLD on individuals and caregivers.

Keywords

frontotemporal dementia; quality of life; *MAPT*; *GRN*; *C9orf72*; tau; TDP-43

Background

There has been growing interest in understanding quality of life effects from chronic illnesses such as Alzheimer's disease and other neurodegenerative disorders. The World Health Organization defines quality of life as "an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" [1]. Quality of life (QOL) is a multi-dimensional construct which includes several domains related to emotional, physical and social well-being. The term health-related quality of life (HRQoL) has been used more

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recently to focus specifically on the effects health, disease states, and medical treatments on quality of life [2]. The cognitive, physical and emotional changes associated with dementia have been associated with lower QOL and increased caregiver burden [3, 4].

There are a number of studies examining the natural history of HRQoL in the context of neurocognitive disorders, although there are conflicting results on the impact of depression, cognitive status and social/demographic variables on quality of life [5]. Even less is known regarding QOL in sporadic or familial frontotemporal lobar degeneration spectrum disorders (hereafter abbreviated FTLD). Although FTLD is less common than ~~Alzheimer's disease,~~ there is tremendous morbidity and emotional distress associated with this disorder. Behavior variant frontotemporal dementia (bvFTD) affects an estimated 50,000–60,000 Americans and represents an estimated 10%−20% of all dementia cases [6]. FTLD tends to present at an earlier age than Alzheimer's disease ~~(AD)~~, and is recognized as one of the most common causes of young onset dementia [7]. FTLD is more often associated with alterations in mood, personality, and behavior. Because FTLD individuals are more likely to develop features earlier in life compared to AD, individuals and caregivers may experience particular challenges in adjusting to changes in life roles, including work and family responsibilities. Younger age has been associated with decreased QOL measures in dementia [8]. Some studies have suggested that caregivers in FTLD have lower HRQoL and higher levels of distress than with AD [9, 10]. In a more recent study comparing caregivers for those with FTLD and AD, the caregivers of those with FTD had a higher HRQoL than AD caregivers, and maintained a higher HRQoL over two years [11]. The trajectory of HRQoL over the course of FTLD is not well understood and requires further research to understand determinants of HRQoL that have the potential to guide appropriate psychosocial interventions for individuals and caregivers [12]. Depression, care burden and unmet care needs in FTLD are associated with lower ratings of QOL in some studies [11, 13, 14]. However, another study showed no association with unmet care and overall ratings of HRQoL in Young Onset Dementia [13]. There has been no clear association found between declining cognitive function and QOL in dementia [5, 15]. One study found that amongst the oldest old, there were high QOL measures in individuals with and without cognitive impairment and that QOL was more strongly associated with depressive symptoms than severity of dementia [16].

HRQoL can be difficult to assess in individuals with cognitive impairment and particularly in those with more advanced disease. Informant or proxy reports of HRQoL are often used in evaluating individuals with dementia ~~in order~~ to gather a fuller picture of HRQoL. Proxy reports of HRQoL have been shown to be a reliable measure with moderate to high levels of agreement with individual based measures [17–19]. However, there have been concerns about bias in proxy measures of HRQoL in dementia and it is important that proxy measures not be used as a substitute for self-assessments of HRQoL [20–23].

In this study the first objective was to examine the correlation between subject HRQoL and clinical symptoms in familial FTLD and caregiver burden. The second objective was to determine whether self-rated HRQoL and informant-rated HRQoL would correlate with each other. We hypothesized that HRQoL for subjects would correlate with clinical

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symptoms in FTLD and caregiver burden, and also hypothesized that the subject and informant HRQoL ratings of the subject would correlate with each other.

Methods

This study was completed as part of a larger longitudinal study, the Longitudinal Evaluation of Familial Frontotemporal Dementia Subjects (LEFFTDS), which included 8 study sites [24]. This study has been approved by the Institutional Review Board (IRB) of each participating site. Written informed consent was obtained from individuals and/or legally authorized representatives. All individuals ~~undergo~~ a detailed interview, comprehensive neurologic examination and neuropsychological assessment. Data were collected between ~~April~~ 2015 and ~~September~~ 2018.

