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Original Research Report

Awareness of Mild Cognitive Impairment and Mild Alzheimer's Disease Dementia Diagnoses Associated With Lower Self-Ratings of Quality of Life in Older Adults

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Abstract

Objective: This study examined how awareness of diagnostic label impacted self-reported quality of life (QOL) in persons with varying degrees of cognitive impairment.

Method: Older adults (n = 259) with normal cognition, Mild Cognitive Impairment (MCI), or mild Alzheimer's disease dementia (AD) completed tests of cognition and self-report questionnaires that assessed diagnosis awareness and multiple domains of QOL: cognitive problems, activities of daily living, physical functioning, mental wellbeing, and perceptions of one's daily life. We compared measures of QOL by cognitive performance, diagnosis awareness, and diagnostic group.

Results: Persons with MCI or AD who were aware of their diagnosis reported lower average satisfaction with daily life (QOL-AD), basic functioning (BADL Scale), and physical wellbeing (SF-12 PCS), and more difficulties in daily life (DEM-QOL) than those who were unaware (all $p \leq .007$). Controlling for gender, those expecting their condition to worsen over time reported greater depression (GDS), higher stress (PSS), lower quality of daily life (QOL-AD, DEM-QOL), and more cognitive difficulties (CDS) compared to others (all $p < .05$).

Discussion: Persons aware of their diagnostic label—either MCI or AD—and its prognosis report lower QOL than those unaware of these facts about themselves. These relationships are independent of the severity of cognitive impairment.

Keywords: Cognitive decline, Cognitive performance, Cognitive impairment, Diagnosis awareness, Self-reported symptoms

Alzheimer's disease dementia (AD) presents a serious challenge to population health in the United States. Currently, over 5 million older Americans have this degenerative disease and that number is expected to continue to increase but there are currently no therapies to slow its progression (U.S. Department of Health and Human Services (USDHHS), 2014). In response to this challenge, the United States has launched an ambitious national plan to discover an effective therapy by 2025 (USDHHS, 2014).

To achieve this goal, older adults are being identified ever earlier in the disease process, such as with mild stage dementia, Mild Cognitive Impairment (MCI), or normal cognition concurrent with one or more Alzheimer's biomarkers. The premise is that early detection will aid opportunities to prevent or slow cognitive decline through

both novel targeted pharmaceutical treatments and lifestyle changes (Sperling, Karlawish, & Johnson, 2013). If effective, individuals diagnosed with these cognitive disorders will live longer without any or with milder cognitive impairments than is currently expected.

This strategy for prevention and intervention is gaining momentum. Several large clinical trials that are currently underway identify individuals who are, at present, experiencing no or mild cognitive impairment but are at risk for dementia based on genetic or biomarker data (Reiman et al., 2011). It is imperative to begin to understand the impact of applying diagnostic labels to groups that have mild or even no symptoms. Understanding quality of life (QOL) in persons along a spectrum of cognitive function from normal cognition (NC) to mild cognitive impairment (MCI) to mild stage Alzheimer's disease dementia (AD) may help to anticipate the treatment needs of these newly emerging patient groups and understand the pragmatic implications of shifts in diagnostic methods. However, to date, few studies have examined QOL in persons with mild stages of cognitive impairment (Bárrios et al., 2013; Pusswald et al., 2015; Teng, Tassniyom, & Lu, 2012), and only a limited few have studied persons along a spectrum from normal cognition to mild stage dementia (Kurz, Scuvee-Moreau, Vernooij-Dassen, & Dresse, 2003; Lapid et al., 2011; Missotten et al., 2008; Ready, Ott, & Grace, 2004).

QOL is a subjective, multidimensional construct typically evaluated across several areas of a person's functioning, including both personal and situational factors. Some measures of QOL focus primarily on health-related domains whereas others reflect one or more of any number of domains. For individuals with dementia, the conceptual framework for QOL often integrates cognitive functioning, physical functioning, social interactions, mental wellbeing, and mood (Whitehouse et al., 1997).

Prior research in dementia and MCI has been equivocal about the relationship between QOL and cognitive decline. Studies reporting a relationship have shown some but not all domains of QOL may be impacted by cognitive decline (Wilson et al., 2013) and those effects may vary depending on the severity of cognitive impairment (Bárrios et al., 2013; Teng et al., 2012). Other studies have not found a relationship at all (Woods et al., 2014) or identified only weak associations between severity of cognitive decline and health-related QOL (Banerjee et al., 2009). Methodologic shortcomings, like proxy-report (Missotten et al., 2008), and the wide-varying definitions across QOL measures (Bowling et al., 2015; Garratt, Schmidt, Mackintosh, & Fitzpatrick, 2002) may explain some but not all of the inconsistency in prior research.

Several studies have relied on the premise that the relationship between QOL and cognitive decline centers on whether, and to what degree, the patient is aware of their impairments. Studies seem to suggest that, for individuals with mild dementia, there is no relationship between their insight into cognitive symptoms and health-related QOL (Banerjee et al., 2009) whereas for those in moderate stages of disease greater insight may be associated with better health-related QOL (Hurt et al., 2010). At more severe stages, anosognosia can limit insight and may be protective against declines in QOL (Conde-Sala et al., 2013).

The purpose of this study was to understand how diagnostic category and awareness of that diagnosis impact QOL in individuals with MCI and mild AD as compared to cognitively typical individuals. Because our QOL measures are self-reported, we expected subjective knowledge of diagnosis to be more influential than actual diagnosis. We also expected that different aspects of QOL may respond differently to cognitive impairment. Specifically, we expected subjective measures of mood and memory to be the most strongly affected and the more objective measures of functioning to be the least strongly affected. This paper specifically does not consider mediators or nonlinear effects, which will be addressed in a later paper.

