J Med Sci 2016;36(1):14-21
DOI: 10.4103/1011-4564.177171

ORIGINAL ARTICLE

Cognitive Function, Depressive Symptoms, Function Level, and Quality of Life in Mild Dementia and Amnestic-mild Cognitive Impairment

Shu Ping Chuang[1], Jo Yung Wei Wu[2], Chien Shu Wang[1], Li Hsiang Pan[3]

[1]Department of Psychiatry, Zuoying Branch of Kaohsiung Armed Forces General Hospital, Kaohsiung, [2]Institute of Allied Health Sciences, College of Medicine, National Cheng Kung University, Tainan, [3]Department of Psychiatry, Kaohsiung Municipal Ta-Tung Hospital, Kaohsiung, Taiwan, Republic of China

Objective: The present study aimed to investigate the relationship among neurocognitive variables, depressive symptoms, functional activities, and the quality of life (QoL) in patients with mild dementia and single-domain amnestic mild cognitive impairment (a-MCI). **Materials and Methods:** Thirty-seven mild dementia patients and thirty a-MCI participants were recruited. All subjects participated in a series of neuropsychological measures (Cognitive Abilities Screening Instrument, family pictures, and digit span), geriatric depression scale-15 (GDS-15), activities of daily living (ADL), The Lawton instrumental ADL scale (IADL) and QoL-Alzheimer's disease. **Results:** Multiple regression analysis revealed that only depressive symptoms was a predictor for the QoL in mild dementia ($\beta = -0.56$, $P < 0.001$). In contrast, all variables were not associated with the QoL in a-MCI. Mildly demented people scored significantly lower on most aspects of cognitive functioning and reported poorer performances on IADL than a-MCI. There were no significant differences on GDS, ADL, and QoL between the two groups. **Conclusion:** Findings indicated that depressive symptoms contributed to the QoL in mild dementia. Interventions targeting depressive symptoms in mild dementia may improve their QoL during their early stages of dementia.

Key words: Cognitive functioning, depressive symptoms, functional level, mild dementia, mild cognitive impairment, quality of life

INTRODUCTION

Treatments in dementia have increasingly focused on aiming to maintain and/or improve their quality of life (QoL).[1,2] Recent studies strove to investigate the linkage between QoL and cognitive functioning; however, the results are conflicting. Demented participants in long-term care institutions were reported to have lower levels of QoL than those with mild cognitive impairment (MCI) and controls, while both cognitive function and behavior symptoms in themselves were predictors of QoL.[3] Wlodarczyk *et al*.[4] showed that mini-mental state examination (MMSE) scores were correlated to patient-QoL in mild to moderate dementia. However, in care home settings, cognitive function was not the predictor of patient-QoL in patients with moderate dementia.[5] Higher QoL in mild to moderate dementia was not significantly correlated with cognitive function.[6] Converging evidence showed that the multinomial MCI group was significantly impaired on scores or total instrumental activities of daily living (IADL) compared to single-domain amnestic-MCI (a-MCI) or controls.[7,8] Although, MMSE has been commonly used,[9] the Cognitive Abilities Screening Instrument (CASI) combines elements from the mostly used tests of global cognitive function[10-13] and is a more detailed assessment of cognition than MMSE. In this study, CASI was used to assess for cognitive functioning and people with mild dementia were recruited and asked to self-report on their QoL. Different stages of dementia can comprise of various profiles in cognitive, functional, and behavioral symptoms. Particularly, cognitive decline is more impaired in the moderate stage of dementia compared to the mild dementia stage and affects language and abstract thought.

Received: August 17, 2015; Revised: September 06, 2015; Accepted: October 27, 2015

Corresponding Author: Prof. Shu Ping Chuang, Department of Psychiatry, Zuoying Branch of Kaohsiung Armed Forces General Hospital, No. 553, Jiunshiau Road, Zuoying District, Kaohsiung 81342, Taiwan, Republic of China. Tel: +886-7-5817121 ext.3308; Fax: +886-7-5818816. E-mail: xota51@ngh.com.tw

How to cite this article: Chuang SP, Wu JY, Wang CS, Pan LH. Cognitive function, depressive symptoms, function level, and quality of life in mild dementia and amnestic-mild cognitive impairment. J Med Sci 2016;36:14-21.

