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Longitudinal changes in quality of life among elderly people with and without dementia

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ABSTRACT

Objective: To study longitudinal changes in the quality of life (QoL) in persons with and without dementia, and explore the factors associated with baseline QoL and changes of QoL over the follow-up period.

Design: Prospective longitudinal study.

Setting: Data were collected from 17 municipalities in Norway in the period from January 2009 to August 2012. A total of 412 persons were included, 254 (61.7 %) persons without dementia and 158 (38.3 %) with dementia at baseline.

Subjects: Persons 70 years of age or older, receiving municipal care services. Main outcome measures include the following: self-rated and proxy-rated QoL over a period of 18 months, cognitive status, functional status, neuropsychiatric symptoms, and demographics.

Results: Longitudinal changes in QoL were small, despite changes in clinical variables. Proxy ratings of patients QoL were lower than the patients' own ratings. Belonging to a group with low QoL trajectory was associated with symptoms of depression, reduced physical and instrumental functioning, and more severe dementia.

Conclusion: Patients and proxies evaluated the patients' QoL differently and QoL did not necessarily correspond with deterioration in clinical parameters. To prevent impaired QoL, we need to address identified factors and keep an approach open to the individual perceptions of QoL.

Key words: quality of life, dementia, municipal care, longitudinal, elderly

Introduction

Dementia is a chronic condition caused by progressive changes in the brain, with no effective cure. The brain changes lead to loss of memory and other cognitive functions, and patients may experience distressing neuropsychiatric symptoms (NPS).

As much of our efforts aim at alleviating the symptoms of dementia, measures of quality of life (QoL) are being increasingly used as outcome scores in clinical practice and research (Thorgrimsen *et al.*, 2003).

In recent years, research on QoL in dementia has evolved considerably with the development and use of disease-specific QoL assessments (Brod *et al.*, 1999; Logsdon *et al.*, 2002; Smith *et al.*, 2005). A 2009 summary of studies showed a consistent association between QoL and depression in dementia, while clinical and sociodemographic characteristics were associated only weakly or not at all with QoL (Banerjee *et al.*, 2009).

Lately, a number of studies have been conducted to uncover QoL changes over time, QoL predictors, and agreement between patient and proxy ratings of QoL in persons with dementia. Results indicate that patient-rated QoL remains fairly stable over

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time and the course of the disease, while proxy ratings of patient QoL are lower and decline over time and across disease stages (Missotten *et al.*, 2007; Tatsumi *et al.*, 2009; Bosboom *et al.*, 2012, 2013; Huang *et al.*, 2015). However, most previous studies are based on small sample sizes up to about 100 participants. Many studies lack controls, and only a few studies have a longitudinal design with longer observation periods than 12 months.

In this study, we aimed at investigating longitudinal changes in patient- and proxy-rated QoL and determining the differences in QoL between persons with and without dementia. Furthermore, we wanted to explore the factors that were associated with changes in QoL during the observation period.

Methods

This was a longitudinal study of a subsample from the CONSIC-study that followed 1,000 home-dwelling individuals with three assessments over a period of 36 months. The sample was recruited from 19 municipalities, both rural and urban, in five counties in eastern part of Norway. To be considered for participation the candidates had to be 70 years and over receiving some kind domiciliary care and having a next of kin who saw them at least once a week. After a random selection was made, 1,795 eligible candidates were contacted, resulting in a final sample of 1,000 people (Wergeland *et al.*, 2014). In the CONSIC-study, QoL was not measured at baseline (BL) but only at an 18-month follow-up (FU), and at a 36-month FU. We included all 412 individuals for whom both QoL assessments were completed. A flowchart of the participants is presented in Figure 1.

Data were collected in the participants' homes and interviews were conducted separately for participants and their proxies. Trained healthcare workers collected data, and participants were examined between January 2009 and August 2012. For more details regarding the data collection process, see Wergeland *et al.* (2014).

Besides demographic data and cohabitation status, the following clinical data were obtained:

Cognitive impairment: Participants were classified as no cognitive impairment, mild cognitive impairment (MCI) according to the Winblad criteria (Winblad *et al.*, 2004), or dementia according to the International Statistical Classification of Diseases and Related Health Problems (ICD-10) criteria (World Health Organization, 1992). The classification was done independently by two experts (GS and SB), based on collected information about cognitive function, activities of daily living (ADL) function, and NPS. If the two experts did not reach consensus, a third expert was consulted. For the analyses in the present study, patients without cognitive impairment and patients with MCI were merged into the category "no dementia."

Quality of Life in Alzheimer's Disease (QoL-AD): It is a dementia-specific instrument assessing QoL. The QoL-AD contains 13 items covering physical health, energy, mood, living situation, memory, family, marriage, friends, self as a whole, ability to do chores around the house, ability to do things for fun, money, and life as a whole (Logsdon *et al.*, 2002). Each item is rated from 1 (poor) to 4 (excellent), resulting in a sum score ranging from 13 to 52. The QoL-AD scale is widely used to assess QoL in patients with dementia. It is recommended because of good psychometric properties in varied cultural settings (Logsdon *et al.*, 2002; Revell *et al.*, 2009; Gomez-Gallego *et al.*, 2014), and has performed well on validity and reliability tests (Logsdon *et al.*, 2002; Thorgrimsen *et al.*, 2003; Gomez-Gallego *et al.*, 2014). The QoL-AD was administered separately to the participants and their proxies. The participants evaluated their own QoL, while the proxies were asked to evaluate the QoL of the participants based on how they believed the participants would evaluate their own QoL. If not more than three items were missing, values were imputed by determining the empirical distribution for each item in the scale and drawing a random number from that distribution for each missing value. To assess dimensions of QoL-AD, we included three subscales previously identified by Revell *et al.* (2009). The dimensions include physical well-being containing the items such as physical health, energy, ability to do chores, and ability to do things for fun; social well-being containing the items such as living situation, family, marriage, friends, and money; psychological well-being containing the items such as mood, memory, self, and life as a whole.