Method

Participants

The sample included 259 individuals recruited from the Penn Memory Center longitudinal cohort study with mild stage AD (n = 68), MCI (n = 92), or NC (n = 99). A diagnosis of AD was defined by the criteria from the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA; McKhann et al., 1984). A diagnosis of MCI was based on the National Alzheimer's Coordinating Center and Peterson criteria (Petersen et al., 1997; Shiloh, 2006). Participants with NC demonstrated performance on neuropsychological testing that was commensurate with similarly aged and educated peers. They did not meet criteria for either AD or MCI. Diagnoses were assigned during routine assessments in the study cohort.

Eligibility

Eligibility criteria were: age ≥ 65, native English speaker, at least 6th grade education, score of 20 or higher on the Mini-Mental State Exam (MMSE), ability to read from a handheld visual acuity card, and able to hear conversational speech. Because interviews were conducted in participants' homes, participants were required to live within one hour drive of the Penn Memory Center. Participants with AD and MCI were required to participate with a knowledgeable informant (study partner), who was a close friend or relative who could provide information about the participant.

Recruitment

Participants were recruited from the Penn Memory Center cohort, which is a registry of individuals interested in being contacted for research studies. Registry members

were sent a letter describing the study. A research assistant called candidates to explain the study in more detail and assess interest in participating. Individuals with NC were contacted directly. Individuals with AD or MCI were contacted through their listed knowledgeable informant. All participants provided written informed consent or, in the case of those not capable, assent while their knowledgeable informants provided written informed consent. Participants received a $20 gift card after each interview to compensate them for their time.

Participant Interviews

The study involved a pair of interviews conducted face-to-face by a trained research assistant. Interviews were conducted at the participant's home, unless they requested to meet at the Penn Memory Center. Interviews were conducted over two sessions to avoid fatigue and were conducted within three months of a participant's most recent Penn Memory Center cohort assessment. Each interview lasted approximately 1–1.5 hr.

Measures

A battery of validated assessments was used to gather information on multiple domains related to cognitive functioning and QOL (Supplementary Table 1). Cognitive functioning was assessed by several performance-based measures. Global cognitive functioning was assessed with the MMSE (Folstein, Folstein, & McHugh, 1975) and Montreal Cognitive Assessment (MoCA) (Nasreddine et al., 2005). Verbal and nonverbal memory were assessed with the Philadelphia Verbal Learning Task (PVLT) (Libon et al., 1997) and Biber Figure Learning Task (BFLT) (Glosser, Cole, Khatri, DellaPietra, & Kaplan, 2002), respectively. Executive function was measured with the test of Graphic Pattern Generation (GPG) (Glosser & Goodglass, 1990). Premorbid crystalized intelligence was assessed via the Wechsler Test of Adult Reading (WTAR) (Wechsler, 2001) and Wechsler Adult Intelligence Scale third edition (WAIS-III) Information subtest (Wechsler, 1997), which tend to be relatively unaffected by normal aging or cognitive decline observed in mild to moderate stages of dementia (Izawa, Urakami, Kojima, & Ohama, 2009; McFarlane, Welch, & Rodgers, 2006; Ryan, 2000).

Participant self-report measures were used to assess multiple domains of QOL: cognitive problems, physical functioning, social interactions, mood, and mental wellbeing (Whitehouse et al., 1997). Cognitive problems were assessed by the Cognitive Difficulties Scale (CDS) (Derouesne et al., 1993; Frank, Lenderking, Howard, & Cantillon, 2011). Distress due to each endorsed problem was assessed using an adapted version of the Global Distress Index (GDI) (Chang, Hwang, Feuerman, Kasimis, & Thaler, 2000). General physical and mental wellbeing were assessed with the Physical Composite Scale (PCS) and Mental Composite Scale (MCS) from the Short Form Health Survey (SF-12)(Ware, Kosinski, & Keller, 1996). Depression, anxiety, and subjective stress were assessed using the Geriatric Depression Scale (GDS) (Yesavage et al., 1982), Beck Anxiety Inventory (BAI) (Beck, Epstein, Brown, & Steer, 1988), and Perceived Stress Scale (PSS) (Cohen, Kamarck, & Mermelstein, 1983), respectively. Functioning in terms of both basic daily activities and those instrumental to personal independence were assessed via the Lawton-Brody Basic and Instrumental Activities of Daily Living scales (B/IADLs) (Lawton & Brody, 1969).

Multiple measures of QOL were used to capture distinct aspects of a person's preferences in daily life. Satisfaction with different areas of life such as physical health, living situation, family, marriage, self, and money were assessed with the QOL-AD (Logsdon, Gibbons, McCurry, & Teri, 1999). Health-related QOL linked to mobility, self-care, usual activity, pain and anxiety were measured by the Euro-QOL (EQ-5D), which also included a single item visual analogue scale to assess overall "health state" (EQ-VAS) (The EuroQol Group, 1990). Degree of difficulty in daily life related to health, well-being, cognitive functioning, social relationships, daily activities, and self-concept was measured by the DEM-QOL (Smith et al., 2005). Higher scores indicate better QOL.

Participants in the AD and MCI study groups were given the AD Insight Questionnaire in order to assess their awareness of their diagnosis and beliefs about prognosis (Hirschman, Joyce, James, Xie, & Karlawish, 2005). Participants were asked questions about their diagnosis, cognitive problems ("Do you have problems with your memory or thinking?" coded as "yes" or "no"), and prognosis ("Will your memory or thinking problems get worse?" coded as "yes" or "no"). For diagnosis, they were asked separate questions about whether they had "Alzheimer's disease" and "Mild Cognitive Impairment." If patients responded "no" to the AD diagnosis question, the interviewer followed with the question, "What about a little bit of Alzheimer's disease?" If patients responded "no", the interviewer followed with the question, "What about dementia?" Participants who responded affirmatively to any of the diagnosis-related items were entered into our analyses as being "aware" of their diagnosis whereas all others were coded "unaware."