IADLs are almost totally lost, and behavioral symptoms increase dramatically with severity.[14,15] In the past, a number of researches have included study samples with a mixture of mildly, moderately or severely demented people, and included them all as the demented patient group. It should be noted, however, that individuals with moderate to severe dementia have more cognitive and functional impairment, causing their inability to express themselves properly, and thus, patients with moderate to severe dementia were not included in this study.

Several studies have found that depression was the most significant factor influencing the QoL of demented people.[5,6,16,17] Other potential determinants such as impairment in the ADL and IADL were significantly associated with the QoL in dementia.[3,4] Several longitudinal studies have reported that people with depression are more at risk to develop dementia and MCI compared to nondepressed participants.[18-20] Dementia often increases a high prevalence of neuropsychiatric symptoms, raises burden to caregivers, and lowers the QoL of the patients.[21] The presence of mobility-related impairment can have a strong impact on the IADL and ADL scores in older people.[22]

The results by Fuh and Wang[23] showed that caregiver distress is the most consistent predictor of informant-QoL rating and that patients' depressive severity is the most significant predictor of patient-QoL. Other researchers also found that reports by either the caregiver (or staff) or the patient regarding the patient-QoL could indicate the unique perspectives of the patient and caregiver.[5,24] QoL as assessed by caregivers and patients could differ due to the use of different versions of patient-QoL assessment. In this study, patient-reported QOL was utilized to assess their QoL. Since medication cannot modify or reverse the whole course of this illness,[25] treatments in dementia have increasingly focused their attention on aiming to maintain or improve their QoL.[26,27] People with MCI probably have a higher risk in developing dementia[28] and factors related to QoL in the two groups may have different profiles in early cognitive impairment. To date, relatively few studies of the predictors or correlates of QoL have included people with a single-domain MCI compared to mild dementia. Therefore, the aim of this study was to compare individuals with mild dementia and the a-MCI group based on their self-reported ratings of their QoL excluding confounding factors. We hypothesized that individuals with mild dementia would show a decrease in cognitive functioning, functional abilities, and more depressive symptoms than the a-MCI group; a comparison between these two groups are examined to determine which factors are significantly associated with QoL.

MATERIALS AND METHODS

Participants

The study protocol was reviewed and approved by Kaohsiung Armed Forces General Hospital Institutional Review Board. Dementia was diagnosed using the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, 4th Edition diagnoses[29] by a senior psychiatrist from the Department of Psychiatry at the Zuoying Branch of Kaohsiung Armed Forces General Hospital in Taiwan. All participants provided written informed consent before entering into this study. Based on diagnosis results, different dementia types were assessed including 28 Alzheimer's disease (AD), 4 vascular dementia, and 5 dementia due to brain damage. Exclusion criteria for dementia and MCI were: Having a current and a history of psychiatric disorder, such as schizophrenia, mood disorder, and substance abuse, other neurologic disorders besides cognitive impairment, severe physical disorder, and behavioral disturbances. All patients were not receiving medication for dementia (such as donepezil, galantamine, memantine, and rivastigmine) at the recruitment of this study. We also excluded people with moderate to severe dementia (due to their inability to correctly express their QoL because of profound cognitive impairment). Thirty participants were diagnosed with MCI according to Petersen,[30] which included specific recommendations for MCI criteria: Subjective memory complaint, normal ADL, normal general cognitive function, and abnormal memory for age and not dementia. In order to gain sample homogeneity, only patients with the same amnesic type of MCI (all amnesic single-domain) were recruited: Subjects should have normal scores of MMSE, maintained scores of ADL and not be diagnosed with dementia (see below).

Measures

Cognitive Abilities Screening Instrument

The CASI has a score range of 0–100 and provides quantitative domains of assessment on attention, concentration and judgment, orientation, short-term memory, long-term memory, language abilities, visual construction, list-generating fluency, and abstraction. The CASI demonstrates good reliability and cross-cultural applicability and is useful in screening dementia, monitoring the progression of disease, and providing profiles of cognitive deterioration.[31]

Quality of life-Alzheimer's disease

QOL-AD is a brief, 13-item instrument used separately to ask participants with dementia and informants to rate participants' QoL across a number of different domains. It has been shown to have very good internal consistency and validity. The items are each rated on a 4-point scale (1 = poor and 4 = excellent), adding up to a total score ranging from 13 to 52, with higher

scores indicating higher QoL. Ratings from the patient-report were used in this study.[32]

