

Running Head: Changes in quality of life outcomes and progression of AD

The relationship between changes in quality of life outcomes and progression of Alzheimer's disease (AD): results from the Dependence in AD in England 2 (DADE2) longitudinal study

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at the time the study was conducted

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Abstract

Objective

The relationship between conventional indicators of Alzheimer's disease (AD) progression and quality of life (QoL) outcomes is unclear. Dependence on others has been recommended as a unifying construct in defining AD severity. This study examined the relationship between indicators of disease severity (including dependence) and changes in QoL and utility over 18-months.

Methods

A multi-centre, cohort study was conducted across 18 UK sites. One hundred and forty five patients with possible/probable AD and their caregivers completed assessments of disease severity (Dependence Scale, Mini-Mental State Examination, Neuropsychiatric Inventory, Disability Assessment for Dementia), dementia-specific QoL (DEMQOL, DEMQOL-Proxy) and generic health-related utility (EQ-5D) at both time points.

Results

There was evidence of individual change in QoL over 18 months, with over 50% of patients reporting either maintenance or improvement of life quality. The EQ-5D proxy suggested a mean decline in QoL whilst the DEMQOL-Proxy indicated overall improvement. In the subsample of people who self-reported QoL and utility, no mean change was evident. Changes in dependence did not explain changes on any QoL or utility outcome. There was a weak association between the EQ-5D proxy and changes in cognition, whereas changes on the DEMQOL-Proxy were partly explained by changes in behavioural disturbance.

Conclusions

The natural progression of AD over 18-months does not lead to inevitable decline in QoL or utility. There are no clear or consistent direct relationships between changes in disease severity and QoL outcomes. The impact of increasing dependence and worsening disease severity is likely buffered by a combination of psychological, social and environmental factors.

Key words: Dementia, utility, wellbeing, disease severity, DEMQOL, EQ-5D

Key messages:

- QoL and utility do not inevitably decline as dementia progresses.
- There are no clear and consistent relationships between markers of disease severity and QoL change.
- The choice of measure may lead to different conclusions about the size, direction and causes of QoL and utility change.
- A better understanding is needed of the mechanisms which allow individuals to report a maintenance or improvement of QoL and utility over time.

Introduction

Within the last decade, cohort studies have explored changes in patient and proxy reports of QoL in relation to the progression of AD. One of the most consistent findings from these studies is the lack of detectable change in QoL when measured at the group level (Selwood *et al.*, 2005; Missotten *et al.*, 2007; Hoe *et al.*, 2009; Livingston *et al.*, 2012; Heggie *et al.*, 2012). Although there is evidence of considerable variation in individual QoL ratings over periods ranging from 20 weeks (Hoe *et al.*, 2009) to 2 years (Missotten *et al.*, 2007), consistent group-level changes are not apparent for either self-report or proxy ratings of QoL. The few studies that have detected group-level decline in QoL over time have often found only small effect sizes and large individual variation, with almost half of patients reporting stable or improved levels of QoL (Lyketsos *et al.*, 2003; Vogel *et al.*, 2012). Baseline severity may have contributed to the differences observed across the longitudinal studies as the 3-year follow up study by Vogel *et al.* was conducted in patients diagnosed early in their disease, when decline may be easier to detect.

Cohort studies have also yet to provide any clarity in determining the factors associated with changes in QoL outcomes. Over a one-year period, Jonsson *et al.* (2006) found that a decline in proxy ratings of utility was associated with worsening cognition and neuropsychiatric symptoms, whilst Vogel *et al.* (2012) report that change in proxy-rated QoL over 3 years was related only to change in function. The strong influence of mood for determining changes in self-reported QoL was a key feature of a 20-week follow up in care home residents (Hoe *et al.*, 2009), whereas Livingston *et al.* (2012) reported that in an 18-month follow-up of those living with AD in the community, social relationships and mental health completely mediated the effect of disease severity on self-reported QoL.