General Medical Health Rating (GMHR): It is a four-category, reliable, and valid global bedside assessment tool staging the severity of physical health (Lyketsos *et al.*, 1999). The score is based on an overall assessment by the caregiver.

Physical Self-Maintenance Scale (PSMS): It is a scale consisting of six items to evaluate functional status in ADL (Lawton and Brody, 1969). Each item is scored from "1" (independent) to "5" (totally dependent), and a mean score is calculated based on the total score divided by six.

Instrumental activities of daily living (IADL): It includes eight items (Lawton and Brody, 1969). Each item is scored "0" (dependent) or "1"

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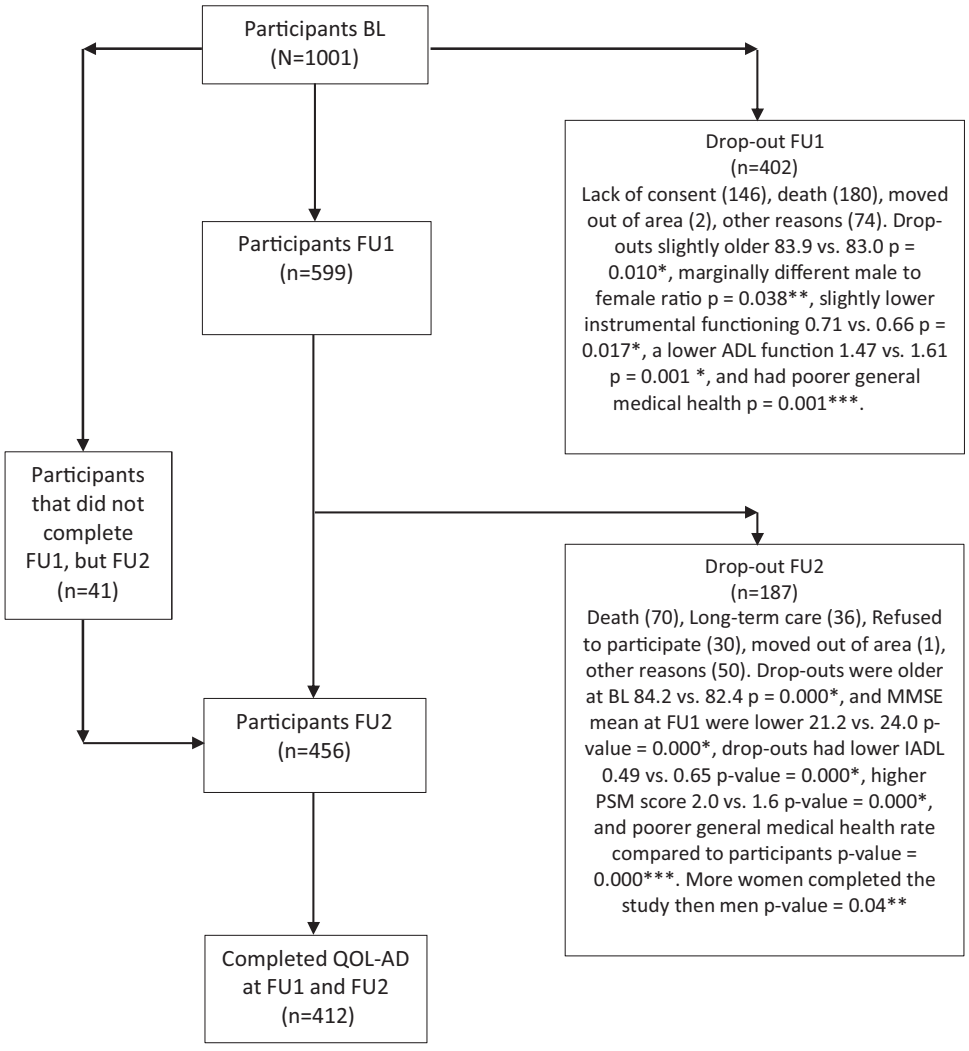

Figure 1. Flow-chart of participant inclusion and drop-out through the study.

(independent), and a mean score is calculated based on the total score divided by eight. For women, all eight items were included in the sum score, while we excluded the items "food preparation," "housekeeping," and "laundry" for men, as these items were not applicable for many male participants in this study (Lawton and Brody, 1969; Wattmo *et al.*, 2013). We calculated a sum score and divided it by the number of items evaluated, thus obtaining a score ranging from 0 = completely dependent to 1 = completely independent in terms of IADL.

Mini-Mental State Examination (MMSE): It is a screening tool that measures cognitive impairment (Folstein '*et al.*, 1975). The maximum score is 30 points.

Clinical Dementia Rating-Sum of Boxes score (CDR-SOB): It is obtained by applying the six-item CDR scale and then summing each of the domain box scores so as to end up with a total score ranging from 0 to 18. The higher the score, the more severe the dementia (O'Bryant *et al.*, 2008).