Inclusion/exclusion criteria

The detailed protocol, inclusion/exclusion criteria and methods for recruitment are described elsewhere [24]. Individuals were eligible for inclusion if they were members of families with a known mutation in one of the three major FTLD-related genes (microtubule associated protein tau (MAPT), progranulin (GRN), or chromosome 9 open reading frame 72 (C9orf72), age 18 or older, and willing to participate and complete required visits and testing (MRI and neuropsychological testing). Each subject is required to have a reliable informant with whom they have personal contact at least weekly. The informant can be a spouse, partner, sibling, parent, child, friend, or relative. Exclusion criteria included presence of a structural brain lesion (e.g., tumor, cortical infarct), presence of another neurologic disorder which could impact findings (e.g., multiple sclerosis), unwillingness to return for follow-up yearly, unwillingness to undergo neuropsychological testing and MR imaging, and no reliable informant.

Clinical dementia rating

Individuals were assessed for the presence or absence of symptoms and symptom severity using the 8-item Clinical Dementia Rating (CDR) plus National Alzheimer's Coordinating Center (NACC) Frontotemporal Lobar Degeneration (FTLD) CDR® plus NACC FTLD scale [25], which is a modification of the standard CDR scale [26]. The CDR combines structured information gathered from both the patient and a knowledgeable informant. It has been used widely in a variety of clinical and research settings including clinical trials in Alzheimer's disease treatments [27]. The Behavior/Comportment and Language domains were added to the original CDR ~~in order~~ to address the variable clinical presentations typical of familial FTLD [25]. Individuals were classified based on CDR® plus NACC FTLD as asymptomatic (CDR® plus NACC FTLD=0), questionable/mild cognitive or behavioral changes (CDR® plus NACC FTLD=0.5), mild dementia (CDR® plus NACC FTLD=1.0), and moderate to severe (CDR® plus NACC FTLD>1) dementia.

Outcome Measures

Quality of life—Subject HRQoL was measured in two ways, first by self-report using the DEMQOL, and second as rated by their informant using the DEMQOL-proxy [18]. The 28-item DEMQOL and 31-item DEMQOL-proxy are dementia specific measures of QOL,

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designed with rigorous psychometric properties and validated to assess QOL in persons with dementia. The DEMQOL is appropriate for self-report in individuals with mild to moderate dementia [18], while the DEMQOL-proxy is more useful for severe dementia [28]. The DEMQOL measures five domains of QOL (daily activities and self-care, health and well-being, cognitive functioning, social relationships and self-concept) and rates overall QOL as very good, good, fair and poor. Cronbach's alpha for the self-report was (0.94) for the 28-item overall score and also acceptable for the four preliminary subscales (daily activities 0.84, memory 0.89, negative emotion 0.84 and positive emotion 0.85) [29]. Cronbach's alpha for the 31-item proxy scale was (0.90) for the overall score and similar for both subscales (functioning 0.90 and emotion 0.85). The DEMQOL and DEMQOL-proxy have been validated in different clinical settings as well as cultures [18, 30–33].

Caregiver burden—Informants completed the Zarit Burden Interview (ZBI) for caregiver burden [34]. This measure includes 22 items related to feelings about caregiving, negative effects of caregiving and perceived stress. For each item, a response of 0 (Never), 1 (Rarely), 2 (Sometimes), 3 (Quite frequently), or 4 (Nearly always) is given. The ZBI categorizes scoring as 0–21 little or no burden, 21–40 mild to moderate burden, 41–60 moderate to severe burden, and 61–88 severe burden. The ZBI has been validated in individuals with dementia and their caregivers in a variety of clinical situations and cultures. [35, 36] The DEMQOL and ZBI data were analyzed from the baseline visit only.