In exploring the associations between AD severity and QoL, it is important to consider the nature and content of the measures used to indicate the progression of AD. Whilst cognition, function and behaviour are commonly the focus for clinicians, it has been noted that each of these single indicators provide somewhat limited and conflicting information on typical AD progression pathways (Loveman *et al.*, 2006). Dependence is a broader construct that reflects the level of assistance required by the person with AD and preliminary research supports associations with clinical endpoints and resource use (Brickman *et al.*, 2002; Scherer, 2008; Zhu *et al.*, 2008). It is possible that the use of a broader measure, such as dependence, may allow further evidence to emerge with regards to the association between AD progression and QoL outcomes. To date, there have only been a few studies linking dependence and QoL in AD. McLaughlin *et al.* (2010) demonstrated a moderate negative correlation between proxy ratings of QoL and dependence in 166 people with mild to moderate AD. Dependency has also been shown to predict the proxy QoL ratings made by staff caring for people with dementia in residential homes (Hoe *et al.*, 2006). More recently, results from the cross-sectional Dependence in Alzheimer's Disease England (DADE) study (Trigg *et al.*, 2012) suggest that self-report and proxy ratings of QoL and utility differ across levels of dependence such that those people who displayed greater dependence on others, were those who were rated as having a lower QoL.

The Dependence in Alzheimer's Disease England 2 (DADE-2) study was an 18-month follow up to the DADE study and provided an opportunity to explore how ratings of QoL and utility change over time and in relation to changes in dependence and other indices of disease progression.

Method

Study design and patient sample

The Dependence in AD in England (DADE) study was conducted across 18 UK sites and recruited 249 people with mild, moderate or severe possible or probable Alzheimer's disease according to the National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria. The evaluation of baseline QoL data from the DADE study has been reported previously (Jones *et al*, submitted).

Eligible participants for the DADE-2 follow-up study were those who participated in the DADE study, were aged 50 years or over and were community-living or institutionalised. Exclusion criteria specified that participants should have no independent source of impairment that could lead to substantive needs for supportive care (due to confounding effects that this would have on the outcome measures) and should not be enrolled in interventional clinical trials of AD treatments. Each participant was required to have a knowledgeable informant who spent at least 4 hours per week caring for the patient.

The study obtained Ethics Committee approval and was conducted in compliance with the Declaration of Helsinki and its amendments. Written informed consent was obtained for the follow-up visit from all patients or caregivers and/or legally acceptable representatives, in accordance with local regulations.

DADE-2 assessment visits were conducted after a period of 18 months (+/- 2 months) from the original DADE visit. All assessments were completed in one follow-up visit and were conducted by trained personnel on sites which are part of the DeNDRoN (Dementias & Neurodegenerative Disease Research Network) networks of the NHS.

Measurements

Quality of Life and Utility

The 28-item DEMQOL and 31-item DEMQOL-Proxy (Smith *et al.*, 2005) provide complementary methods for evaluating disease-specific health-related quality of life (HRQoL) in dementia. The DEMQOL and DEMQOL proxy have been shown to demonstrate psychometric properties comparable with the best available dementia-specific measures (Smith *et al.*, 2007). The DEMQOL gives a score of 28-112 and the DEMQOL-Proxy a score of 31-124, with a higher score indicating better QoL. The DEMQOL proxy was completed for all participants and the patient-reported DEMQOL was only completed by patients with MMSE scores of ≥ 10

The EQ-5D (EUROQOL Group, 1990) was used to provide generic HRQoL utility ratings for the patient (self-rating and proxy). Utility preference weights were derived from a UK population (Dolan, 1997). The EQ-5D has been demonstrated to be applicable to people with mild to moderate dementia and caregivers as proxies (Kunz, 2010). EQ-5D proxy ratings were obtained for all patients in the study, whereas self-report ratings were only obtained from those with a MMSE score of ≥ 10 .

Dependence

The Dependence Scale (DS; Stern *et al.*, 1994) is a 13-item questionnaire developed to measure the amount of assistance AD patients need due to impairments in cognition, function and behaviour. It is administered to the caregiver and scale items assess relatively subtle types of dependence, such as need for reminders and cueing in daily activities, as well as grosser forms of dependence (e.g. need for assistance in self-care activities). The sum of items provides a total dependence score from 0-15, with a higher score indicating more dependence on others.