Neuropsychiatric Inventory (NPI): It assesses NPS (Cummings *et al.*, 1994). The scale considers 12 types of NPS. The presence of symptoms and their frequency and intensity are assessed based on an interview with the closest carer. A higher score denotes more severe NPS. Three

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sub-syndromes of NPI were identified (NPI-Agitation, NPI-Psychosis, and NPI-Affective) based on a principal component analysis with direct oblimin rotation. For details, see Ydstebo *et al.* (2015).

Cornell Scale for Depression in Dementia (CSDD): It is a 19-item dementia-specific depression screening tool. Each item is scored zero (absent), one (mild), two (severe), or unable to evaluate, and the total score (0–38) is calculated by adding the item scores (Alexopoulos *et al.*, 1988).

Statistical analysis

Demographic factors and clinical symptoms were described by means and standard deviations (SD). Categorical variables are described as frequencies and percentages. The group differences were analyzed by Student's *t*-test (with no equal variance assumption) for continuous variables and by χ^2 or Fisher's exact test for categorical variables. The distribution of continuous variables was assessed by inspecting the histograms.

By means of an exploratory approach, group-based trajectory models using censored normal mixture were estimated to identify potential distinct homogeneous subgroups of participants, following similar profiles from BL to FU in patient- and proxy-rated QoL-AD. The aim was to describe the longitudinal change within each subgroup as well as to assess the differences among the groups. According to this approach, the groups are identified in a post-hoc matter, where the group belonging is determined based on individual profiles. Several statistical criteria were applied in the process. Akaike's Information Criterion (AIC) and Bayesian Information Criterion (BIC) were used to ascertain the best-fitting models, where smaller values of AIC and BIC denote better fit. Other criteria were reasonable sample sizes in each group, non-overlapping 95% confidence intervals (CI), and average within-group probability larger than 0.7. The group-based trajectory models were estimated using plugin STATA command TRAJ (Jones and Nagin, 2013).

The agreement between groups of patients and their proxies was assessed by kappa statistic applying guidelines for interpretation suggested by Cicchetti (1994), where a statistic below 0.40 is considered to be of poor clinical significance, while 0.40–0.59 is fair, 0.60–0.74 is good, and 0.75–1.00 indicates excellent clinical significance.

Bivariate and multiple nominal regression models were estimated to identify potential characteristics associated with group membership. The interaction terms between all variables and the dichotomous variable dementia were included into the multiple-regression models. Models were further reduced by AIC. Significant interactions imply that there are differences between persons with and without dementia regarding associations between group membership and clinical and/or demographic characteristics.

The results for QoL ratings were presented as odds ratios (OR) with the corresponding 95% CI and p values. ORs were calculated separately for persons with and without dementia for variables included into interaction terms. However, as the analyses generated vast amounts of information, main findings for the subdimensions of QoL-AD are only reported in text. The Statistical Package for Social Science (SPSS) version 23 for Windows and STATA version 14 were used for the data analysis.

Ethical considerations

The study was approved by the regional ethics committee (registration number 2010/119). All participants gave informed written consent.

Results

Study population

A total of 412 participants were included, 254 (61.7%) persons without dementia and 158 (38.3%) with dementia at BL. The demographic and clinical characteristics of the study population are presented in Table 1. Between BL and FU, 103 participants were admitted to permanent nursing home stay, of whom 92 (89%) had dementia at BL.

Three trajectory groups based on the patients' QoL scores at BL and the changes in QoL over time (G1 $n = 80$, G2 $n = 249$, G3 $n = 83$) and three trajectory groups based on the proxies' QoL scores at BL and the changes in QoL over time (G1 $n = 165$, G2 $n = 199$, G3 $n = 48$) were identified, each following a distinct trajectory (Figure 2). The BL QoL mean scores for the patients were G1 = 31.1 (SD = 9.8), G2 = 38.2 (SD = 12.5), G3 = 44.3 (SD = 9.6), and for the proxies; G1 = 30.6 (SD = 12.2), G2 = 38.5 (SD = 13.5), G3 = 43.0 (SD = 10.3). For both patient- and proxy-rated QoL, G1 represents the participants with the lowest QoL score at BL. The QoL score was significantly different between the three groups, as judged by non-overlapping 95% CI, both for patients and proxies. The average probabilities for within-group membership were all above 0.80. The QoL remained stable in patient-rated G1 and G3, while there was a statistically significant reduction in the QoL scored by the patients in G2 by a mean of 1.04 points (p = 0.008) (Figure 2). Changes in proxy-rated QoL were not significant in any of the