Participant demographics—Of the 345 individuals initially enrolled, 17 were excluded based on diagnosis and 16 were excluded due to discrepant information between clinical diagnosis and CDR score, leaving a final sample of 312 individuals. This cohort of 312 individuals included symptomatic mutation carriers, asymptomatic mutation carriers, and non-carrier family controls. The demographic information is summarized in Table 1. Participants had a mean age of 48.5 years (range 18–80), with a mean of 15.5 years of education, and were predominantly white (297, 95%) and not Hispanic or Latino (305, 98.1%). There were slightly more females (169, 54.3 %) than males (142, 45.7%). The most common informant was a spouse (137, 52.3%).

Data Analysis

The first step in the data analysis consisted of summarizing key variables by CDR® plus NACC FTLD score. Then, to investigate the association of QOL, both subject- and informant-reported, with CDR® plus NACC FTLD and ZBI, Pearson correlation coefficients were used. Weighted kappa statistics using linear weighting with corresponding 95% confidence intervals were used to assess agreement between the subject and informant HRQoL ratings of the subject. The weighted kappa statistic was computed amongst everyone in the data as well as in CDR® plus NACC FTLD subgroups (0 vs. ≥ 0.5) to assess whether or not agreement is different between symptomatic and asymptomatic individuals and in subgroups based on whether or not the informant was a spouse to assess whether or not agreement varies by relationship. Data analysis was completed using SAS version 9.4 (SAS Institute, Cary, NC).

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Results

Participant clinical characteristics

The clinical characteristics of participants are summarized in Table 1. The majority of primary clinical phenotypes are clinically normal (75.6%), followed in order of decreasing frequency by bvFTD ± ALS (14.4%), MCI (8.0%), Primary Progressive Aphasia (1.3%), and Corticobasal Syndrome (0.6%). Participants with higher CDR® plus NACC FTLD scores were significantly older than those who were asymptomatic. ($p<0.0001$)

QOL and caregiver burden

Table 2 shows age, HRQoL ratings, and Zarit caregiver burden scores for all 312 participants broken down by CDR® plus NACC FTLD. Two hundred thirty six (75.6%) subjects were asymptomatic (CDR® plus NACC FTLD=0), 31 (9.9%) were questionably/minimally symptomatic (CDR® plus NACC FTLD=0.5), and 45 (14.4%) were definitely symptomatic (CDR® plus NACC FTLD≥1). Of those who were definitely symptomatic who were further categorized by symptom severity, 16 (5.1%) had mild (CDR® plus NACC FTLD=1), 21 (6.7%) moderate (CDR® plus NACC FTLD=2), and 8 (2.6%) severe (CDR® plus NACC FTLD=3) symptoms. There were 257 individuals who completed the self-report DEMQOL, 264 caregivers who completed the DEMQOL-proxy, and 262 caregivers who completed the ZBI. Majority of the scores on both the DEMQOL (89%) and DEMQOL-proxy (91%) ranged from good to very good ~~quality of life~~, and a smaller percentage showed fair to poor quality of life. The ZBI scores were low (mean score=10.5) when all informants were grouped together, indicating little or no caregiver burden. However, ZBI scores were higher among informants of individuals with mild and moderate symptoms (CDR® plus NACC FTLD=1 and 2), indicating mild to moderate caregiver burden (mean ZBI scores 32.6 and 35.3, respectively). Informants of individuals who were severely symptomatic (CDR® plus NACC FTLD=3) showed low caregiver burden (mean ZBI score11.8). The F-test for age indicates that at least one CDR® plus NACC FTLD group is different in terms of age than the other groups. Asymptomatic individuals in the group with CDR® plus NACC FTLD=0 are younger than the other groups, which is not surprising.