Cognition

The Mini-Mental State Examination (MMSE; Folstein *et al.*, 1975) is a brief 30-point questionnaire that is used to screen for cognitive impairment. Scores ranging from 20-26 indicate some cognitive impairment; 10-19 indicate moderate to severe cognitive impairment, and below 10, very severe cognitive impairment.

Function

The Disability Assessment for Dementia (DAD; Gelinas *et al.*, 1999) is a measure of instrumental and basic activities of daily living in AD patients. The scale contains 40 items and gives a total score from 0-100, with a higher score indicating better activity performance.

Behavioural disturbance

The Neuropsychiatric Inventory (NPI; Cummings *et al.*, 1994) assesses psychopathology in dementia patients. It evaluates the severity of neuropsychiatric disturbances common in dementia and scores range from 0-144, with higher scores representing more severe neuropsychiatric symptoms.

Analysis

All study endpoints are summarised using descriptive statistics. Effect sizes (ES) for change scores were calculated in relation to baseline standard deviations. Pearson's correlation coefficient was used to examine bivariate relationships between changes in study variables. Repeated measures t-tests were used to assess significance of changes in study variables across the 18-month period. Due to multiple univariate analyses, $p < 0.01$ was used as the level for significance. To examine association between disease severity indicators and QoL, whilst controlling for baseline scores, ordinary least squares multiple regression was used. A stepwise method of entry was employed due to the exploratory nature of the analysis. A significance level of $p < 0.01$ was used for beta values in the regression of EQ-5D data due to kurtosis in the distribution of change scores.

Results

For the purpose of the present analysis, 145 participants were included. This is the number of participants who completed an assessment of dependence at DADE baseline and DADE-2 follow-up visits. Baseline demographics of these 145 patients and scores on all measures at both baseline and follow-up are summarized in Table 1. Also provided, are the details of a smaller subsample of individuals ($n = 70$) who were able to complete follow-up assessments for self-reported QoL and utility (Subsample A).

Assessment of Change in Study Variables

Paired samples t-tests were used to explore significant differences in mean scale scores between baseline (T1) and 18-month follow-up (T2), for dependence, clinical variables and QoL outcomes (see Table 1). Dependence scores were significantly higher at T2 than T1 ($t_{144} = -6.45$, $p < 0.001$) showing a mean increase in sample dependence of 1.18 points ($ES = 0.37$) over the 18 months.

There were also significant reductions in scores on the MMSE ($ES = 0.46$; $t_{128} = 7.42$, $p < 0.001$) and DAD ($ES = 0.41$; $t_{142} = 8.50$, $p < 0.001$), indicating a reduction in cognitive ability and activities of daily living (ADL) function over time. There was no significant difference in NPI scores ($t_{124} = 0.22$, $p > 0.05$) across the two time points. A similar pattern of change was demonstrated within Subsample A, although the size of change was reduced across the measures.

Insert Table 1 here

Within the whole sample data, utility ratings on the EQ-5D proxy scale fell significantly by 0.1 points over the two time periods ($ES = 0.34$; $t_{134} = 3.64$, $p < 0.001$) whereas there was a significant increase of 4.84 points in QoL ratings on the DEMQOL-Proxy ($ES = 0.34$; $t_{138} = -4.50$, $p < 0.001$), suggesting that proxies were rating the QoL of participants as significantly better after 18 months. However within Subsample A, neither proxy nor self-reported QoL and utility ratings showed any significant mean change over the 18 months.

Examination of the distribution of change scores on QoL and utility measures suggests that there is considerable individual variation across the 18-months. Figure 1 shows the distribution of QoL and utility change scores for the whole sample. Although there were no mean changes in QoL and utility within Subsample A, examination of the distribution of change scores on both proxy and self-report measures suggests that within this subsample there are positive and negative changes occurring for individuals. For the EQ-5D there were approximately equal proportions of participants who reported utility values better, worse or the same as baseline (27.6%, 39.1% and 33.3% respectively). For the EQ-5D proxy 45.6% of the sample were judged as having lower utility but there were almost a third (30.9%) for whom proxies reported an improvement in utility. For the DEMQOL self-report 40% of participants reported a reduction in QoL however this was offset by a larger proportion (57.1%) reporting a QoL improvement. The DEMQOL proxy demonstrated a high proportion of participants as having an improved (55.1%) as opposed to reduced (40.6%) QoL.