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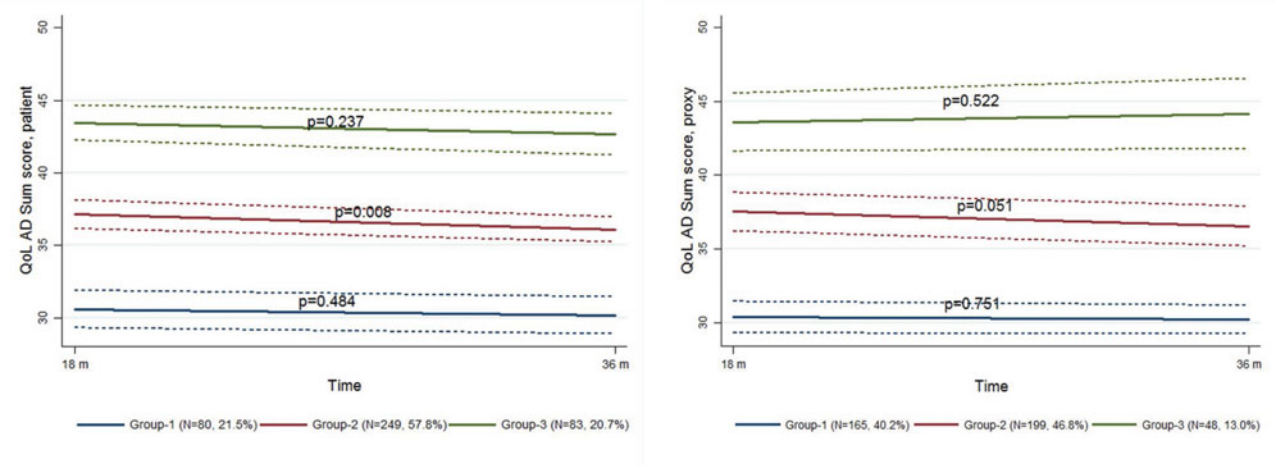
Table 1. Demographic and clinical variables for all participants, and comparisons of participants with and without dementia at BL

	TOTAL, $N = 412$		NO DEMENTIA, $N = 254$, SD		DEMENTIA, $N = 158$		p VALUE
Age (SD)	83.9	(5.4)	83.0	(5.1)	85.4	(5.4)	<0.001**
Gender female (%)	301	(73.1)	190	(74.8)	111	(70.3)	0.361*
Living with relative (%)	166	(40.7)	74	(29.1)	92	(59.7)	<0.001*
Admitted to NH before FU (%)	103	(25)	11	(4.3)	92	(58.2)	<0.001*
Physical health (GMHR) (%)							
–Poor	36	(9.2)	21	(8.7)	15	(9.9)	<0.001**
–Fair	153	(39.0)	76	(31.5)	77	(51.0)	
–Good	159	(40.6)	110	(45.6)	49	(32.5)	
–Excellent	44	(11.2)	34	(14.1)	10	(6.6)	
PSMS (SD)	1.6	(0.7)	1.3	(0.5)	2.0	(0.70)	<0.001**
IADL (SD)	0.7	(0.3)	0.8	(0.2)	0.4	(0.25)	<0.001***
Cognitive status MMSE (SD)	24.0	(5.6)	27.5	(2.0)	18.1	(4.7)	<0.001**
CDR-SOB	3.8	(4.4)	1.2	(1.6)	7.8	(4.2)	<0.001**
QoL-AD (SD)							
Patient-reported	37.0	(4.5)	37.6	(5.5)	36.1	(5.4)	0.010**
Physical well-being	9.2	(2.6)	9.3	(2.6)	8.9	(2.7)	0.126**
Social well-being	16.4	(2.4)	16.7	(2.2)	15.8	(2.7)	0.001**
Psychological well-being	11.3	(2.1)	11.6	(2.1)	10.8	(2.1)	0.001**
Proxy-reported	35.5	(6.1)	37.3	(5.9)	32.7	(5.5)	<0.001**
Physical well-being	8.9	(2.9)	9.6	(2.9)	7.8	(2.5)	<0.001**
Social well-being	16.1	(2.3)	16.5	(2.1)	15.5	(2.4)	<0.001**
Psychological well-being	10.5	(2.5)	11.2	(2.2)	9.4	(2.5)	<0.001**
Neuropsychiatric symptoms NPI (SD)	6.6	(10.8)	3.5	(6.5)	11.4	(13.9)	<0.001**
NPI subsyndromes (SD)							
–Agitation	2.2	(4.6)	2.3	(0.8)	4.3	(6.3)	<0.001**
–Psychosis	0.6	(2.0)	0.1	(0.6)	1.3	(3.0)	<0.001**
–Affective	2.6	(4.8)	1.7	(3.8)	4.0	(5.8)	<0.001**
CSDD (SD)	4.1	(4.7)	3.0	(3.8)	5.9	(5.3)	<0.001**

SD = Standard deviation; NH = nursing home; FU = follow-up; GMHR = General Medical Health Rating; PSMS = Physical Self-Maintenance Scale; IADL = Instrumental activity of daily living; MMSE = Mini-Mental State Examination; CDR-SOB = Clinical Dementia Rating-Sum of Boxes; QoL-AD = Quality of Life in Alzheimer's Disease; NPI = Neuropsychiatric Inventory; NPI-Agitation = agitation/aggression, euphoria, disinhibition, aberrant motor behavior, and irritability, NPI-Psychosis = delusions and hallucinations, NPI-Affective = depression, anxiety, and apathy; CSDD = Cornell Scale for Depression in Dementia.
*Fisher's exact test, **Student's t-test (equal variances not assumed), ***χ^2-test.



P-values refer to change in QoL from baseline to FU within each group.

Figure 2. Trajectories for 18-months change in patient- and proxy-rated QoL-AD. p values refer to change in QoL from baseline to follow-up within each group.