Correlations of HRQoL with CDR and ZBI

Utilizing a Pearson correlation (Table 3), CDR® plus NACC FTLD was negatively correlated with HRQoL, both self-reported ($r=-0.20$, $n=257$, $p=0.001$) and informant-rated ($r=-0.32$, $n=264$, $p<0.0001$). ZBI score was negatively correlated with both self-report ($r=-0.22$, $n=229$, $p=0.0009$) and informant DEMQOL ($r=-0.36$, $n=253$, $p<0.0001$).

Subject and Informant HRQoL *rating agreement*

Using weighted kappa statistics to measure agreement between the subject and informant ratings of subject HRQoL (Table 4), there was fair agreement ($\kappa=0.36$, $n=232$, $p<0.0001$ between subject and informant QOL ratings, regardless of CDR® plus NACC FTLD (0 $\kappa=0.30$, $n=180$, $p<0.0001$, ≥0.5 $\kappa=0.40$, $n=52$, $p<0.0001$), and regardless of whether informants are spouses ($\kappa=0.47$, $n=112$, $p<0.0001$) or not ($\kappa=0.26$, $n=97$, $p=0.0007$).

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Discussion

In this study cohort of FTLD kindreds that include symptomatic mutation carriers, asymptomatic mutation carriers, and non-carrier family controls, the main finding is that HRQoL was negatively correlated with clinical status and caregiver burden.

In general the individuals reported high levels of HRQoL with the majority of participants and informants rating HRQoL as either good or very good, even amongst those with dementia (i.e., higher CDR® plus NACC FTLD scores). Higher CDR® plus NACC FTLD scores were negatively correlated with HRQoL ratings, indicating that HRQoL decreases with poorer clinical status, i.e., as individuals become symptomatic. This finding suggests that even mild FTLD features may have a negative impact on HRQoL. Similar to the findings presented here, several studies have indicated a negative correlation with HRQoL and early cognitive changes. In one study, the presence of a memory complaint was associated with lower QOL in individual(s) with MCI but not for normal controls [37]. In another study, MCI was associated with lower self-reported psychological QOL compared to controls [38]. A study of cognitively normal participants showed significantly higher QOL scores compared to those with MCI based on both subject and informant measures [39], and a similar study found reduced QOL in MCI by both participant and proxy reports [40]. In addition, individuals reported higher levels of QOL compared to their caregivers. These four studies in MCI also found that depressive and neuropsychiatric symptoms correlated with lower ratings of QOL. However, not all studies have supported this association with MCI and lower QOL. One study compared QOL measures for those with AD, MCI, and normal controls, and found that while caregivers rated QOL lower in AD than in controls, MCI was not associated with decreased QOL [23]. Furthermore, the self-report measures of QOL did not show any differences across the 3 groups. The trajectory decreased QOL over the course dementia, from preclinical/asymptomatic to early cognitive changes, and finally clinically significant dementia remains unclear. There is even less available evidence regarding HRQoL over the course of FTLD specifically.

This current study, which includes a high risk familial FTLD cohort, provides a unique opportunity to follow changes in HRQoL longitudinally. Additional work on HRQoL with this cohort will provide more insights on how FTLD impacts QOL in individuals and informants, particularly with regard to phenoconversion from asymptomatic to overtly symptomatic FTLD. Though not specific to FTLD, one study found that decreases in HRQoL preceded the diagnosis of all cause dementia and AD in a community sample, suggesting that changes in HRQoL could be a predictor of cognitive decline [41]. This LEFFTDS cohort may provide an opportunity to test if a similar effect could be seen in FTLD.