Insert Figure 1 here

Associations between Change Scores

Pearson's correlation coefficients were used to explore bivariate associations between change scores (Time 2 – Time 1) for dependence, changes in clinical indicators and changes in QoL and utility measures (see Table 2). Changes in DS scores showed significant bivariate associations with changes in MMSE ($r_{128} = -0.26$, $p < 0.01$) and DAD scores ($r_{142} = -0.42$, $p < 0.001$) such that worsening cognition and function were associated with increases in dependence. There was little association between the change scores on the different QoL and utility measures. Only the change scores on the self-report EQ-5D and DEMQOL were significantly correlated ($r_{68} = 0.43$, $p < 0.01$).

Insert Table 2 here

Changes in Disease Severity and Associations with QoL Outcomes

Changes in dependence showed no significant bivariate associations with changes in any of the QoL or utility measures (see Table 2). To further explore any relationship between changes in dependence and QoL outcomes, the sample was split into two groups according to DS change scores: negative/no change (DS change -7 to 0) and positive change in scores (DS change 1-7). Independent t-tests confirmed that there were no significant differences between the two groups for any of the QoL or utility scales (see Table 3).

Insert Table 3 here

As shown in Table 2, Pearson correlations between change scores on QoL outcomes and changes on the MMSE, DAD and NPI were calculated. These suggest that changes on the EQ-5D, EQ-5D proxy and DEMQOL are not significantly associated with changes in any of these three clinical indicators. Changes in the DEMQOL-Proxy displayed weak but significant associations with changes on the NPI ($r_{119} = -0.29$, $p < 0.01$) such that increases in the severity of neuropsychiatric disturbances over time are associated with a reductions in QoL ratings by proxies.

Multivariate Analysis of QoL and Utility Changes

The factors associated with changes in QoL and utility were further explored using multiple linear regression. For each QoL and utility indicator a stepwise regression was conducted whereby scores for DS change, MMSE change, DAD change and NPI change were considered for entry into an exploratory model. Alongside these four possible explanatory variables, the baseline scores for the particular QoL or utility measure were also entered, to control for the fact that the magnitude of change can be dependent on baseline ratings. Final models are shown in Table 4.

Insert Table 4 here

For the EQ-5D self-report and DEMQOL, no measure of disease progression was able to account for variation in QoL or utility. Only baseline ratings from these two measures were significant within the final regression models. There was an inverse relationship, such that lower baseline scores were predictive of larger increases in QoL and higher baseline scores with lower improvements or deterioration in QoL. For changes in EQ-5D proxy ratings, baseline scores and MMSE change scores

were significant explanatory variables, such that lower baseline scores and improvement in cognition were associated with larger increases in proxy utility ratings. For changes in DEMQOL-Proxy ratings, baseline scores and change in NPI scores were significant such that lower baseline scores and decreasing neuropsychiatric disturbance were associated with larger improvements in QoL ratings.

Discussion

The study aimed to explore changes in QoL and utility over an 18-month period and its relationship with different indices of disease progression, including dependence. Findings suggest that there is a large amount of individual variation in QoL and utility, with over 50% of participants reporting maintenance or improvement in QoL and utility. The mean change data is inconclusive across the different measures of QoL and utility and different conclusions can be drawn depending on which measure is used.