Wechsler Memory Scale-III-Family Pictures I

The family pictures (FP) was used to evaluate the patient's processing of complex, meaningful, and visual presented information. Participants were introduced to a "family portrait" colored drawings of six members (mother, father, grandfather, grandmother, son, and daughter) and their dog for 10 s. The portrait contained four family members appearing in four different scenes. Participants were asked to remember who the character was, what their positions are, and what the characters were doing.[33]

Wechsler Memory Scale-III

Forward and reverse digit span was used to measure working memory. Participants are presented with a series of digits (e.g., digit span forward and backward) and asked to immediately reiterate the series of digit.[33]

Geriatric depression scale-15

The geriatric depression scale (GDS) is a self-reported questionnaire of depression in older adults. It consists of 15 questions about how participants have felt over the past week and is responded through a "Yes/No" format. Higher scores suggest that more depressive symptoms are present.[34]

Activities of daily living

The measurement assessed participant's mobility, self-care, and independence in 10 domains, including bowels, bladder, feeding, grooming, dressing, transferring from bed to chair and back, toilet use, mobility around house or ward, indoors, and stairs and bathing. Total scores ranged from 0 to 20, with higher scores indicating higher functioning.[35]

Lawton instrumental activities of daily living scale

This measurement assesses participants' independent living skills and is used to identify how a person is functioning at the present time and for recognizing the improvement or deterioration over time in 8 domains. Total scores range from 0 (low function, dependent) to 8 (high function, independent).[36] A clinical psychologist conducted the assessments of ADL and IADL to the participant and the informant. When the information provided by the participant was not consistent with the informant, the informant's version was applied.

Clinical Dementia Rating

The clinical dementia rating is a semi-structured interview of patients and informants. It assesses cognitive functioning rated on a 5-point scale from 6 domains, namely memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care (0: No impairment; 0.5: Questionable impairment; 3: Severe impairment).[37]

Mini-mental state examination

The test is widely used for cognitive impairment. The normative cut-off values for the Chinese version adjusted to education were used. Subjects with a-MCI scored 15 on MMSE if they had ≤6 years of education, and 24 on MMSE if they had >7 years of education.[38]

Statistical analysis

Data analysis was carried out using SPSS 16.0 (Statistical Package for the Social Sciences). Bivariate statistics using Pearson correlation were generated to understand the interrelationship among neuropsychological variables, functional abilities (ADL and IADL), depressive symptoms, and QoL. Comparisons of age, education, sex, religion, place of residence, and physical disorder between demented participants and MCI were performed using two sample *t*-tests or Chi-square statistics as appropriate and clinical measures were conducted using one-way analysis of covariance, controlling education and gender as covariates. Corrections for multiple testing were used according to the Bonferroni method to obtain results significant at a corrected alpha level of 0.05. Multiple regression analyses were used to explore significant predictors among neuropsychological variables, ADL, depressive symptoms, and QoL. The alpha level was set at 0.05 per comparison.

RESULTS

Descriptive statistics for participant's demographics are presented in Table 1. There were no significant differences in age, place of residence, physical disorder, and religion between demented patients and a-MCI participants. All participants were married, and none of them used alcohol or smoked. The demented group (mean = 5.9, standard deviation [SD] =4.4) had lower education years than the a-MCI group (mean = 8.8, SD = 4.0; $P = 0.007$) and the demented group consisted of more females ($P = 0.04$). Clinical characteristics of the demented patients and a-MCI participants are shown in Table 2; all clinical measures showed significant differences in mildly demented group and a-MCI group, except for attention (domain of CASI), digit span (forward), GDS, ADL, and QoL. Correlations among neuropsychological variables, depressive symptoms, IADL, ADL, and QoL in mild dementia and a-MCI are shown in Tables 3 and 4 (Demographics that were not associated with the QoL in both groups were not shown in the Table). The domains of CASI, the FP, digit span forward and backward were not correlated with the QoL in mild dementia, whereas, in contrast, only language and domain of CASI was correlated with the QoL in a-MCI ($r = 0.39$, $P < 0.05$, are not shown in Table).

The present study aimed to understand the extent to which neuropsychological variables, depressive symptoms, ADL, and IADL were related to the patient's QoL. Four multiple regression analyses were performed, which are shown in Table 5.