In individuals with dementia, it can be more difficult to assess HRQoL due to the inherent impairments in memory, language, and executive function, as well as the decreased insight that is particularly common in some FTLD syndromes. This is an increasing concern with more advanced stages of dementia. Therefore proxy/informant measures of HRQoL have often been used in dementia, though this method also has its limitations. In this study we examined both self-report and proxy reported HRQoL, and demonstrated fair agreement

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between the two. This cohort is relatively young, with a mean age of 48.5 years, and the majority of the informants are spouses, and likely caregivers. The differences between self-reported and proxy-rated measures could reflect of the impaired awareness and insight regarding behavioral, cognitive and functional changes in FTLD and the resulting impact on HRQoL on the part of the symptomatic patient [42]. There may also be factors related to the informant or caregiver that create bias in reporting HRQoL. There are multiple possible sources of bias related to proxy reports of HRQoL for individuals with dementia. Informants may have difficulty objectively evaluating subject HRQoL, such as projecting their own sense of HRQoL onto the dementia patient [20]. Studies in AD have indicated that proxy reports tend to underestimate a patient's QOL, and proxy reports can vary based on the emotional state of the caregiver and the nature of the relationship between the caregiver and patient [21, 43, 44]. A 2001 study of 40 caregivers found that dementia severity, caregiver depression and caregiver burden negatively affected caregivers' assessments of patient QOL [45]. This study also indicated that proxy reports differ based on their own assessment versus how they believe the dementia patient would respond. The tendency for informants to report lower QOL compared to patient self-report, has also been demonstrated in MCI [40]. Both patient-reported and proxy measures of QOL impart valuable information. Further research is needed to develop best practices for incorporating both self-reports and proxy reports of QOL in FTLD.

This study found that caregiver burden as measured on the ZBI was negatively correlated with patient HRQoL. This is consistent with our hypothesis that as individuals experience a lower quality of life, based on decreased functional status and higher symptoms burden, caregivers are likely to experience increased caregiver demands and distress. This finding is consistent with other studies in dementia [46, 47]. In this current study, caregivers of asymptomatic and minimally symptomatic participants rated caregiver burden in the "little or no burden" category, while caregivers of those with mild to moderate dementia were generally in the "mild to moderate burden" category. However, individuals with the highest symptoms severity showed low levels of caregiver burden. The significance and possible causes of this finding are unclear. It is possible that at the advanced stages of FTLD, caregivers are seeking out additional supports such as home care or moving individuals to long-term care environments, and subsequently have a lower level of caregiver burden. Though there was a significant increase in caregiver burden associated with reductions in HRQoL, overall there were fairly low levels of caregiver burden reported. This is consistent with the generally good ratings of HRQoL within this cohort.

There has been increasing interest in understanding the factors contributing to HRQoL in dementia generally and in FTLD specifically. In addition, there is a strong desire to offer interventions that may help maintain or improve HRQoL for individuals with dementia. There are studies showing potential benefits for a variety of interventions to improve quality of life in dementia [48] and FTLD more specifically [49]. Interventions with evidence of benefit include neurorehabilitation, behavioral therapy, caregiver education~~s~~, strategies to improve self-efficacy, occupational therapy, and physical exercise programs, and cognitive stimulation programs. ~~In order to~~ better target HRQoL in FTLD, it will be important to have a better understanding of the factors that influence HRQoL in FTLD and how HRQoL may change over the course of illness. This study provides preliminary data on the natural course

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of HRQoL and caregiver burden as disease severity progresses. Additional studies are needed to further explore individual and disease related factors that may influence HRQoL and therefore be a target for intervention studies.

There are several limitations to this study. This study does not examine other possible determinants of HRQoL such as depression, behavioral symptoms or level of care needs. This study does not provide longitudinal data on HRQoL to examine changes over time through the course of disease progression. However, this cohort is part of a longitudinal study and this information will be analyzed as the study continues.

The strengths of this study include that it is one of the few studies to examine HRQoL in a FTLD cohort. This study is unique in being able to track HRQoL ratings of kindred individuals in familial FTLD who are not yet symptomatic or diagnosed with FTLD. This study ~~utilizes~~ a measure of HRQoL designed specifically for use in dementia individuals, and has the benefits of providing both self-rating and informant rating of HRQoL.