Both of the self-report measures, the EQ-5D and the DEMQOL, failed to show group-level change over the 18 months. However the self-report data was obtained from only those participants with higher MMSE scores. This means that those who deteriorated significantly over the 18-months were unlikely to provide self-report QoL information at follow up. The data supports the suggestion that the self-report subsample included participants who experienced less deterioration over time and the proxy QoL and utility ratings for this sample also showed no mean change. Within the whole sample data, the proxy ratings of QoL and utility provided conflicting results. The EQ-5D proxy data suggested an overall decline in utility for the whole sample and yet the DEMQOL-Proxy data indicated an overall improvement in life quality. Measures of cognition (MMSE), function (DAD) and dependence (DS) all displayed significant decline over the 18 months in both the whole sample and the self-report subsample, suggesting that dementia had progressed. The only marker of disease severity that showed no significant change was behavioural disturbance (NPI).

Although cross-sectional data has suggested links between dependence and QoL (Trigg *et al.*, 2012) these relationships were not evident in the change scores. Changes on the DS showed no association with change in QoL or utility within univariate or multivariate analyses. Changes to EQ-5D proxy ratings were partly explained by changing cognition whereas changes on the DEMQOL-Proxy were associated with changes in the severity of behavioural disturbance, although these associations were relatively weak. The association between the DEMQOL-Proxy and NPI may explain why the DEMQOL-Proxy was the one measure that actually reported an overall improvement in QoL for the whole sample. NPI scores remained stable over the 18 months and this lack of deterioration may have led to more positive evaluations of life quality by the caregiver. Both of the self-report measures of QoL and utility failed to show significant associations with changes to any of the measures of disease progression. In fact the strongest predictor of change on each of the four QoL outcomes was the baseline score for that measure, such that higher baseline scores were more likely to be reduced at follow-up and vice versa. This finding has been replicated in other cohort studies (Selwood *et al.*, 2005; Hoe *et al.*, 2009; Vogel *et al.*, 20012) and may reflect regression towards the mean in longitudinal QoL data. In order to avoid misinterpreting changes in QoL, it is important that studies assessing the impact of intervention or treatment carefully control for baseline measurements.

The finding that QoL and utility do not inevitably decline as dementia progresses concurs with several other studies that have shown similar results, using both proxy and self-report measures (Selwood *et al.*, 2005; Missotten *et al.*, 2007; Hoe *et al.*, 2009; Livingston *et al.*, 2012; Heggie *et al.*, 2012). Several reasons have been proposed for the lack of a direct link between changes in disease severity and QoL outcomes. For self-report measures of QoL it may be that reduced insight suppresses the impact of worsening symptoms and functioning on the QoL reported by the person with AD (Trigg *et al.*, 2011). Alternatively it may be that the person with AD is able to accommodate and adapt to gradual changes in cognition, function and behaviour, thus reducing the impact on more holistic outcomes such as wellbeing and life quality (Livingston *et al.*, 2012). Theories such as response shift (Sprangers & Schwartz, 1999) also provide an explanatory mechanism whereby the person adjusts expectations and internal standards, in response to deterioration in health, thereby reducing fluctuations in self-reported QoL. Research also indicates that caregiver factors such as burden and depression may influence the QoL ratings that proxies provide (Conde-Sala *et al.*, 2009; Schiffczyk *et al.*, 2010). It may also be that participation in studies and trials impacts on patient and caregiver perceptions of support and this might serve to buffer the QoL reports obtained. A further consideration is the impact of participant drop-out within longitudinal studies. It may be that those who experience significant declines in QoL are also those more likely to be lost to follow-up.

Although mean self-report scores on the DEMQOL and the EQ-5D showed no significant group-level changes, there was considerable evidence of individual change. Previous studies have found the EQ-5D and other self-report measures to be responsive to changes in the QoL of people with dementia (Hounsome *et al.*, 2011; Perales *et al.*, 2013), which suggests that such change is not solely attributable to measurement error. In fact the EQ-5D and DEMQOL self-report were the only QoL and utility measures to display a significant association. The correlation between the change scores on these different measures was moderate in size and suggests that people with AD are able to provide consistent and meaningful information via self-report. The challenge for future research is to determine the key factors that influence these ratings.