Standard demographics, including age, gender, race, ethnicity, years of education, and handedness were collected directly from NC participants and from knowledgeable informants of AD and MCI participants. All procedures involving human subjects were approved by the local Institutional Review Board.

Statistical Analysis

Because the distributions of many of the outcome measures were skewed, we used nonparametric statistics that offered satisfactory alternatives to their parametric equivalents with

little loss of statistical power (Kitchen, 2009). Chi-square test and the Kruskall–Wallace test with Dunn's test for multiple comparisons were used to assess central tendency of the distributions of measures (Dinno, 2015). In separate analyses, an uncorrected Dunn's test was used as a follow-up to the Kruskall–Wallace test to compare each domain of QOL in the NC group to the MCI and AD groups.

To estimate the effect of one's belief about their prognosis on domains of QOL, we used the diagnosed group of 160 participants. For each domain, we entered patient self-awareness of their diagnosis, either MCI or AD respectively, and prognosis into regression models, either OLS or logistic as appropriate. For these analyses, we statistically controlled for patient gender. We used a log transformation on the GDS to improve model fit. The BAI and B/IADL scales were entered as binary variables. The cut point for these variables separated one-third of the sample into the high group.

To minimize the influence of floor and ceiling effects and measurement error, we created a composite score to assess performance-based memory (Wilson, Beckett, Bennett, Albert, & Evans, 1999). The Cognitive Composite Score (CCS) was calculated as the average of the z-scores from the: PVLT immediate memory, PVLT long-term memory, BFLT immediate memory, and BFLT long-term memory. This score was standardized to the NC group so that this group had an average of zero and *SD* of 1.0. The Cronbach α for the score was 0.95. We used the CCS to assess if and how diagnostic label changed the relationship between domains of QOL and memory impairment. In these analyses, we used two-stage nested regression models, either OLS or logistic as appropriate. In the first stage, we estimated the initial R-squared value of the CCS and the QOL domain. In the second stage, we assessed the change in the R-squared value when diagnostic label was added to the stage 1 model.

All analyses were conducted in Stata version 14.0.

Results

Participant Characteristics

The study groups did not differ on age, race, right-handedness, or the percentage of college graduates (all $p > .05$, Table 1). The MCI group had fewer women (46%) than both the NC (73%) and AD (63%) groups. On all but two measures, the average cognitive performance of the three study groups differed consistently with the NC group performing relatively strongest, the AD group performing weakest, and the MCI group's performance falling between the two (all $p < .01$). The study groups did not appear to differ in premorbid cognitive ability (WTAR, $p = .06$) or perseverations in nonverbal memory (BFLT, $p = .91$).

Awareness of Impairment and Diagnosis by Diagnostic Label

Most older adults in the MCI and AD groups reported at least some memory problems, 97% and 94%, respectively (Table 2). However, the MCI group reported greater cognitive difficulty (mean = 42.3) than those in either the NC (mean = 33.0) or AD (mean = 35.4) groups (CDS; $p = .007$). When asked if they had more memory problems than most other people, the MCI group (45%) was similarly as likely as the AD group (36%) to answer affirmatively ($p = .06$). The MCI and AD groups were also similarly as likely to believe their memory problems would worsen over time ($p = .06$).

The MCI and AD groups were asked whether they believed that they were diagnosed with AD or MCI. Those in the MCI group were more likely to be aware that they had a diagnosis of MCI (63%) than those in the AD group were to be aware that they had a diagnosis of AD (34%). Over one-third (37%) of patients formally diagnosed with AD or MCI were unaware that they had such a diagnosis.

QOL by Diagnostic Label

On average, the MCI and AD groups reported relatively less satisfaction with daily life (QOL-AD) and greater difficulty in daily life related to health, well-being, cognitive functioning, social relationships, activities, and self-concept (DEM-QOL) compared to those in the NC group (both $p \leq .03$). On average, the MCI group reported higher depression (GDS, mean = 7.1) and lower overall mental wellbeing (SF-12 MCS, mean = 51.6) as compared to both the NC and AD groups (all $p < .001$). The MCI group also reported feeling more stress (PSS mean = 12.6) than the NC group (mean = 9.8, $p = .01$). In contrast, the AD group reported, on average, lower general physical wellbeing (SF-12 PCS) compared to the NC group and greater impairment in instrumental functioning (IADLs) compared to both the NC and AD groups (all $p \leq .045$).

There were no statistically discernable differences in anxiety (BAI), health-related QOL (EQ-5D), global health (EQ-VAS), or basic functioning (DEM-QOL Daily Activities Scale; BADLs, all $p \geq .18$). In multivariable regression analyses that statistically controlled for the difference in the percentage of women across study groups, all results were similar to those from the bivariate analyses.

Impact of Diagnostic Label on Relationships Between Memory Impairment and QOL

To assess whether diagnostic label of MCI or AD impacted relationships between self-reported QOL and performance-based memory impairment, we used a two-stage nested regression model. In the first stage, we estimated the amount of variability explained (R^2) in a QOL domain by memory impairment (CCS). In the second stage, we added diagnostic label to the model to estimate the change in the explained variance (ΔR^2) (Table 3).