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Table 2. Baseline data in the different trajectory groups (cases with at least one missing covariate excluded). G1 = group with lowest QoL

PATIENT-RATED QOL	G1 ($N = 65$)	G2 ($N = 204$)	G3 ($N = 74$)
Dementia, *n* (%)	28 (43.1)	88 (43.1)	15 (20.3)
Age, mean (SD)	81.9 (5.0)	82.1 (5.2)	82.8 (5.5)
Living alone, *n* (%)	41 (63.1)	115 (56.4)	53 (71.6)
MMSE, mean (SD)	23.2 (5.7)	23.4 (5.8)	26.0 (5.0)
GMHR, *n* (%)			
Poor/fair	44 (67.7)	102 (50.0)	10 (13.5)
Good/excellent	21 (32.3)	102 (50.0)	64 (86.5)
CDR-SOB, mean (SD)	4.3 (4.0)	4.1 (4.4)	1.7 (3.3)
IADL, mean (SD)	0.60 (0.26)	0.62 (0.31)	0.79 (0.24)
PSMS, mean (SD)	1.81 (0.74)	1.60 (0.66)	1.26 (0.43)
CSDD, mean (SD)	6.09 (5.58)	3.95 (4.60)	2.27 (2.85)
NPI-Agitation, mean (SD)	2.46 (5.39)	2.43 (5.03)	1.09 (2.93)
NPI-Psychosis, mean (SD)	0.62 (2.45)	0.74 (2.28)	0.18 (1.00)
NPI-Affective, mean (SD)	4.00 (6.26)	2.91 (4.92)	1.01 (2.45)
Proxy-rated QoL	G1 ($N = 137$)	G2 ($N = 160$)	G3 ($N = 46$)
Dementia, *n* (%)	80 (58.4)	46 (28.7)	5 (10.9)
Age, mean (SD)	81.6 (5.3)	82.9 (5.1)	81.7 (5.4)
Living alone, *n* (%)	74 (54.0)	101 (63.1)	34 (73.9)
MMSE, mean (SD)	21.9 (6.1)	24.7 (5.2)	27.4 (3.2)
GMHR, *n* (%)			
Poor/fair	82 (59.9)	64 (40.0)	10 (21.7)
Good/excellent	55 (40.1)	96 (60.0)	36 (78.3)
CDR-SOB, mean (SD)	5.74 (4.33)	2.65 (3.68)	0.45 (1.40)
IADL, mean (SD)	0.51 (0.29)	0.71 (0.27)	0.89 (0.17)
PSMS, mean (SD)	1.84 (0.70)	1.44 (0.59)	1.17 (0.38)
CSDD, mean (SD)	6.39 (5.32)	2.86 (3.55)	0.76 (1.21)
NPI-Agitation, mean (SD)	3.37 (5.97)	1.64 (3.87)	0.30 (1.33)
NPI-Psychosis, mean (SD)	1.15 (2.92)	0.29 (1.37)	0.0 (0.0)
NPI-Affective, mean (SD)	4.91 (6.26)	1.58 (3.23)	0.07 (0.25)

QoL = Quality of life; SD = standard deviation; MMSE = Mini-Mental State Examination; GMHR = General Medical Health Rating; CDR-SOB = Clinical Dementia Rating-Sum of Boxes; IADL = Instrumental activity of daily living; PSMS = Physical Self-Maintenance Scale; CSDD = Cornell Scale for Depression in Dementia; NPI = Neuropsychiatric Inventory; NPI-Agitation = agitation/aggression, euphoria, disinhibition, aberrant motor behavior, and irritability; NPI-Psychosis = delusions and hallucinations; NPI-Affective = depression, anxiety, and apathy.

three groups. The agreement between groups of patients and proxies was poor with a κ of 0.22.

Table 2 presents descriptive statistics for the patients in each trajectory group. Bivariate analyses for patient-rated QoL, as presented in Table 3, show that the chances of belonging to G1 versus G3 were higher for persons with a dementia diagnosis, more cognitive impairment (MMSE), more severe dementia (CDR-SOB), lower instrumental functioning (IADL), and more affective symptoms (NPI-Affective). The chances of belonging to G1 versus G2 and G1 versus G3 were higher for persons with poor/fair physical health (GMHR), lower functional ADL (PSMS), and more depressive symptoms (CSDD).

Bivariate analyses for proxy-rated QoL (Table 3) show that the chances of belonging to G1 versus G2 and G1 versus G3 were higher for persons with a dementia diagnosis, more cognitive impairment (MMSE), poor/fair physical health (GMHR), more severe dementia (CDR-SOB), lower instrumental functioning (IADL), lower functional ADL (PSMS), more depressive symptoms (CSDD), more agitation (NPI-Agitation), and more affective symptoms (NPI-Affective), while the chances of belonging to G1 versus G2 were higher for persons with lower age and more psychosis (NPI-Psychosis), while the chances of belonging to G1 versus G3 were lower for persons living alone.

Nominal regression analysis in patient-rated QoL

Multivariate analyses presented in Table 3 show that more depressive symptoms (CSDD) were associated with the higher chances of belonging to G1

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Table 3. Results from bivariate and multiple nominal regression of trajectories for patient- and proxy-rated QoL-AD. Multiple models were reduced by AIC, odds ratios are presented for persons with and without dementia for variables which were a part of interaction with dementia diagnosis