Evidence from this study and others (Missotten *et al.*, 2007; Livingston *et al.*, 2012; Vogel *et al.*, 2012) points to the lack of a clear direct relationship between changes in disease severity and changes in QoL or utility. The maintenance and improvement of QoL reported by many people with AD in this study, suggests the possible buffering influence of other psychological, social and environmental factors. These need exploring if we are to properly understand how and why QoL changes for the individual across the natural course of the disease and in response to treatment and intervention. We also need to be mindful of the fact that different QoL and utility measures may lead us to very different conclusions about the direction, magnitude and causes of change. Careful interpretation is needed when drawing conclusions from QoL outcomes and individual scores should be considered alongside sample means in order to capture the true nature of changes.

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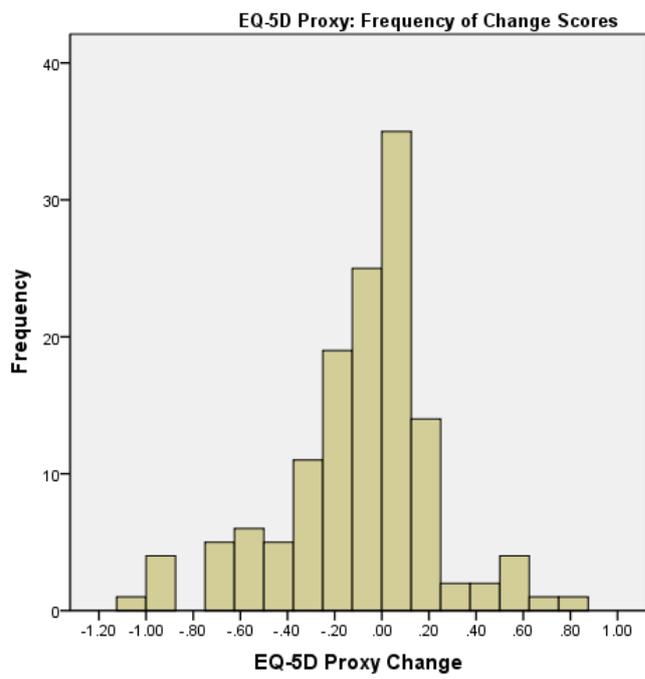
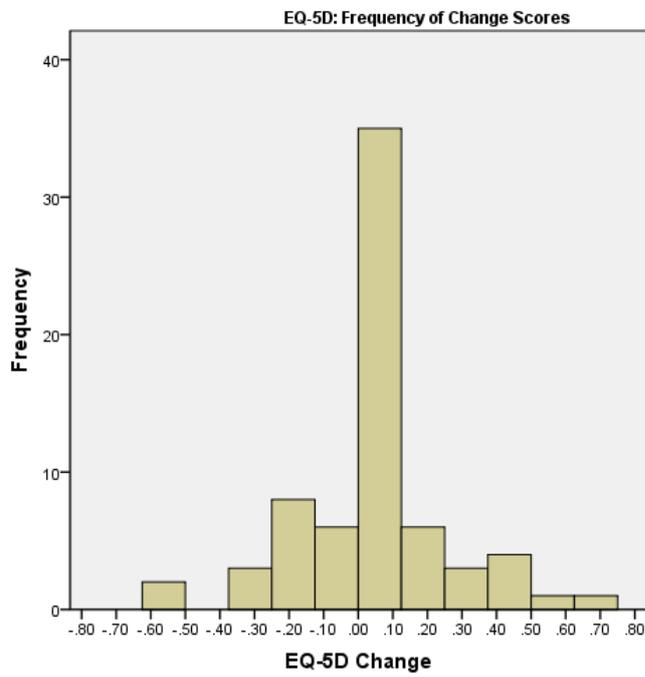
Table 1: Demographics, clinical status and QoL/utility scores of all participants included in follow-up and the subsample who completed self-reported QoL/utility follow-up (Subsample A)