A small proportion of variance in each mental wellbeing (SF-12 MCS, 3%), basic functioning (BADLs, 2%), and the degree individuals had difficulty in daily life related

Table 1. Demographics and Cognitive Measures by Diagnostic Group

	Variable	Normal control (n = 99)	Mild cognitive impairment (n = 92)	Alzheimer's disease (n = 68)	p value[a]
Demographics	Age (years), mean (*SD*)	79.2 (7.1)	78.1 (6.4)	78.2 (6.5)	.44
	Female, n (%)	72 (72.7)	42 (45.6)	43 (63.2)	<.001
	African American, n (%)	9 (9.1)	8 (8.7)	4 (5.9)	.73
	College graduate, n (%)	66 (66.7)	55 (59.8)	38 (55.9)	.34
	Right handed, n (%)	94 (95.0)	82 (89.1)	64 (94.1)	.48
Memory	Cognitive Composite Score, mean (*SD*)	0.0 (1.0)	–2.4 (1.5)	–4.1 (1.1)	.001
	PVLT-Immediate memory, mean (*SD*)	39.2 (4.2)	29.5 (6.7)	23.2 (6.3)	.001
	PVLT-Long Delay, mean (*SD*)	7.5 (2.0)	4.0 (2.9)	1.1 (1.9)	.001
	PVLT-Intrusions, mean (*SD*)	1.6 (3.1)	6.1 (6.0)	8.3 (7.8)	<.001
	PVLT- Perseverations, mean (*SD*)	0.9 (1.7)	1.6 (2.0)	1.0 (1.7)	.01
	BFLT-Immediate memory, mean (*SD*)	93.5 (22.1)	53.4 (28.6)	22.7 (19.7)	<.001
	BFLT-Long Delay, mean (*SD*)	21.4 (5.4)	11.2 (7.4)	3.2 (5.4)	.001
	BFLT-Intrusions, mean (*SD*)	0.1 (0.5)	0.2 (0.5)	1.0 (2.9)	<.001
	BFLT-Perseverations, mean (*SD*)	0.1 (0.4)	0.1 (0.4)	0.1 (0.3)	.91
Global Cognition	MMSE, mean (*SD*)	29.2 (1.0)	27.3 (2.2)	24.4 (2.7)	.001
	MoCA, mean (*SD*)	26.8 (2.3)	22.0 (3.2)	18.6 (3.7)	.001
Cognitive	WTAR IQ, mean (*SD*)	114.1 (9.2)	110.6 (11.0)	110.8 (11.0)	.06
Reserve	WAIS-III IS, mean (*SD*)	14.6 (2.5)	12.0 (2.9)	9.5 (2.2)	<.001
Executive	GPG unique designs, mean (*SD*)	16.2 (2.5)	13.8 (3.3)	11.7 (4.2)	<.001
Function	GPG generation rule violations, mean (*SD*)	0.7 (1.3)	1.7 (3.0)	2.9 (3.7)	<.001

Note: AD = Alzheimer's disease; BFLT = Biber Figure Learning Task; GDS = Geriatric Depression Scale; GPG = Graphic Pattern Generation; IQ = Intelligence Quotient; MCI = Mild Cognitive Impairment; MMSE = Mini-Mental State Exam; MoCA = Montreal Cognitive Assessment; PVLT = Philadelphia Verbal Learning Task; WAIS-III IS = Wechsler Adult Intelligence Scale third edition Information subtest; WTAR = Wechsler Test of Adult Reading.

[a]Chi-square test with 2 degrees of freedom for categorical variables. For rank variables, Kruskall–Wallis test with correction for ties for the other variables.

to health, well-being, cognitive functioning, social relationships, activities, and self-concept (DEM-QOL, 3%) was explained by differences in the severity of memory impairment (all $p \leq .04$). For each, the explained variance increased when diagnostic label was added to the model, 4%, 4%, and 15% respectively (all $p \leq .006$).

Variability in each self-reported cognitive difficulties (CDS), depression (GDS), anxiety (BAI), stress (PSS), health-related quality of life (EQ-5D), and satisfaction with daily life (QOL-AD) was only reliably explained when diagnostic label was included in the model with memory impairment (all $p \leq .006$). In all but two of these models, the diagnostic label of MCI was the strongest of the predictors (all $p \leq .006$). In addition, variability in both physical wellbeing and instrumental functioning was reliably related to differences in memory impairment (SF-12 PCS, IADLs, both $p \leq .03$). These relationships were no better accounted for when diagnostic label was included in the model with memory impairment (all $p \geq .30$).

Awareness of Impairment and Diagnosis by Awareness of Diagnostic Label

To assess whether self-reported QOL was related to a person's belief that they did or did not have a diagnosis of MCI or AD, we compared self-reported cognitive problems, quality of daily life, mental and physical wellbeing, and functioning by awareness of diagnosis. Of the 160 study persons diagnosed with either MCI or AD, 63% (101 out of 160) acknowledged, or were aware of, having such a diagnosis. The remaining 59 were unaware that they had such a diagnostic label.

Among persons diagnosed with MCI or AD, those who were and were not aware of their diagnostic label demonstrated similar cognitive functioning (MoCA, $p = .30$) and impairments in memory (CCS, $p = .14$). Both groups, independent of awareness, performed below the NC group on these measures (all $p < .001$). Those who were unaware of their diagnostic label, however, reported fewer cognitive difficulties (CDS, mean = 30.4) than those who were aware (mean = 44.7, $p < .001$). This average cognitive difficulty of the unaware group appeared similar to the NC group ($p = .13$) (Table 4).

On average, the group that was unaware that they had a diagnosis of MCI or AD reported greater satisfaction with daily life (QOL-AD) and less difficulty in daily life related to health, well-being, cognitive functioning, social relationships, activities, and self-concept (DEM-QOL) than the group that was aware of their diagnosis (all $p < .001$). This group that was unaware of their diagnosis reported better global health (EQ-VAS, $p < .001$) and health-related quality of life (EQ-5D) than the group that was aware of their diagnostic label and the NC group (all $p \leq .002$).

