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Trajectories of quality of life in early-stage dementia: individual variations and predictors of change

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Key words:
Caregiver; depression; quality of relationship; Alzheimer’s disease; vascular dementia

Key points:
- Reliable change in self-rated quality of life scores was observed in 25% of participants with early-stage dementia at 20-month follow-up.
- A better perceived quality of relationship with the carer was associated with an increase in self-rated quality of life at 20-month follow-up.
- In this sample, use of acetylcholinesterase-inhibiting medication appeared to be associated with a decline in self-rated quality of life at 20-month follow-up.

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Abstract

Background: Little evidence is available about how quality of life (QoL) changes as dementia progresses.

Objectives: We explored QoL trajectories over a 20-month period and examined what predicted change in QoL.

Method: Fifty-one individuals with a diagnosis of Alzheimer’s, vascular or mixed dementia (PwD) participating in the MIDAS study rated their QoL using the QoL-AD scale at baseline and at 20-month follow-up. PwD also rated their mood and quality of relationship with the carer. In each case the carer rated his/her level of stress and perceived quality of relationship with the PwD.

Results: There was no change in mean QoL score. Nearly one-third of PwD rated QoL more positively at 20-month follow-up and nearly one-third rated QoL more negatively. These changes could be regarded as reliable in one-quarter of the sample. Participants taking AChEI medication at baseline were more likely to show a decline in QoL score. There were no other significant differences between those whose scores increased, decreased or stayed the same on any demographic or disease-related variables, or in mood or perceived quality of relationship with the carer. While baseline QoL score was the strongest predictor of QoL at 20 months, the quality of relationship with the carer as perceived by the PwD was also independently a significant predictor.

Conclusions: There is a degree of individual variation in QoL trajectories. Use of AChEI medication appears linked to decline in QoL score, while positive relationships with carers play an important role in maintaining QoL in early-stage dementia.
Trajectories of quality of life in early-stage dementia: individual variations and predictors of change

It has been argued that, despite considerable research, little is known about the quality of life (QoL) of people living with dementia (Banerjee et al., 2009; Hoe et al., 2009; Selwood et al., 2005). This may be partly because it has been studied in relation to a relatively limited set of factors (St John and Montgomery, 2010). Numerous studies demonstrate that a large proportion of the variance in QoL scores, whether self-rated by people with dementia (PwD) or proxy-rated by carers, remains unexplained by commonly-measured patient and caregiver factors including symptoms, comorbidity, carer burden, and basic demographic variables such as age, gender, education and marital status (Naglie et al., 2011a; Naglie et al., 2011b). Depressed mood is a common predictor of low QoL scores, but no clear associations emerge with cognitive function, behavioural symptoms or functional ability (Banerjee et al., 2009; Naglie et al., 2011a). Even with the inclusion of additional factors such as difficulties in the caregiving relationship, studies have only accounted for 38% of the variance in QoL scores (Menne et al., 2009).

If little is known about what predicts QoL in cross-sectional analyses, even less is known about how QoL changes as dementia progresses or what factors influence such changes. Follow-up studies are few, and typically involve small samples, so the trajectory of QoL and the factors associated with change in QoL remain to be clearly established. Studies with care home residents have variously reported no change in mean scores at 20 weeks (Hoe et al., 2009) and 1 year (Selwood et al., 2005), or significant decline in mean scores at 2 year follow-up (Lyketsos et al., 2003). Findings from community-dwelling samples with mild to moderate dementia have been similarly variable. PwD self-ratings did not change over 2 years (Tatsumi et al., 2009) but proxy ratings declined at 16 month (Vogel et al., 2012) or 2 year (Tatsumi et al., 2009) follow-up. In a
mixed community and care home sample ranging from mildly to severely impaired, QoL increased at 1 year before decreasing at 2 year follow-up (Missotten et al., 2007).