	PATIENT-RATED QOL						PROXY-RATED QOL					
			MULTIPLE MODELS						MULTIPLE MODELS			
	BIVARIATE MODELS		WITHOUT DEMENTIA		DEMENTIA		BIVARIATE MODELS		WITHOUT DEMENTIA		DEMENTIA	
VARIABLES	OR (95% CI)	p VALUE	OR (95% CI)	p VALUE	OR (95% CI)	p VALUE	OR (95% CI)	p VALUE	OR (95% CI)	p VALUE	OR (95% CI)	p VALUE
Dementia												
Group-1 – ref.	1						1	-				
Group-2	1.02 (0.57; 1.77)	0.993					0.29 (0.18; 0.47)	<0.001				
Group-3	0.34 (0.16; 0.71)	0.005					0.09 (0.03; 0.23)	<0.001				
Age[1]												
Group-1 – ref.	1	–					1	–	1	–	1	–
Group-2	1.01 (0.96;1.06)	0.763					1.05 (1.01;1.10)	0.027	1.14 (1.06;1.23)	0.001	1.03 (0.96;1.11)	0.443
Group-3	1.04 (0.97;1.10)	0.289					1.01 (0.94;1.07)	0.881	1.07 (0.96;1.18)	0.214	1.34 (1.06;1.69)	0.014
Living alone												
Group-1 – ref.	1	–					1	–				
Group-2	0.76 (0.43;1.35)	0.342					1.46 (0.91;2.32)	0.113				
Group-3	1.48 (0.72;3.02)	0.285					2.41 (1.15;5.06)	0.020				
MMSE[1]												
Group-1 – ref.	1	–					1	–				
Group-2	1.01 (0.96;1.05)	0.806					1.09 (1.04;1.14)	<0.001				
Group-3	1.11 (1.04;1.19)	0.003					1.32 (1.18;1.47)	<0.001				
GMHR												
Poor/fair												
Group-1 – ref.	1	–	1	–	1	–	1	–				
Group-2	0.48 (0.27;0.86)	0.014	0.69 (0.30;1.59)	0.387	0.30 (0.09;0.93)	0.037	0.45 (0.28;0.71)	0.001				
Group-3	0.08 (0.03;0.17)	<0.001	0.24 (0.08;0.74)	0.013	0.01 (0.00;0.11)	<0.001	0.19 (0.09;0.41)	<0.001				
Good/excellent – ref.	1	–	1	–	1	–	1	–				
CDR-SOB[1]												
Group-1 – ref.	1	–	1	–	1	–	1	–	1	–	1	–
Group-2	0.99 (0.93; 1.05)	0.670	0.89 (0.64;1.22)	0.452	1.06 (0.90;1.25)	0.509	0.83 (0.78; 0.89)	<0.001	0.70 (0.55;0.90)	0.005	0.94 (0.86;1.04)	0.248
Group-3	0.81 (0.73; 0.90)	<0.001	0.38 (0.21;0.30)	0.002	1.19 (0.88;0.26)	0.259	0.40 (0.27; 0.59)	<0.001	0.22 (0.10;0.49)	<0.001	0.72 (0.51;1.02)	0.062
IADL[1]												
Group-1 – ref.	1	–	1	–	1	–	1	–	1	–	1	–
Group-2	1.15 (0.46; 2.92)	0.763	1.08 (0.82;1.42)	0.578	0.73 (0.56;0.96)	0.022	11.8 (4.9; 28.1)	<0.001				
Group-3	12.8 (3.45; 47.5)	<0.001	1.03 (0.72;1.49)	0.861	0.63 (0.39;1.04)	0.069	1274 (132;12295)	<0.001				
PSMS[1]												
Group-1 – ref.	1		1	–	1	–	1	–				
Group-2	0.66 (0.45; 0.97)	0.034	1.02 (0.92;1.12)	0.754	0.88 (0.81;0.96)	0.005	0.39 (0.26; 0.57)	<0.001				
Group-3	0.17 (0.08; 0.36)	<0.001	0.97 (0.80;1.17)	0.749	0.79 (0.66;0.94)	0.008	0.06 (0.02; 0.19)	<0.001				

Table 3. Continued

	PATIENT-RATED QOL						PROXY-RATED QOL					
			MULTIPLE MODELS						MULTIPLE MODELS			
	BIVARIATE MODELS		WITHOUT DEMENTIA		DEMENTIA		BIVARIATE MODELS		WITHOUT DEMENTIA		DEMENTIA	
VARIABLES	OR (95% CI)	p VALUE	OR (95% CI)	p VALUE	OR (95% CI)	p VALUE	OR (95% CI)	p VALUE	OR (95% CI)	p VALUE	OR (95% CI)	p VALUE
CSDD[1,2]												
Group-1 – ref.	1		1	–	1	–	1				–	
Group-2	0.92 (0.87; 0.97)	0.003	0.91 (0.84; 0.99)	0.026	0.83 (0.77; 0.88)	<0.001	0.92 (0.85; 1.00)				0.042	
Group-3	0.81 (0.74; 0.89)	<0.001	0.92 (0.82; 1.04)	0.178	0.51 (0.40; 0.65)	<0.001	0.77 (0.61; 0.98)				0.037	
NPI-Agitation[1]												
Group-1 – ref.	1		1	–	1	–	1	–				
Group-2	1.00 (0.95; 1.06)	0.967	1.05 (0.88;1.25)	0.616	1.04 (0.96;1.13)	0.304	0.93 (0.88; 0.98)	0.006				
Group-3	0.91 (0.83; 1.00)	0.062	1.32 (1.04;1.68)	0.021	0.96 (0.81;1.15)	0.679	0.67 (0.50; 0.90)	0.008				
NPI-Psychosis[1]												
Group-1 – ref.	1						1	–				
Group-2	1.03 (0.90; 1.17)	0.707					0.81 (0.70; 0.93)	0.004				
Group-3	0.82 (0.62; 1.07)	0.139					0.23 (0.02; 2.45)	0.221				
NPI-Affective[1,3]												
Group-1 – ref.	1		1		–	1	–	1	–	1		–
Group-2	0.97 (0.92; 1.01)	0.154	0.98 (0.92; 1.06)		0.655	0.85 (0.80; 0.91)	<0.001	0.85 (0.76;0.95)	0.004	0.96 (0.88;1.05)		0.329
Group-3	0.82 (0.74; 0.92)	0.001	0.86 (0.75; 0.99)		0.045	0.38 (0.21; 0.67)	0.001	0.41 (0.19;0.91)	0.029	1.01 (0.61;1.68)		0.963