	Baseline Scores (T1)					18 Month Follow-up (T2)					Change Scores (T2-T1)					P value	Partial η^2
	n	Mean	SD	Min	Max	n	Mean	SD	Min	Max	n	Mean	SD	Min	Max		
Whole Sample																	
Age	145	77.78	9.24	53	102												
Male	57																
Female	88																
DS	145	7.79	3.14	0	14	145	8.98	3.44	0	15	145	1.18	2.21	-7	7	<0.001	0.22
MMSE	145	14.99	7.00	3	26	129	12.64	8.57	0	27	129	-3.26	4.99	-23	9	<0.001	0.30
DAD	144	47.26	28.58	0	100	144	35.41	29.54	0	100	143	-11.80	16.60	-71.18	50	<0.001	0.33
NPI	131	20.96	18.11	1	106	136	20.80	18.60	1	119	125	-0.37	18.53	-53	43	ns	
DEMQOL-Proxy	143	97.26	14.11	60	123	141	102.48	11.61	71	124	139	4.84	12.68	-32	48	<0.001	0.12
EQ-5D Proxy	140	0.70	0.29	-0.09	1	140	0.60	0.33	-0.17	1	135	-0.10	0.32	-1.02	0.81	<0.001	0.09
Subsample A																	
Age	70	78.19	8.48	53	102												
Male	31																
Female	39																
DS	70	5.99	2.60	0	13	70	6.77	2.84	0	15	70	0.78	2.32	-7	7	<0.01	0.10
MMSE	70	20.69	3.45	10	26	70	19.40	4.67	10	27	70	-1.28	3.84	-11	9	<0.01	0.10
DAD	70	65.78	22.24	15	100	70	57.44	22.54	5.41	100	70	-8.33	16.23	-54.12	31.35	<0.001	0.21
NPI	61	16.13	15.72	1	86	65	17.68	15.65	1	89	58	1.56	15.57	-49	40	ns	
DEMQOL-Proxy	70	97.61	14.06	63	123	69	100.38	12.56	71	124	69	2.51	11.39	-32	38.57	ns	
EQ-5D Proxy	69	0.76	0.23	0.05	1	69	0.74	0.23	-0.17	1	68	-0.02	0.22	-0.6	0.61	ns	
DEMQOL	70	95.20	13.73	54	112	70	96.43	12.35	63	112	70	1.22	8.60	-24	18	ns	
EQ-5D	70	0.81	0.22	0	1	69	0.83	0.18	0.01	1	69	0.02	0.21	-0.61	0.66	ns	

ns = non-significant

DS = Dependence Scale; MMSE = Mini-Mental State Examination; DAD = Disability Assessment for Dementia;
NPI = Neuropsychiatric Inventory;

Figure 1: Change from baseline scores on QoL and utility measures



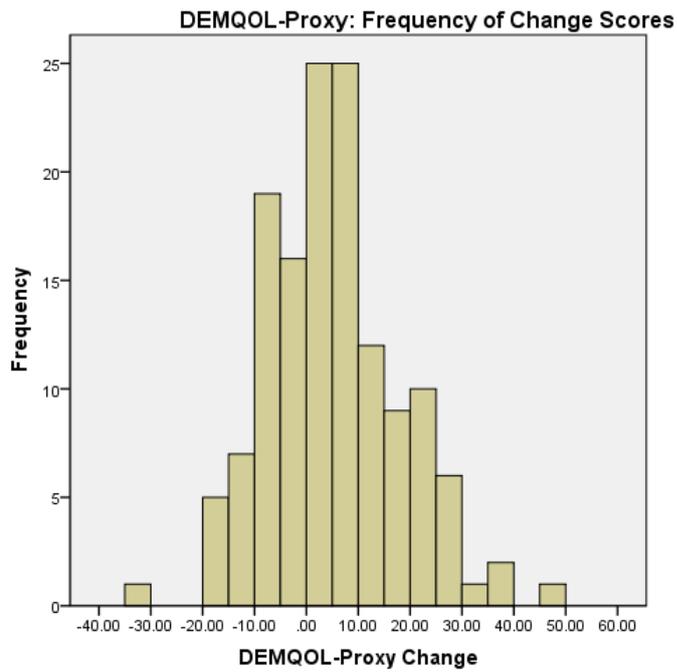
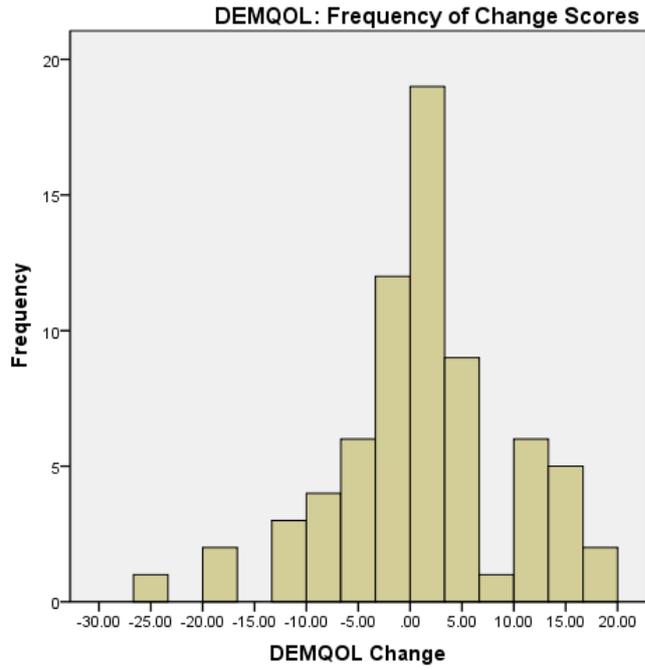


