Participant–Informant Relationships Affect Quality of Life Ratings in Incipient and Clinical Alzheimer Disease

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Objective: *Clinical trials in incipient and clinical Alzheimer disease (AD) often include informant-reported outcomes. Whereas 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 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, the Functional Activities Questionnaire (FAQ), and the Neuropsychiatric Inventory (NPI).* **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.* (Am J Geriatr Psychiatry 2016; ■■:■■–■■■■–■■–■■)

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Alzheimer disease (AD) is a neurodegenerative condition characterized by progressive cognitive deficits, behavioral abnormalities, and functional disabilities. Because 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.

Although informant reports represent an important source of information regarding disease progression,[6] because of their subjective nature they also have limitations. 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 for 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] Other studies, however, 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—although 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 among 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 the UCLA Medical Center, the Olive View-UCLA Medical Center, and the Marina Campus of the Centinela-Freeman Medical Center. Inclusion criteria included: 1) participant age of 50 years or older, 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 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 or more 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