Table 1: Sociodemographic characteristics of mildly demented patients and a-MCI participants

	Mean±SD/*n*/%		*P*
	Demented patients *n*=37	a-MCI participants *n*=30	
Age (years)	77.7±8.6	77.6±9.1	0.94
Education (years)	5.9±4.4	8.8±4.0	0.007**
Sex (%)			
Male	12 (32)	17 (57)	0.04*
Female	25 (68)	13 (43)	
Religion (%)			
Buddhist and Taoists	14 (37.9)	13 (43.3)	0.09
Christians	5 (13.5)	9 (30.0)	
No religion	18 (48.6)	8 (26.7)	
Place of residence (%)			
Live alone in community	3 (8.1)	2 (6.7)	0.48
Retirement home	4 (10.9)	1 (3.3)	
Live with family in community	30 (81)	27 (90)	
Physical disorder (%)			
None	10 (27.1)	11 (36.7)	0.71
Diabetes	12 (32.4)	9 (30)	
Hypertension	13 (35.1)	10 (33.3)	
Cancer	2 (5.4)	0 (0)	

a-MCI = Single-domain amnestic mild cognitive impairment. *P<0.05; **P<0.01

Table 2: Clinical characteristics of patient group and a-MCI group

	Patient group *n*=37	a-MCI group *n*=30	*P*
Cognitive Abilities Screening Instrument (CASI)	50.91 (14.28)	81.93 (10.09)	<0.001*
Attention	5.81 (1.41)	6.80 (1.12)	0.003
Concentration and judgment	3.27 (2.83)	7.03 (2.70)	<0.001*
Orientation	6.59 (3.46)	15.73 (3.52)	<0.001*
Recent memory	2.40 (1.93)	7.13 (3.26)	<0.001*
CI1shown in table 1 remote remotememory	6.54 (2.85)	9.66 (0.75)	<0.001*
Language abilities	8.48 (2.12)	9.96 (0.18)	<0.001*
Visual construction	6.75 (3.49)	9.76 (0.67)	<0.001*
List-generating fluency	4.02 (2.00)	6.30 (1.98)	<0.001*
Abstraction	6.45 (2.23)	9.33 (2.24)	<0.001*
The family pictures	3.83 (3.84)	10.03 (7.29)	<0.001*
Digit span			
Forward	9.08 (2.03)	10.86 (2.81)	0.005
Backward	2.89 (2.07)	4.67 (1.89)	<0.001*
Total	11.91 (3.86)	14.90 (4.23)	<0.001*
Geriatric depression scale	7.63 (1.95)	7.13 (3.01)	0.678
Activities of daily living	87.56 (18.58)	98.16 (10.04)	0.020
The lawton instrumental activities of daily living scale	11.94 (5.03)	21.43 (3.81)	<0.001*
Quality of life-alzheimer's disease	31.05 (4.43)	35.96 (6.71)	0.004

*P<0.001 (Bonferroni corrected). Note. The data are expressed as mean (standard deviation). a-MCI = Single-domain amnestic mild cognitive impairment

As summarized in Table 5, depressive symptoms emerged to contribute significantly as a predictor of mild demented participant's QoL (adjusted $r^2 = 0.26$, $P < 0.05$). Other variables were not significant predictors of QoL. Table 5 presents the details of beta weights of contributing variables. All variables did not predict the QoL in the a-MCI group (data not shown).

DISCUSSION

The results of our study demonstrated that individuals with mild dementia displayed more impairment in almost all of the cognitive measures and in IADL compared to the a-MCI group. This study showed a significantly negative correlation between depressive symptoms and QoL in mildly demented patients. Our finding was similar to that of Bhattacharya *et al*.[39] who found that depression was inversely associated with patient-rated QoL in mild dementia. In this study, we used CASI (more quantitative domains of cognitive abilities), other than MMSE and functional abilities, all of which were expected to show an impact on QoL, but our results were unforeseen. Previous studies have also found inconsistent results. Wlodarczyk *et al*.[4] represented that MMSE scores were correlated to patient-QoL in mild to moderate dementia (the patients receive donepezil treatment). Missotten *et al*.[3] reported MMSE, ADL, IADL correlated significantly with informant-QoL of dementia (not classified subtypes) in long-term care institution. Findings by Ready *et al*.[40] indicated that QoL is moderately related with greater dementia severity. On the other hand, Hoe *et al*.[5] found no significant correlation between MMSE scores and patient-QoL in patients with moderate dementia in residential care homes. Higher QoL of moderate to severe dementia was not correlated with cognitive function at baseline, but improvement in QoL was associated with increased cognitive performances and reduced depression.[3] Thus, the discrepancy in the findings may be due to several factors, including the severity of dementia, receiving medical treatment, residence of place or not excluding confounding factors (such as psychiatric disorder, neurological disorder, severe physical disorder, and dementia-behavioral symptoms).