Table 2: Pearson correlations between change scores on study measures

	DS Change	EQ-5D Change	EQ-5D Proxy Change	DEMQOL Change	DEMQOL - Proxy Change	MMSE Change	DAD Change
EQ-5D Change	-.10						
EQ-5D Proxy Change	-.12	.19					
DEMQOL Change	-.08	.43*	.21				
DEMQOL-Proxy Change	-.01	.04	.12	.17			
MMSE Change	-.26*	.02	.22	.03	.08		
DAD Change	-.42*	.06	.13	-.09	.04	.43*	
NPI Change	-.14	.09	-.05	-.26	-.29*	-.18	-.25*

* p < 0.01

DS = Dependence Scale; MMSE = Mini-Mental State Examination; DAD = Disability Assessment for Dementia;

NPI = Neuropsychiatric Inventory

Table 3: QoL change scores by two Dependence Scale change groups: reduced dependence/no change and increased dependence

	DS Change -7 to 0			DS Change 1-7			t-test
	n	Mean	SD	n	Mean	SD	p
EQ-5D Change	35	0.04	0.24	34	0	0.18	ns
EQ-5D Proxy Change	55	-0.06	0.23	80	-0.12	0.37	ns
DEMQOL Change	35	2.14	9.85	35	0.31	7.16	ns
DEMQOL-Proxy Change	56	4.38	10.99	83	5.16	13.76	ns

ns = $p > 0.05$

DS = Dependence Scale

Table 4: Linear regression models for QoL and utility change: contribution of change in disease severity and baseline QoL/utility ratings

Score	Model Significance	R ²	Variable	Beta	SE Beta	Standardised beta	t
EQ5D Change	F(1,56) = 31.25**	0.35	(Constant)	0.50	0.09		5.49**
			EQ5D baseline	-0.60	0.1	-0.59	-5.59**
EQ5D Proxy Change	F(2,100) = 15.86**	0.24	(Constant)	0.26	0.06		3.92**
			EQ5D Proxy baseline	-0.42	0.08	-0.42	-4.87**
			MMSE change	0.01	0.005	0.20	2.30*
DEMQOL Change	F(1,56) = 13.90**	0.19	(Constant)	27.39	7.07		3.87**
			DEMQOL baseline	-0.27	0.07	-0.44	-3.72**
DEMQOL-Proxy Change	F(1,104) = 12.43**	0.19	(Constant)	58.80	6.64		8.85**
			DEMQOL-Proxy baseline	-0.56	0.06	0.61	-8.34**
			NPI change	-0.15	0.06	0.18	-2.48*

* P < 0.05

** p < 0.001

MMSE = Mini-Mental State Examination; NPI = Neuropsychiatric Inventory