QoL = Quality of life; OR = odds ratio; CI = confidence interval; Coeff. = coefficient; SE = standard error; ref = reference value; MMSE = Mini-Mental State Examination; GMHR = General Medical Health Rating; CDR-SOB = Clinical Dementia Rating-Sum of Boxes; IADL = instrumental activity of daily living; PSMS = Physical Self-Maintenance Scale; CSDD = Cornell Scale for Depression in Dementia; NPI = Neuropsychiatric Inventory NPI-Agitation = agitation/aggression, euphoria, disinhibition, aberrant motor behavior, and irritability; NPI-Psychosis = delusions and hallucinations; NPI-Affective = depression, anxiety, and apathy.

[1]Odds for one-unit change.

[2]No interaction between dementia diagnosis and CSDD present, i.e. odds are the same for those without and with dementia.

[3]No interaction between dementia diagnosis and NPI-Affective among patients present, i.e. odds are the same for those without and with dementia.

versus G2, while more affective symptoms (NPI-Affective) were associated with higher chances of belonging to G1 versus G3, independently of dementia diagnosis.

Persons with dementia and poor/fair physical health (GMHR) and lower ADL functioning (PSMS) were more likely to belong to G1 versus G2 and G1 versus G3. Lower instrumental functioning (IADL) for persons with dementia increased the chances of belonging to G1 versus G2.

Among persons without dementia the chances of belonging to G1 versus G3 increased with poor/fair physical health (GMHR), a higher score on the CDR-SOB scale, and a lower score on NPI-Agitation.

Nominal regression analysis in proxy-rated QoL

As presented in Table 3, more symptoms of depression (CSDD) were associated with higher chances of belonging to G1 versus G2 and G1 versus G3, independently of dementia diagnosis.

For persons with dementia, higher age was associated with lower chances of belonging to G1 versus G3. For persons without dementia, higher age was associated with lower chances for belonging to G1 versus G2. In addition, a higher score on the CDR-SOB scale as well as more affective symptoms (NPI-Affective) were associated with higher chances of belonging to G1 versus G2 and G1 versus G3.

Discussion

This study assessed longitudinal changes in QoL in persons with and without dementia and explored the factors that were associated with changes in QoL. We found three different BL levels and trajectories of QoL in both patient- and proxy-rated QoL.

The changes in QoL scores during the 18-month observation period were, however, small and mostly non-significant.

The type of QoL-trajectory group membership was associated with the severity of the symptoms of depression, dementia severity, physical health, physical and instrumental functioning, NPI-Agitation, and age, with small variations between patient- and proxy-rated QoL-AD. However, we observed that the agreement between patient- and proxy-rated QoL-AD was poor, implying that patients and proxies assess QoL differently.

While former studies have demonstrated significant reductions in proxy-rated QoL for patients with dementia over an 18–24-month period (Lyketsos *et al.*, 2003; Tatsumi *et al.*, 2009; Bosboom *et al.*, 2013; Bosboom and Almeida, 2016; Conde-Sala *et al.*, 2016a), this was not found in our study, neither for the cohort as a whole nor for the respective trajectory groups.

We saw a statistically significant QoL reduction in only one of the patient-rated trajectory groups. The total decline in QoL was, however, small and has probably only minor clinical implications.

The lack of changes to QoL could be explained by the inclusion of a larger and more heterogenic population in our study with a broader variety in age and cognitive and functional limitations than previous studies. Considering the highly subjective nature of QoL assessments (Ready and Ott, 2003) there is also a possibility that the individuals general positive or negative life perceptions has a stronger influence than dementia on their QoL evaluation. In total, the lack of QoL changes supports a former proposition that BL QoL is more strongly associated to later QoL than to QoL changes (Conde-Sala *et al.*, 2016b).

The agreement between patient ratings and their proxy ratings regarding QoL trajectory affiliation showed a low kappa score of 0.22 (Cicchetti, 1994). Such discrepancies between patient self-ratings and proxy ratings have been reported in several previous publications (Logsdon *et al.*, 2002; Tatsumi *et al.*, 2009; Thorgrimsen *et al.*, 2003; Andrieu *et al.*, 2016). Nonetheless, Bosboom *et al.* found the agreement to be reasonably high, though proxy ratings were systematically lower than patient self-ratings (Bosboom *et al.*, 2012).

The discrepancy we found might also be – as suggested by others – a result of proxy bias from higher carer burden (Andrieu *et al.*, 2016) or carers' depression (Logsdon *et al.*, 2002), causing proxies to project their own QoL onto the participants. Unfortunately, this study design does not comprise these factors.