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Table 1.

Baseline demographic and clinical characteristics by mutation status

	Carrier (N=149)	Not a carrier (N=105)	Not tested (N=58)	Total (N=312)
Age at visit	49.15 (14.25)	48.90 (13.47)	46.35 (15.58)	48.54 (14.25)
Sex				
Male	71 (48.0%)	48 (45.7%)	23 (39.7%)	142 (45.7%)
Female	77 (52.0%)	57 (54.3%)	35 (60.3%)	169 (54.3%)
Education (yrs)	15.77 (2.51)	15.29 (2.50)	15.40 (2.27)	15.54 (2.47)
Race				
White	140 (94.6%)	101 (96.2%)	56 (96.6%)	297 (95.5%)
Black or African American	0 (0.0%)	0 (0.0%)	1 (1.7%)	1 (0.3%)
American Indian or Alaska Native	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (0.3%)
Asian	7 (4.7%)	1 (1.0%)	1 (1.7%)	9 (2.9%)
Other (Specify)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
Unknown	0 (0.0%)	2 (1.9%)	0 (0.0%)	2 (0.6%)
Ethnicity				
Not Hispanic or Latino	143 (96.6%)	104 (99.0%)	58 (100.0%)	305 (98.1%)
Hispanic or Latino	3 (2.0%)	0 (0.0%)	0 (0.0%)	3 (1.0%)
Unknown	2 (1.4%)	1 (1.0%)	0 (0.0%)	3 (1.0%)
Informant relationship				
Wife	43 (34.1%)	16 (18.2%)	7 (14.6%)	66 (25.2%)
Husband	33 (26.2%)	22 (25.0%)	16 (33.3%)	71 (27.1%)
Other relative	22 (17.5%)	27 (30.7%)	15 (31.3%)	64 (24.4%)
Other	11 (8.7%)	5 (5.7%)	4 (8.3%)	20 (7.6%)
Friend/companion	9 (7.1%)	9 (10.2%)	5 (10.4%)	23 (8.8%)
Daughter	4 (3.2%)	6 (6.8%)	1 (2.1%)	11 (4.2%)
Son	4 (3.2%)	3 (3.4%)	0 (0.0%)	7 (2.7%)
Primary clinical phenotype				
Clinically Normal	90 (60.4%)	97 (92.4%)	49 (84.5%)	236 (75.6%)
bvFTD +/− ALS	38 (25.5%)	1 (1.0%)	6 (10.3%)	45 (14.4%)
MCI	15 (10.1%)	7 (6.7%)	3 (5.2%)	25 (8.0%)
Primary Progressive Aphasia	4 (2.7%)	0 (0.0%)	0 (0.0%)	4 (1.3%)
Corticobasal Syndrome	2 (1.3%)	0 (0.0%)	0 (0.0%)	2 (0.6%)
QoL, self-rated *				
Poor	2 (1.7%)	1 (1.1%)	1 (2.0%)	4 (1.6%)
Fair	10 (8.5%)	11 (12.5%)	3 (5.9%)	24 (9.3%)
Good	48 (40.7%)	26 (29.5%)	22 (43.1%)	96 (37.4%)
Very good	58 (49.2%)	50 (56.8%)	25 (49.0%)	133 (51.8%)
QoL, informant-rated **				
Poor	3 (2.4%)	1 (1.1%)	2 (4.5%)	6 (2.3%)