In contrast, we found that the QoL in a-MCI was not associated with depression, cognitive functioning,

Table 3: Correlations among neuropsychological variables, depressive symptoms, IADL, ADL and quality of life of mild dementia (n=37)

Variables	1	2	3	4	5	6	7	8
CASI	-							
FA	0.389*	-						
Digit span (forward)	0.425**	0.300	-					
Digit span (backward)	0.510**	0.252	0.356*	-				
GDS	0.023	0.226	−0.115	0.008	-			
IADL	0.290	0.191	−0.027	−0.155	0.088	-		
ADL	0.017	−0.208	−0.132	−0.212	0.057	0.573**	-	
Quality of life-alzheimer's disease	0.027	0.007	0.180	−0.108	−0.567**	0.243	0.177	-

CASI = Cognitive abilities screening instrument; FA = Family pictures; GDS = Geriatric depression scale; IADL = The Lawton instrumental activities of daily living scale; ADL = Activities of daily living. *P<0.05; **P<0.01

Table 4: Correlations among neuropsychological variables, depressive symptoms, IADL, ADL and quality of life of a-MCI (n=30)

Variables	1	2	3	4	5	6	7	8
CASI	-							
FA	0.530**	-						
Digit span (forward)	0.138	0.101	-					
Digit span (backward)	0.454*	0.282	0.385**	-				
GDS	−0.167	−0.248	0.136	0.249	-			
IADL	0.636**	0.571**	−0.033	0.321	−0.263	-		
ADL	0.578**	0.260	−0.143	0.265	−0.180	0.814**	-	
Quality of life-Alzheimer's Disease	0.104	0.236	0.252	−0.068	−0.347	0.201	0.083	-

CASI = Cognitive abilities screening instrument; FA = Family pictures; GDS = Geriatric depression scale; IADL = The Lawton instrumental activities of daily living scale; ADL = Activities of daily living; a-MCI = Single-domain amnestic mild cognitive impairment. *P<0.05; **P<0.01

and functional activities. Inconsistently, Teng *et al*.[41] indicated that depression scores were negatively correlated with subject-QoL in MCI people (mix of amnestic and nonamnestic). A recent study found that QoL was negatively associated with depressive mood and memory complaints while it was positively correlated with the self-efficacy of MCI (not classified subtypes).[42] A potential explanation may be the method selection of the MCI group. Our study cases included single-domain a-MCI which may complicate results. The differences of cognitive functioning between mild dementia and a-MCI were significant, indicating that mild dementia have lower scores in most aspects of cognition than a-MCI, except for attention (domain of CASI) and digit span (forward). People of subjective memory complaint with impaired digit showed wider cognitive decline in verbal memory and fluency compared to the normal digit span group, impaired digit span scores indicate an earlier sign for conversion of subjective memory complaint to MCI.[43] In the present study, no significant difference was shown in the digit span (forward) scores between the a-MCI and mild dementia groups, indicating that mild dementia still possessed these abilities, but not in backward digit span. Forward digit span does not have such a working memory burden as backward digit span.[44] The backward digit span involved mental double tracking in that both the memorizing and the reversing must operate simultaneously, and in this study, it seems that mildly demented people failed to possess this ability. Thus, if people with a-MCI have poor performance on backward digit span, it is possible that these people may be considered to have a higher risk of developing dementia.

Compared to a-MCI, mildly demented people also showed poorer performances on IADL. People with single-domain a-MCI performed similarly to the normal controls on IADL.[45] According to the results by Luck *et al*.,[46] MCI subtypes with IADL impairment increased the conversion rate to dementia, implying that IADL impairment is a risk factor for developing dementia. Gold[47] concluded that multiple-domain MCI was more impaired than single-domain MCI on IADL,

Table 5: Multiple regression predicting quality of life from demographic characteristics and clinical measures in mildly demented participants (n=37)

Variables	B	SE	Beta	t	P
Age	0.09	0.08	0.18	1.07	0.292
Education	0.15	0.18	0.15	0.82	0.415
Gender	3.28	1.75	0.35	1.87	0.070
Residence	0.61	1.25	0.15	0.48	0.629
CASI	0.55	0.07	0.17	0.71	0.483
FA	−0.15	0.28	−0.13	−0.53	0.600
Digit span (forward)	−0.19	2.34	−0.11	−0.08	0.936
Digit span (backward)	−0.82	2.14	−0.38	−0.38	0.702
Digit span	0.49	2.32	0.43	0.21	0.832
Depressive symptoms	−1.28	0.35	−0.56	−3.65	0.001
ADL	0.05	0.04	0.21	1.02	0.315
IADL	0.16	0.19	0.18	0.85	0.400