In addition to group trends, it is important to consider individual variations in QoL appraisals and trajectories, and to investigate underlying factors (Vogel et al., 2012). Whether mean scores remained the same or declined, all these follow-up studies have noted considerable individual variation (Vogel et al., 2012), although little attention has been paid to establishing what constitutes a reliable change. In one study of care home residents, over one-third improved and one-third declined (Hoe et al., 2009), and in another, half the sample improved and half declined (Selwood et al., 2005). It has been suggested that increases or reductions in QoL score are not directly attributable to changes in clinical variables (Clare et al., 2011; Missotten et al., 2007). The effect of depression remains unclear; one study found that lower baseline depression scores predicted better self-rated QoL at 20 weeks (Hoe et al., 2009), but another found no effect of depression at 2-year follow-up (Lyketsos et al., 2003). Recent findings suggest that social and interpersonal factors may play a stronger role; for example, a reciprocal relationship between carer stress and perceived quality of relationship and observer-rated PwD well-being six months later has been reported (Burgener and Twigg, 2002).

In this study, we assessed the impact of PwD depression and perceived quality of relationship with the carer, and carer stress and perceived quality of relationship with the PwD, at baseline on PwD self-ratings of QoL at 20-month follow-up. The following research questions were addressed:

1. What was the profile of QoL trajectories?
2. Were different QoL trajectories associated with baseline differences in key characteristics (age, gender, socio-economic status, and years of education) or illness-related variables (diagnosis, functional ability, neuropsychiatric symptoms, and use of acetylcholinesterase-inhibiting medication)?
3. Did PwD mood and perceived quality of relationship with the carer at baseline, and carer stress and perceived quality of relationship with the PwD at baseline, predict PwD QoL scores at 20-month follow-up?

Methods

Design
We examined QoL in a community-dwelling sample of people with early-stage Alzheimer’s, vascular or mixed dementia participating in the Memory Impairment and Dementia Awareness Study (MIDAS). MIDAS was a longitudinal, multi-method study of awareness in people with early-stage dementia. Participants were assessed on entry (n = 101) and again at approximately 12 (n = 66) and 20 month (n = 51) time-points. Ethical approval was granted by the relevant University and NHS Ethics Committees. As part of a previous, more general analysis, MIDAS data showed no change in mean QoL score across all three time-points for the whole sample (Clare et al., 2011). This paper presents data from the 51 participants who completed the assessment at both baseline and 20-month follow-up, and analyses data from these two time-points only.

Participants
Participants were recruited from Memory Clinics in North Wales, UK. Inclusion criteria were an ICD-10 diagnosis of Alzheimer’s disease (AD), vascular dementia (VaD) or mixed Alzheimer’s and vascular dementia (World Health Organisation, 1992), a score of 18 or above on the Mini-Mental State Examination (MMSE) (Folstein et al., 1975), ability to communicate verbally in English, and availability of a spouse, partner, other family member or friend (‘carer’) who was willing to contribute. Exclusion criteria were concurrent major depression, psychosis or other neurological disorder, and past history of neurological disorder, stroke or brain injury. Fifty-one participants
completed the assessment at both time-points, and in each case a carer also contributed. Sample characteristics are summarised in Table 1.

Measures

The following measures from the MIDAS data set were used in the present analysis.

(a) Measures completed by the PwD

Quality of life was assessed with the Quality of Life in Alzheimer’s Disease (QoL-AD) scale (Logsdon et al., 1999). Mood was assessed with the depression sub-scale of the Hospital Anxiety and Depression Scale (HADS) (Snaith and Zigmond, 1994). Perceived quality of relationship with the carer was assessed with the Positive Affect Index (Bengtson and Schrader, 1982).

(b) Measures completed by the carer

Carers rated functional ability of the PwD on the Functional Activities Questionnaire (Pfeffer et al., 1982), the number and severity of neuropsychiatric symptoms in the PwD on the Neuropsychiatric Inventory Questionnaire (Kaufer et al., 2000), and their own levels of stress on the Relative Stress Scale (Greene et al., 1982). Perceived quality of relationship with the PwD was assessed with the Positive Affect Index (Bengtson and Schrader, 1982).