Both groups that were and were not aware of their diagnostic label, reported greater impairment in activities instrumental to daily life than the NC group (IADLs,

Table 2. Awareness of Diagnosis, Self-reported Memory Problems, Quality of Life, Mental Wellbeing, and Physical Functioning by Diagnostic Group (*N* = 259)

	Characteristics	Normal control[a] (*n* = 99)	Mild cognitive impairment[a] (*n* = 92)	Alzheimer's disease[a] (*n* = 68)	*p* value[b]
Diagnosis beliefs	Reports having MCI, *n* (%)	N/A	58 (63.0)	31 (46.3)	.035
	Reports having AD, *n* (%)	N/A	9 (9.8)	23 (33.8)	<.001
	Reports either MCI or AD, *n* (%)	N/A	62 (67.4)	39 (57.4)	.19
Self-reported memory problems	CDS, mean (*SD*)	33.0 (16.5)[y]	42.3 (20.7)[x,z]	35.4 (19.1)[y]	.007
	Has any problems w/ thinking or memory, *n* (%)	N/A	89 (96.7)	64 (94.4)	.42
	More memory problems than most others, *n* (%)[c]	6 (6.0)	41 (44.6)	24 (35.8)	.06[d]
	Expects memory to worsen, n (%)	N/A	67 (72.8)	40 (58.8)	.06
Quality of life (QOL)	EQ-5D, mean (*SD*)	0.81 (0.18)	0.79 (0.21)	0.83 (0.22)	.24
	EQ-VAS, mean (*SD*)	81.8 (14.4)	81.1 (16.2)	83.8 (17.4)	.22
	QOL-AD, mean (*SD*)	42.2 (4.5)[y,z]	40.3 (5.4)[x]	40.6 (6.1)[x]	.03
	DEM-QOL, mean (*SD*)	98.9 (7.2)[y,z]	91.8 (10.5)[x]	93.7 (10.6)[x]	<.001
	Health and wellbeing, mean (*SD*)	47.3 (4.4)[y,z]	43.7 (6.0)[x]	44.4 (6.7)[x]	<.001
	Cognitive function, mean (*SD*)	25.6 (2.3)[y,z]	23.4 (3.4)[x]	23.6 (3.5)[x]	<.001
	Social relationships, mean (*SD*)	18.6 (1.7)[y]	17.6 (2.4)[x,z]	18.2 (2.4)[y]	.02
	Daily activities, mean (*SD*)	7.4 (1.0)	7.1 (1.2)	7.5 (0.8)	.18
Mood and wellbeing	GDS, mean (*SD*)	3.9 (3.3)[y]	7.1 (5.4)[x,z]	4.9 (4.6)[y]	<.001
	BAI, mean (*SD*)	5.3 (5.2)	6.9 (5.9)	6.5 (5.9)	.18
	PSS, mean (*SD*)	9.8 (4.8)[y]	12.6 (6.7)[x]	11.3 (6.3)	.01
	SF-12 MCS, mean (*SD*)	55.7 (6.0)[y,z]	51.6 (7.6)[x,z]	53.5 (6.6)[y]	<.001
Physical functioning	IADLs, mean (*SD*)	8.9 (1.7)[y,z]	9.9 (2.6)[x,z]	12.3 (4.7)[x,y]	<.001
	BADLs, mean (*SD*)	6.4 (0.9)	6.6 (1.2)	6.8 (1.9)	.49
	SF-12 PCS, mean (*SD*)	46.1 (10.0)[z]	47.6 (10.9)	49.7 (9.0)[x]	.045

Note: AD = Alzheimer's disease; BADLs = Basic Activities of Daily Living Scale; BAI = Beck Anxiety Inventory; CDS = Cognitive Difficulties Scale; EQ = EuroQOL; GDS = Geriatric Depression Scale; IADLs = Instrumental Activities of Daily Living Scale; MCI = Mild Cognitive Impairment; MCS = Mental Composite Scale; N/A = Nonapplicable; PCS = Physical Composite Scale; PPS = Perceived Stress Scale; QOL = Quality of Life; SF-12 = Short Form Health Survey; VAS = Visual Analog Scale.

[a]Statistical significance ($p < .05$) determined by Dunn test and shown by: "x" = different from NC group, "y" = different from MCI group, "z" = different from AD group. [b]Kruskall–Wallis test with correction for ties for the other variables. [c]Single item from Geriatric Depression Scale (GDS). [d]*p* value from comparison of Mild Cognitive Impairment and Alzheimer's disease groups.

both $p \leq .02$). But, the group that was unaware of their diagnostic label reported, on average, better basic functioning (BADLs) and physical wellbeing (SF-12 PCS) than the group that was aware of their diagnostic label (both $p \leq .007$).

The group that was aware of their diagnostic label was much more likely (78%) to believe their symptoms would worsen over time compared to the group that was unaware of their diagnosis (47%, $p < .001$). Statistically controlling for gender, those who expected their condition to worsen reported greater depression (GDS), higher stress (PSS), more cognitive difficulties (CDS), lower satisfaction with their daily life (QOL-AD) and greater difficulty in daily life related to health, well-being, cognitive functioning, social relationships, daily activities, and self-concept (DEM-QOL) compared to the group that had such a diagnosis but did not expect their condition to worsen (all $p < .05$; data not shown). No between-group differences were found in anxiety (BAI), physical wellbeing (SF-12 PCS), mental wellbeing (SF-12 MCS), global health status (EQ-VAS), health-related quality of life (EQ-5D), or activities of daily living (IADLs; BADLs; all $p > .05$).