Model 1: Adjusted R^2=0.02; ΔR^2=0.13; (F=1.242. P=0.313). Model 2: Adjusted R^2=−0.07; ΔR^2=0.05; (F=0.39. P=0.850). Model 3: Adjusted R^2=0.26; ΔR^2=0.27; (F=13.32. P=0.001). Model 4: Adjusted R^2=0.33; ΔR^2=0.09; (F=2.50. P=0.103). CASI = Cognitive Abilities Screening Instrument; FA = Family pictures; ADL = Activities of daily living; IADL = The Lawton instrumental activities of daily living scale

and mild IADL changes in MCI may be a strong predictor for incident dementia. Although depressive symptoms were not associated with QoL in this study, Pearson's correlation showed that shopping, doing laundry, using the telephone, and handling finances (domains of IADL) were negatively associated with depressive symptoms (r = -0.36 ~ -0.73, P < 0.05), suggesting that when these independent skills weakened, people with a-MCI may feel distressed and consider it as a sign of deteriorating health status or reduced self-efficacy. The link between depressive symptoms and QoL was only found in patients with mild dementia, but not a-MCI. It is possible that people with a-MCI may perceive their cognitive decline as a normal decline and maintained a good health status (self-rated memory and perceived health status not measured in this study). Kosteniuk *et al*.[48] found that elevated depressive symptoms were negatively associated with self-rated memory and QoL for the patients with dementia, but not in the MCI group (the type of two groups were not classified).

In this study, we excluded confounding factors to investigate, which clinical measures impacted QoL in the two groups. A few limitations should be noted. The small sample size in the present study may have limited the strength of the primary findings, which require confirmation in a larger mild dementia and a-MCI sample. In this study, we used QOL-AD, which specifically examined the QoL in AD. Other measurements of QOL may be considered for future research. The cross-sectional nature of our study did not allow us to test the causal effect of clinical measures on QoL in this study. A longer follow-up is needed to test subsequent factors associated with the QoL. Another potential limiting factor was that the findings might not be referred to the different stages of dementia, subgroups of MCI and other cognitive impaired adults. Other factors, such as economic status, perceived stress level, self-efficacy, and health status, could be considered in investigating their relationship with the QoL in these two groups.

CONCLUSION

In summary, our data suggested that more depressive symptoms were associated with a lower QoL in mild dementia patients, but not in a-MCI. Our results suggest that interventions targeting depressive symptoms in mild dementia may be the most effective in improving QoL for these individuals.[49,50]

Acknowledgment

This study was supported by grant from Zuoying Branch of Kaohsiung Armed Forces General Hospital, Kaohsiung, Taiwan (ZBH103-15).

Financial support and sponsorship

Zuoying Branch of Kaohsiung Armed Forces General Hospital, Kaohsiung, Taiwan (ZBH103-15).

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Whitehouse PJ. Harmonization of dementia drug guidelines (United States and Europe): A report of the International Working Group for the harmonization for dementia drug guidelines. Alzheimer Dis Assoc Disord 2000;14 Suppl 1:S119-22.
2. Moniz-Cook E, Vernooij-Dassen M, Woods R, Verhey F, Chattat R, De Vugt M, *et al.* A European consensus on outcome measures for psychosocial intervention research in dementia care. Aging Ment Health 2008;12:14-29.
3. Missotten P, Squelard G, Ylieff M, Di Notte D, Paquay L, De Lepeleire J, *et al.* Quality of life in older Belgian people: Comparison between people with dementia, mild cognitive impairment, and controls. Int J Geriatr Psychiatry 2008;23:1103-9.
4. Wlodarczyk JH, Brodaty H, Hawthorne G. The relationship between quality of life, Mini-Mental State Examination, and the instrumental activities of daily living in patients with Alzheimer's disease. Arch Gerontol Geriatr 2004;39:25-33.