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	Carrier (N=149)	Not a carrier (N=105)	Not tested (N=58)	Total (N=312)
Fair	13 (10.4%)	5 (5.3%)	1 (2.3%)	19 (7.2%)
Good	44 (35.2%)	32 (33.7%)	17 (38.6%)	93 (35.2%)
Very good	65 (52.0%)	57 (60.0%)	24 (54.5%)	146 (55.3%)
CDR® plus NACC FTLD				
0	90 (60.4%)	97 (92.4%)	49 (84.5%)	236 (75.6%)
0.5	20 (13.4%)	7 (6.7%)	4 (6.9%)	31 (9.9%)
1	12 (8.1%)	0 (0.0%)	4 (6.9%)	16 (5.1%)
2	19 (12.8%)	1 (1.0%)	1 (1.7%)	21 (6.7%)
3	8 (5.4%)	0 (0.0%)	0 (0.0%)	8 (2.6%)
ZBI*	14.74 (16.03)	5.38 (8.44)	9.40 (13.69)	10.47 (13.97)

Values presented are N (%) for categorical variables and mean (standard deviation) for continuous variables. Data presented above are based on non-missing values for each variable only.

* DEMQOL.

** DEMQOL-proxy.

*** Zarit Burden Interview.

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Table 2.

Age, QOL Ratings, and ZBI by CDR® plus NACC FTLD

	CDR® plus NACC FTLD					
	All (n=312)	**0 (n=236)**	**0.5 (n=31)**	**1 (n=16)**	**2 (n=21)**	**3 (n=8)**
Age at Visit *	48.5 (14.2)	45.6 (14.1)	55.8 (10.1)	58.7 (9.0)	59.1(12.5)	59.0 (10.4)
QOL, self-reported **						
Very good	133 (51.8%)	117 (58.2%)	9 (32.1%)	5 (38.5%)	1 (7.7%)	1 (50.0%)
Good	96 (37.4%)	68 (33.8%)	12 (42.9%)	5 (38.5%)	11 (84.6%)	0 (0.0%)
Fair	24 (9.3%)	13 (6.5%)	6 (21.4%)	3 (23.1%)	2 (16.7 %) 1 (7.7%)	1 (50.0%)
Poor	4 (1.6%)	3 (1.5%)	1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
QOL, informant-rated ***						
Very good	146 (55.3%)	126 (62.7%)	9 (34.6%)	4 (28.6%)	6 (30.0%)	1 (33.3%)
Good	93 (35.2%)	68 (33.8%)	9 (34.6%)	8 (57.1%)	7 (35.0%)	1 (33.3%)
Fair	19 (7.2%)	5 (2.5%)	7 (26.9%)	1 (7.1 %)	6 (30.0 %)	0 (0.0%)
Poor	6 (2.3%)	2 (1.0%)	1 (3.8%)	1 (7.1%)	1 (5.0%)	1 (33.3%)
ZBI ****	10.5 (14.0)	5.9 (8.6)	15.5 (16.2)	32.6 (16.2)	35.3 (12.8)	11.8 (10.2)

* The ANOVA F-test p-value for comparing Age at Visit across **CDR® plus NACC FTLD** is <.0001.

** DEMQOL.

*** DEMQOL-proxy.

**** Zarit Burden Interview

Values presented are N (%) for categorical variables and mean (standard deviation) for continuous variables Data presented above are based on non-missing values for each variable only.

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Table 3.

Pearson Correlations with P-Values

	CDR® plus NACC FTLD	ZBI
QOL, self-reported *	−0.20 (.001)	−0.22 (.0009)
QOL, informant-rated **	−0.32 (<.0001)	−0.36 (<.0001)

* DEMQOL.

** DEMQOL-proxy.

Data presented above are based on non-missing values for each variable only.

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Table 4.

Weighted Kappa for Subject and Informant QOL Rating Agreement

	Weighted Kappa (95% CI)	P-Value
Everyone	0.36 (0.25, 0.46)	<.0001
CDR® plus NACC FTLD=0	0.30 (0.16, 0.43)	<.0001
CDR® plus NACC FTLD≥0.5	0.40 (0.20, 0.59)	<.0001
Spouse as Informant	0.47 (0.32, 0.62)	<.0001
Non-Spouse as Informant	0.26 (0.11, 0.40)	.0007

Data presented above are based on non-missing values only.