Another confounding factor could be that the participants' lack of insight causes an overestimation of their own QoL (Conde-Sala *et al.*, 2016a). There is also a possibility that patients undergo a process of adaption to their disability and thus perceive their QoL as higher than their proxies do (Banerjee *et al.*, 2009).

Characteristics associated with QoL

More severe depressive symptoms were associated with lower QoL in both patient- and proxy-rated QoL in our study, independent of dementia status. Also, more affective symptoms covering the items depression, anxiety, and apathy in the NPI were associated with lower QoL in patient ratings independent of dementia status and in

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proxy ratings for persons without dementia. This relation has been described in several previous studies confirming that depressive symptoms are strongly associated with QoL (Banerjee *et al.*, 2009; Tatsumi *et al.*, 2009; Bosboom *et al.*, 2012, 2013; Heggie *et al.*, 2012; Andrieu *et al.*, 2016; Conde-Sala *et al.*, 2016b). We should therefore stress the importance of addressing depression as part of our care services.

Furthermore, being in the two lowest categories of physical health (GMHR) considerably reduced the chance of belonging to the higher QoL trajectories, independent of dementia status for patient-rated QoL, indicating that physical health affects QoL regardless of cognitive functioning. Contrary to our findings, a previous study (Huang *et al.*, 2015) could not find any association with QoL and comorbidity.

Low ADL functioning (PSMS) and low instrumental functioning (IADL) were associated with lower patient-rated QoL in persons with dementia. The association between functional ability and QoL has more often been described with proxy ratings (Banerjee *et al.*, 2009; Tatsumi *et al.*, 2009). However, in more recent studies, associations between limitations in IADL and low patient-rated QoL (Andrieu *et al.*, 2016), and between poorer functional ability (ADL) and low patient-rated QoL (Conde-Sala *et al.*, 2016b) (Heggie *et al.*, 2012), could be found.

Higher age was associated with higher proxy-rated QoL independent of dementia status. This association has been reported in a previous study, where it was interpreted as representing various levels of expectation and social support with age (Banerjee *et al.*, 2006).

In contrast to previous studies (Conde-Sala *et al.*, 2014; Huang *et al.*, 2015), we found no association between dementia severity and patient-rated QoL. As suggested previously (Bosboom *et al.*, 2012; Andrieu *et al.*, 2016), persons with dementia gradually lose insight as the disease progresses; thus, a link between dementia severity and QoL in this group is less likely with patient ratings. Proxies, to the contrary, are more likely to evaluate the patient's QoL from a disease and disability perspective rather than from an individual perspective (Bosboom *et al.*, 2012; Andrieu *et al.*, 2016). However, in our study, more cognitive impairment (CDR-SOB) was associated with a lower QoL in proxy and patient-rated QoL in participants without dementia.

We also found that higher NPI-Agitation scores were associated with higher patient-rated QoL in persons without dementia. We do not fully comprehend this finding in our population but suggest that this could indicate that the NPI may not be an appropriate assessment for persons without cognitive impairments, or that this result illustrates the difference in opinions between proxy and patient ratings, as NPI was also rated by proxy.

Limitations and strengths of the study

As QoL was first evaluated 18 months after the inclusion of patients in the original CONSIC-study, there is a possibility of selection bias towards participants with better health outcomes.

Approximately, 100 participants were admitted to nursing homes between BL and FU observation, resulting in a more heterogenic study population at FU. Data on relevant domains associated with QoL changes in dementia, such as carer burden and carers' depression, could have added more depth to the analysis if they had been included in the data collection. The observation period was probably too short to catch changes in QoL over time in such a heterogenic population.

We used the QoL-AD to assess QoL in all participants, although it has only been validated for use in persons with dementia. However, only one of 13 items in the questionnaire refers to memory impairment. We therefore consider the results as sufficiently reliable to compare QoL in persons with and without dementia.

The strengths of the study were the large cohort of 412 persons that included persons with dementia as well as persons without dementia. A further advantage was the data collection organized by experts in the field. It provided a rich characterization of clinical parameters with standard outcome measures. Another plus was the QoL assessment taken from both the patients' and the proxies' points of view, with a scale well adapted for use in longitudinal studies (Selwood *et al.*, 2005).

Conclusion

In this study, we found that, despite significant changes in clinical parameters, patient- and proxy-rated QoL in an elderly population did not change substantially over a period of 18 months.

We confirmed findings from previous studies that patients and proxies evaluate the patients' QoL differently. QoL is an important aspect of person-centered care, but obviously QoL was determined not only by the clinical aspects we examined, especially in patients with dementia. Thus, we need to focus on the patients' personalities, comprising their history and culture as well as their beliefs, values, family relations, and individual perceptions of QoL.

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The foremost factors associated with lower QoL in our study sample were more severe symptoms of depression, NPI-Affective symptoms, and poorer physical health for the whole population, while low functional abilities were only associated with low QoL for persons with dementia. Efforts aiming at preventing low or decreasing QoL at any stage of dementia should, therefore, target these factors as well as keeping a person-centered approach open to the individual perceptions of QoL.

Conflicts of interest

None.

Description of authors' roles

A. E. Ydstebø designed the study and wrote the paper. S. Bergh organized the data collection and supervised the development of the paper. G. Selbæk organized the data collection and supervised the development of the paper. J. Šaltytė Benth was responsible for the statistical design of the study and for carrying out the statistical analysis. K. Brønnick supervised the development of the paper. C. Vossius supervised the design of the study and the development of the paper.

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