5. Hoe J, Hancock G, Livingston G, Orrell M. Quality of life of people with dementia in residential care homes. Br J Psychiatry 2006;188:460-4.
6. Woods B, Thorgrimsen L, Spector A, Royan L, Orrell M. Improved quality of life and cognitive stimulation therapy in dementia. Aging Ment Health 2006;10:219-26.
7. Farias ST, Mungas D, Reed BR, Cahn-Weiner D, Jagust W, Baynes K, *et al.* The measurement of everyday cognition (ECog): Scale development and psychometric properties. Neuropsychology 2008;22:531-44.
8. Burton CL, Strauss E, Bunce D, Hunter MA, Hultsch DF. Functional abilities in older adults with mild cognitive impairment. Gerontology 2009;55:570-81.
9. Folstein MF, Folstein SE, McHugh PR. "Mini-Mental State". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189-98.
10. Teng EL, Chui HC. The modified Mini-Mental State (3MS) Examination. J Clin Psychiatry 1987;48:314-8.
11. Graves AB, Larson EB, Edland SD, Bowen JD, McCormick WC, McCurry SM, *et al.* Prevalence of dementia and its subtypes in the Japanese American population of King County, Washington state. The Kame project. Am J Epidemiol 1996;144:760-71.
12. White L, Petrovitch H, Ross GW, Masaki KH, Abbott RD, Teng EL, *et al.* Prevalence of dementia in older Japanese-American men in Hawaii: The Honolulu-Asia aging study. JAMA 1996;276:955-60.
13. Chang JW, Pai MC, Chen HL, Guo HR, Su HJ, Lee CC. Cognitive function and blood methylmercury in adults living near a deserted chloralkali factory. Environ Res 2008;108:334-9.
14. Galasko D. An integrated approach to the management of Alzheimer's disease: Assessing cognition, function and behaviour. Eur J Neurol 1998;5 Suppl 4:9-17.
15. Mega MS, Cummings JL, Fiorello T, Gornbein J. The spectrum of behavioral changes in Alzheimer's disease. Neurology 1996;46:130-5.
16. Samus QM, Rosenblatt A, Steele C, Baker A, Harper M, Brandt J, *et al.* The association of neuropsychiatric symptoms and environment with quality of life in assisted living residents with dementia. Gerontologist 2005;45:19-26.
17. Bhattacharya S, Vogel A, Hansen ML, Waldorff FB, Waldemar G. Generic and disease-specific measures of quality of life in patients with mild Alzheimer's disease. Dement Geriatr Cogn Disord 2010;30:327-33.
18. Saczynski JS, Beiser A, Seshadri S, Auerbach S, Wolf PA, Au R. Depressive symptoms and risk of dementia: The Framingham heart study. Neurology 2010;75:35-41.
19. Goveas JS, Espeland MA, Woods NF, Wassertheil-Smoller S, Kotchen JM. Depressive symptoms and incidence of mild cognitive impairment and probable dementia in elderly women: The women's health initiative memory study. J Am Geriatr Soc 2011;59:57-66.
20. Byers AL, Covinsky KE, Barnes DE, Yaffe K. Dysthymia and depression increase risk of dementia and mortality among older veterans. Am J Geriatr Psychiatry 2012;20:664-72.
21. Khoo SA, Chen TY, Ang YH, Yap P. The impact of neuropsychiatric symptoms on caregiver distress and quality of life in persons with dementia in an Asian tertiary hospital memory clinic. Int Psychogeriatr 2013;25:1991-9.
22. Wilms HU, Riedel-Heller SG, Angermeyer MC. Limitations in activities of daily living and instrumental activities of daily living capacity in a representative sample: Disentangling dementia-and mobility-related effects. Compr Psychiatry 2007;48:95-101.
23. Fuh JL, Wang SJ. Assessing quality of life in Taiwanese patients with Alzheimer's disease. Int J Geriatr Psychiatry 2006;21:103-7.
24. Ready RE, Ott BR, Grace J. Insight and cognitive impairment: Effects on quality-of-life reports from mild cognitive impairment and Alzheimer's disease patients. Am J Alzheimers Dis Other Demen 2006;21:242-8.
25. World Health Organization. Dementia: A Public Health Priority. Geneva: World Health Organization; 2012.
26. Whitehouse PJ. Harmonization of dementia drug guidelines (United States and Europe): A report of the international working group for the harmonization for dementia drug guidelines. Alzheimer Dis Assoc Disor 2000;14:119-22.
27. Moniz-Cook E, Vernooij-Dassen M, Woods R, Verhey F, Chattat R, De Vugt M, *et al*. A European consensus on outcome measures for psychosocial intervention research indementia care. Aging Ment Health 2008;12:14-29.
28. Schneider JA, Arvanitakis Z, Leurgans SE, Bennett DA. The neuropathology of probable Alzheimer disease and mild cognitive impairment. Ann Neurol 2009;66:200-8.
29. Spitzer R, Williams J, Gibbon M, First M. Structured Clinical Interview for DSM-IV. New York: Biometrics Research; 1994.
30. Petersen RC. Mild cognitive impairment clinical trials. Nat Rev Drug Discov 2003;2:646-53.
31. Lin KN, Wang PN, Liu HC, Teng EL. Cognitive abilities screening instrument, Chinese version 2.0 (CASI C-2.0): Administration and clinical application. Acta Neurol Taiwan 2012;21:180-9.