Discussion

In a sample of 259 older adults with mild stage AD, MCI, or NC, we found that the MCI and AD groups were similarly likely to report that they had more memory problems than most other people and to expect those memory problems to worsen over time. Compared to the NC group, the MCI and AD groups were also relatively less satisfied with daily life (QOL-AD) and reported greater difficulty in daily life related to health, well-being, cognitive functioning, social relationships, daily activities, and self-concept (DEM-QOL).

The MCI group, however, differed from both persons with mild stage dementia and normal cognition in a number of ways. They reported lower psychological wellbeing—higher depression (GDS) and lower overall mental wellbeing (SF-12 MCS)—than both the NC and AD

Table 3. Two-stage Nested Regression of Memory Impairment (CCS) on Self-reported Memory Problems, Quality of Life, Mental Wellbeing, and Physical Functioning ($N = 259$)

		Stage 1 ($N = 259$)			Stage 2 ($N = 259$)				
	Outcome	CCS mean	R^2	p value	CCS mean	MCI mean	AD mean	ΔR^2	p value
Memory problems	CDS	−0.61	.004	.29	0.2	9.7**	3.1	.09	<.001
	More memory problems than most[a]	−0.05***	.06	<.001	−0.02	0.5	0.7	.08	<.001
Quality of life	EQ-5D	−0.01	.01	.10	−0.01	−0.1***	−0.3	.07	<.001
	EQ-VAS	−0.59	.01	.21	−0.6	−5.5*	−3.2	.02	.07
	QOL-AD	0.14	.003	.37	0.2	−3.4***	−2.6*	.07	<.001
	DEM-QOL	0.82**	.03	.006	0.4*	−8.3***	−9.4***	.15	<.001
Mental mood and wellbeing	GDS[b,c]	−0.13	.003	.36	−0.2	3.1**	2.6	.08	<.001
	BAI[a,d]	−0.16	.004	.34	−0.1	3.3***	2.8*	.06	<.001
	PSS	−0.28	.01	.12	0.1	4.6**	3.6**	.10	<.001
	SF-12 MCS	0.55**	.03	.008	0.2	−2.7*	−4.1**	.04	.004
Physical functioning	IADLs[a,e]	−0.67	.14	<.001	0.01	0.7	0.1	.01	.30
	BADLs	−0.05	.02	.04	−0.03	0.6	−0.2	.04	.006
	SF-12 PCS	−0.84	.03	.03	−0.8	−0.5	0.1	.01	.90

Note: AD = Alzheimer's disease; BADLs = Basic Activities of Daily Living Scale; BAI = Beck Anxiety Inventory; CCS = Cognitive Composite Score; CDS = Cognitive Difficulties Scale; EQ = Euro-QOL; GDS = Geriatric Depression Scale; IADLs=Instrumental Activities of Daily Living Scale; MCI = Mild Cognitive Impairment; MCS = Mental Composite Scale; PCS = Physical Composite Scale; PPS = Perceived Stress Scale; QOL = Quality of Life; SF-12 = Short Form Health Survey; VAS = Visual Analog Scale.

[a]Logistic regression, with pseudo R-squared reported, and significance based on Wald chi-square test. All others are ordinary least squares (OLS) regression. [b]Single item from Geriatric Depression Scale (GDS). [c]Log transformed to improve statistical fit. [d]Score greater than 7 points. [e]Score greater than 1 point.

*$p < .05$, **$p < .01$, ***$p < .001$.

groups. They also reported greater situational stress than the NC group (PSS). These findings are in contrast to their reports of general physical health and basic functioning (EQ-5D; EQ-VAS; BADLs), which appeared unaffected by differences in cognitive decline, and physical wellbeing and instrumental functioning (SF-12 PCS, IADLs), which differed only between the AD and NC groups.

These findings suggest reasons for why prior studies' results appear contradictory, such as reporting no or weak relationships between cognitive decline and QOL (Banerjee et al., 2009; Woods et al., 2014) while other studies report robust associations (Wilson et al., 2013). First, the relationship between cognitive decline and QOL varies by domain. In particular, the physical domain seems relatively unaffected by cognitive impairment while the psychological domain is affected. This finding makes sense as amongst persons with cognitive impairments in the AD spectrum (in contrast to Parkinson's disease), physical function is not impaired until the moderate to severe stage of dementia when persons need assistance with basic activities of daily living. Second, the relationship may be curvilinear. Individuals with MCI report lower psychological QOL than either those with NC or AD. This suggests the subjective experience of cognitive decline is complicated. "Mild cognitive impairment" may not be felt as a "mild" impairment in wellbeing.

There are a number of plausible reasons for why psychological domains of QOL showed a curvilinear relationship with cognitive decline. In our study, we examined diagnostic label, prognostic expectation, and "awareness" of diagnosis. In two-stage nested regression models, we found that, when added to a model with memory impairment, diagnostic label increased the amount of statistical variability explained in all QOL domains except for those related to physical health and instrumental functioning (SF-12 PCS, IADLs). We found that an older adult's expectation for their prognosis impacted many domains of QOL, including depression (GDS), stress (PSS), satisfaction and ease in daily life (QOL-AD, DEM-QOL), and cognitive difficulties (CDS).

Our findings suggest that the relationship between QOL and cognitive decline could be impacted or anticipated, at least in part, by diagnostic label and patient expectations of prognosis. This has pragmatic implications for current and future clinical practice. When a clinician discloses the diagnosis and prognosis of MCI or mild stage AD the process may cause a patient to experience additional symptoms. Therefore, before a diagnostic work-up, a clinician ought to explain to the patient that he or she may experience declines in how they feel about themselves and reassure the patient that there will be clinical follow-up of their mood and wellbeing. Such disclosure and assessment of wellbeing may help to mitigate the impact of disclosure. Whether initial disclosure of these risks and assurance of support alter these relationships would be useful to know.