32. Logsdon RG, Gibbons LE, McCurry SM, Teri L. Assessing quality of life in older adults with cognitive impairment. Psychosom Med 2002;64:510-9.
33. Wechsler D. WMS-III Administration and Scoring Manual. San Antonio, TX: The Psychological Corporation, Harcourt Brace Jovanovich; 1997.
34. Sheikh JI, Yesavage JA. Geriatric Depression Scale (GDS): Recent evidence and development of a shorter version. Clin Gerontol 1986;5:165-73.
35. Collin C, Wade DT, Davies S, Horne V. The barthel ADL index: A reliability study. Int Disabil Stud 1988;10:61-3.
36. Lawton MP, Brody EM. Assessment of older people: Self-maintaining and instrumental activities of daily living. Gerontologist 1969;9:179-86.
37. Morris JC. The Clinical Dementia Rating (CDR): Current version and scoring rules. Neurology 1993;43:2412-4.
38. Guo NW, Liu HC, Wong PF, Liao KK, Yan SH, Lin KP, *et al*. Chinese version and norms of Mini-Mental State Examination. J Rehabil Med 1988;16:52-9.
39. Bhattacharya S, Vogel A, Hansen ML, Waldorff FB, Waldemar G. Genetic and disease-specific measures of quality of life in patients with mild Alzheimer's disese. Dement Geriatr Cogn Disord 2010;30:327-33.
40. Ready RE, Ott BR, Grace J, Fernandez I. The cornell-brown scale for quality of life in dementia. Alzheimer Dis Assoc Disord 2002;16:109-15.
41. Teng E, Tassniyom K, Lu PH. Reduced quality-of-life ratings in mild cognitive impairment: Analyses of subject and informant responses. Am J Geriatr Psychiatry 2012;20:1016-25.
42. Maki Y, Yamaguchi T, Yamagami T, Murai T, Hachisuka K, Miyamae F, *et al.* The impact of subjective memory complaints on quality of life in community-dwelling older adults. Psychogeriatrics 2014;14:175-81.
43. Kurt P, Yener G, Oguz M. Impaired digit span can predict further cognitive decline in older people with subjective memory complaint: A preliminary result. Aging Ment Health 2011;15:364-9.
44. Black FW. Digit repetition in brain-damaged adults: Clinical and theoretical implications. J Clin Psychol 1986;42:770-82.
45. Tam CW, Lam LC, Chiu HF, Lui VW. Characteristic profiles of instrumental activities of daily living in Chinese older persons with mild cognitive impairment. Am J Alzheimers Dis Other Demen 2007;22:211-7.
46. Luck T, Luppa M, Wiese B, Maier W, van den Bussche H, Eisele M, *et al.* Prediction of incident dementia: Impact of impairment in instrumental activities of daily living and mild cognitive impairment-results from the German study on ageing, cognition, and dementia in primary care patients. Am J Geriatr Psychiatry 2012;20:943-54.
47. Gold DA. An examination of instrumental activities of daily living assessment in older adults and mild cognitive impairment. J Clin Exp Neuropsychol 2012;34:11-34.
48. Kosteniuk JG, Morgan DG, O'Connell ME, Crossley M, Kirk A, Stewart NJ, *et al.* Prevalence and covariates of elevated depressive symptoms in rural memory clinic patients with mild cognitive impairment or dementia. Dement Geriatr Cogn Dis Extra 2014;4:209-20.
49. Kverno KS, Black BS, Nolan MT, Rabins PV. Research on treating neuropsychiatric symptoms of advanced dementia with non-pharmacological strategies, 1998-2008: A systematic literature review. Int Psychogeriatr 2009;21:825-43.
50. Moyle W, Hsu MC, Lieff S, Vernooij-Dassen M. Recommendations for staff education and training for older people with mental illness in long-term aged care. Int Psychogeriatr 2010;22:1097-106.