Future clinical practice is likely to include routine disclosure of information about one's risk of cognitive decline to cognitively normal patients, such as is being done currently in large clinical trials where patient volunteers, who are at present experiencing no or mild cognitive impairment, are

Table 4. Self-reported Memory Problems, Quality of Life, Mental Wellbeing, and Physical Functioning by Cognitive Typicality and Awareness of Diagnosis ($N = 259$)

		Cognitively normal (NC) ($n = 99$)	Patients believe self-normal (BCN) ($n = 59$)	Patients believe self-diagnosed (DX) ($n = 101$)			
Outcome		Mean (*SD*)	Mean (*SD*)	Mean (*SD*)	*p* value[a] (NC vs BCN)	*p* value[a] (NC vs DX)	*p* value[a] (BCN vs DX)
Cognitive performance	MoCA	26.8 (2.3)	20.2 (4.1)	20.8 (3.6)	<.001	<.001	.30
	CCS	0.0 (1.0)	−3.36 (1.53)	−2.97 (1.67)	<.001	<.001	.14
Cognitive problems	CDS	33.0 (16.5)	30.4 (16.3)	44.7 (20.5)	.13	<.001	<.001
	More memory problems than most others[a]	6.0[b]	28.8[b]	48.0[b]	<.001	<.001	<.02
	Expects memory to worsen	N/A	47 (50.3)[b]	78 (41.5)[b]	N/A	N/A	<.001
Quality of life	EQ-5D	0.86 (0.13)	0.91 (0.12)	0.82 (0.2)	.005	.07	<.001
	EQ-VAS	81.9 (14.4)	86.5 (15.9)	79.8 (16.8)	.005	.002	.002
	QOL-AD	42.2 (4.5)	42.5 (5.3)	39.2 (5.5)	.37	<.001	<.001
	DEM-QOL	98.9 (7.2)	98.0 (7.3)	89.4 (10.9)	.23	<.001	<.001
	Health and wellbeing	47.3 (4.4)	47.0 (4.6)	42.2 (6.5)	.35	<.001	<.001
	Cognitive function	25.6 (2.3)	25.1 (2.4)	22.6 (3.6)	.07	<.001	<.001
	Social relationships	18.6 (1.7)	18.4 (2.2)	17.5 (2.5)	.39	.005	.006
	Daily activities	7.4 (1.0)	7.5 (1.0)	7.1 (1.1)	.11	.07	.006
Mental mood and wellbeing	GDS	3.9 (3.3)	4.5 (4.1)	7.1 (5.5)	.28	<.001	<.001
	BAI	5.3 (5.2)	4.4 (5.3)	8.0 (5.8)	.07	<.001	<.001
	PSS	9.8 (4.8)	9.1 (5.2)	13.7 (6.6)	.18	<.001	<.001
	SF-12 MCS	55.7 (6.0)	54.2 (6.4)	51.4 (7.5)	.08	<.001	.006
Physical functioning	IADLs	8.9 (1.7)	10.7 (4.0)	11.0 (3.8)	.02	<.001	.06
	BADLs	0.5 (1.1)	0.5 (1.7)	1.0 (1.8)	.15	.008	.001
	SF-12 PCS	46.1 (10.0)	51.0 (8.4)	47.0 (10.8)	<.001	.17	.007

Note: AD = Alzheimer's disease; BADLs = Basic Activities of Daily Living Scale; BAI = Beck Anxiety Inventory; CCS = Cognitive Composite Score; CDS = Cognitive Difficulties Scale; EQ = Euro-QOL; GDS = Geriatric Depression Scale; IADLs = Instrumental Activities of Daily Living Scale; MCI = Mild Cognitive Impairment; MCS = Mental Composite Scale; MoCA = Montreal Cognitive Assessment; N/A = Nonapplicable; PCS = Physical Component Scale; PPS = Perceived Stress Scale; QOL = Quality of Life; SF-12 = Short Form Health Survey; VAS = Visual Analog Scale.

[a]*p* values are uncorrected Dunn's pairwise comparison test following Kruskall–Wallace rank test. [b]Mean of a dichotomous variable, equivalent to proportion affirmatively endorsed.

being identified as at risk for dementia based on genetic or biomarker data (Reiman et al., 2011). We found that, among persons with a diagnostic label of MCI or AD, those who were aware of their diagnosis generally reported lower satisfaction with daily life (QOL-AD), basic functioning (BADL Scale), and physical wellbeing (SF-12 PCS) along with greater difficulty in daily life related to health, well-being, cognitive functioning, social relationships, activities, and self-concept (DEM-QOL) than those who were unaware. Our findings are consistent with the limited prior research conducted in this area. Lineweaver, Bondi, Galasko, & Salmon (2014) found, for example, that older adults who have knowledge of being an ApoE4 carrier, a gene associated with lifetime risk of late-onset AD, report more cognitive symptoms and perform worse on measures of memory than adults who are ApoE4 carriers but do not know this information about their genetic risk (Lineweaver et al., 2014).

As advances in diagnostics and treatment of AD are translated from research into clinical care, novel diagnoses, like "preclinical AD" or "asymptomatic AD", may be introduced into health care to define patients who are cognitively normal but at risk for cognitive decline in order to guide the prescribing of pharmacological treatments aimed at preventing these declines. Our results offer early evidence that suggests such advances in diagnostics will bring opportunities and challenges to the field of health care. Appropriate use of these novel diagnostics is likely to require tailored assessment to determine patients should or should not undergo screening. It may also require strategies for ongoing monitoring to identify safety concerns if and when a patient might begin to experience declines. Technologies and protocols will need to be developed and implemented to support these processes and health care providers will need to be adequately trained in order to accommodate the safe and effective use of these new diagnoses.

In our study, we found that of 160 older adults diagnosed with either MCI or AD, 63% were aware of having such a diagnosis while 37% were unaware. We did not investigate why some patients were unaware of their diagnosis. There are several possible reasons why some patients were unaware of their diagnosis. For example, they may not have been told their diagnosis or they may have been told but forgot—especially if years had passed since they learned the information. Some patients may have been confused as to whether they had a diagnosis of AD or MCI, particularly if, for instance, they were initially diagnosed with MCI and then later were diagnosed with AD, or they were treated by multiple providers with differing opinions. However, this is unlikely to be an explanation in our study as we broadly defined an "aware" patient as one who endorsed either condition or more generally "dementia" or "a little Alzheimer's disease." It is possible that some unaware patients were experiencing anosognosia whereby they were unable or unwilling to recognize their impairments. The percentage of patients with anosognosia is highly variable in clinical populations, ranging from about 27% upwards to 80% (Turró-Garriga et al., 2016; Verhülsdonk et al., 2016). Understanding the degree to which anosognosia that can develop in neurodegenerative diseases is protective against declines in QOL for persons with AD dementia may be useful for understanding and addressing the burdens that may be placed on individuals who are cognitively typical yet diagnosed with AD dementia.

Our sample showed expected differences in average cognitive performance based on diagnostic group whereby the NC group performed relatively strongest, the AD group performed weakest, and the MCI group performed between the two. In our two-stage nested regression models, in which we aimed to understand if and how diagnostic label changed the relationship between domains of QOL and memory impairment, we did not statistically control for differences in executive function across the three study groups. In preliminary analyses including executive dysfunction, as measured by the GPG, slightly increased the variance explained by diagnostic label, but it also inflated the model's variance as it shared a multicollinear relationship with memory impairment. This finding is consistent with prior research on the collinear relationship between memory impairment and executive function in Alzheimer's disease (Baudic et al., 2006; Chan, Shum, Toulopoulou, & Chen, 2008). As a consequence of omitting executive function from our final analyses, our results may underestimate the actual amount of variance explained by diagnostic label. In our analyses that compared patients who were and were not aware of their diagnoses, variability in cognitive performance is unlikely to have affected our results. As shown in Table 4, aware and unaware patients showed similar performance on global measures of cognition (MoCA) and memory (CCS). The two groups were also similar across on all other cognitive measures with the exception of crystalized knowledge (WAIS Information subtest), which showed a statistically but not clinically significant difference.

In sum, our findings suggest some reasons for contradictory findings in previous studies. First, the relationship between cognitive impairment and QOL varies by domain. Second, the relationship may be curvilinear for some domains. Third, perhaps most problematic, the relationship varies depending on whether individuals are aware of their diagnostic label. Our study offers important information because public policy to address cognitive impairment in older adults favors early detection and diagnosis. Medicare's annual wellness visit now includes the detection of "any cognitive impairment" (The Patient Protection and Affordable Care Act (PPACA), 2010) and the U.S. National Alzheimer's Project Act includes goals of early diagnosis and prevention (Fins & Rodríguez del Pozo, 2011). Our findings help to identify psychological processes underlying relationships between cognitive decline and QOL, which is particularly relevant as AD is transformed from a clinical disease to one defined by biological measures along a continuum of cognitive performance so as to include not only

persons with cognitive symptoms but well persons without symptoms (Ihara, 2011).

This study was carried out at a single site. The results may not generalize to populations with other characteristics. In addition, we did not test hypotheses about mediating variables, that is, whether cognitive decline per se or decline in metacognition about cognition could be responsible for any effects. Likewise, a decline in mood and increase in depressive symptoms can affect other self-reported QOL measures because those suffering from depression are generally more negative about a wide range of aspect of their lives. These hypotheses can be tested in a later paper.

Our findings suggest that one might change the relationship between decline and self-reported QOL by simply informing an individual of their diagnosis. However, these data do not answer the causal question of whether learning a diagnosis leads to a change. Future research is needed to understand why some patients are unaware of their diagnoses and to understand possible causal relationships between learning a diagnosis and declines in quality of life. For example, an experiment which varied whether participants were told their diagnosis and its prognosis could assist in discovering whether this is true.

In our study, we examined diagnostic label, prognostic expectation, and "awareness" of diagnosis as factors that could explain the curvilinear relationship between cognitive decline and some domains of QOL. However, there are other plausible explanations for this relationship. For instance, studies of personal happiness suggest that self-ratings of happiness behave as though each person has a "set point." Thus, bad fortune such as a diagnosis of MCI will cause a decline in subjective wellbeing, but that decline decays over time and the person returns to his state prior to the event. This phenomenon is notably observed as well with good news, as winning the lottery provides a real but decaying happiness (Wilson & Gilbert, 2005). A diagnosis of mild stage AD dementia or MCI may create an initial decline in QOL which then rebounds over time, a phenomenon known as the "disability paradox" (Albrecht & Devlieger, 1999).

Further research is needed to understand what drives the impact of awareness of diagnosis and prognosis on QOL. If, over time, people do not adjust to MCI or AD, then a treatment that delays the time before the disability seen in AD dementia (i.e., extends the time in MCI), may in turn extend a period of poor quality of life (compared to persons with either normal cognition or mild stage AD dementia). To discover whether this is true, measures of QOL domains ought to be included in the outcome measures of clinical trials that are testing treatments to prevent cognitive decline. Research should examine the neural correlates of these relationships and the nature of self "stigma" associated with having an MCI or mild stage AD dementia diagnosis.

Supplementary Material

Supplementary data are available at *The Journals of Gerontology, Series B: Psychological and Social Sciences* online.

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Conflict of Interest

None reported.

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