Procedure

Participants and carers were visited at home by the researchers, unless they preferred to attend the University, and were each seen separately. The baseline MIDAS assessment typically took two or three sessions to complete. The assessment at 20 months was of shorter duration, typically one or two sessions. Informed consent was obtained from both PwD and carer at each time-point.
**Statistical analyses**

Repeated measures ANOVA was used to compare mean QoL scores at baseline and 20-month follow-up. Participants were divided into three similar-sized groups consisting of those whose scores at 20-month follow-up, relative to baseline, increased by 3 points or more, decreased by 3 points or more, or stayed the same (± 2 points), in line with Hoe et al. (2009). Scores obtained by these groups on baseline variables were compared using ANOVA, chi-square, or the Mantel-Haenzsel test for linear-by-linear association in IBM SPSS Statistics v.20, as appropriate. A reliable change index (Evans et al., 1998) was calculated for the QoL-AD, based on a Cronbach’s alpha of .8 for the MIDAS baseline data set. Finally, regression analysis using the stepwise method in IBM SPSS Statistics v.20 examined baseline predictors of QoL score at 20-month follow-up for the whole sample. The assumptions of equal variability and normality for the residuals were assessed and were found to hold.

**Results**

Mean scores for the 51 participants who provided self-ratings on the QoL-AD at baseline and 20-month follow-up are summarised in Table 2. There was no difference in mean scores across these two time points ($F_{1,50} = .03, p = .87$). The stable group mean score masked a degree of individual variation, with individual change scores ranging from +15 to -10 points.

((Table 2 near here))

Relative to baseline, twenty participants (39%) gave the same rating plus or minus 2 points, 15 (30%) rated their QoL more positively with scores increasing by 3 points or more, and 16 (31%) rated their QoL less positively with scores decreasing by 3 points or more. Mean scores for each of...
these three groups at each time point are summarised in Table 2. Baseline scores for each of the three groups on the other variables of interest are summarised in Table 3. There were no significant differences between the groups at baseline in age, gender, socio-economic status, years of education, dementia diagnosis, MMSE score, depression scores, or perceived quality of relationship with the carer. There were also no significant differences between the groups in carer-rated functional ability or neuropsychiatric symptoms or in carer stress or perceived quality of relationship with the PwD. However, the groups did differ significantly in use of acetylcholinesterase-inhibiting (AChEI) medication at baseline; participants treated with AChEI medication at baseline were more likely to show a decline in QoL at 20-month follow-up. Baseline mean scores for QoL did not differ significantly for those taking and not taking AChEI medication (mean on medication 37.52, sd 5.53; mean not on medication 36.42, s.d. 4.66; $F_{1,49} = 5.9$, $p = .05$).

Of the 25 participants treated with AChEI medication, 23 had a diagnosis of AD, 1 had a diagnosis of mixed AD and vascular dementia, and 1 had a diagnosis of vascular dementia; of the 26 participants not receiving AChEI medication, 8 had a diagnosis of AD, 8 had a diagnosis of mixed AD and vascular dementia, and 10 had a diagnosis of vascular dementia. However, as noted above, diagnosis in itself did not result in differences in QoL ratings between the groups.

Calculation of the reliable change index indicated that a change of 6 points or more in either direction was required to be confident that alteration in QoL-AD score was not due to measurement unreliability. At 20-month follow-up, 6 participants (12% of the sample) increased their scores by 6 points or more, and 6 (12% of the sample) decreased their scores by 6 points or more, relative to baseline score. Thus, approximately one-quarter of the sample could be considered to have shown reliable changes in QoL.
Regression analysis examined baseline predictors of QoL score at follow-up for the whole sample. QoL score at baseline was entered at the first step and accounted for 35% of variance. At the second step, PwD depression score and perceived quality of relationship score were included, together with carer stress and perceived quality of relationship scores. All five variables were retained in the model, which accounted for 38% of variance, but only baseline QoL score and PwD quality of relationship score were individually significant. A further regression analysis including just these two variables accounted for 39% of variance, with both QoL and quality of relationship individually significant, indicating that higher baseline quality of relationship scores were associated with increases in QoL score at follow-up. Thus, while QoL score at baseline was a strong predictor of subsequent QoL score at follow-up, the perception held by the PwD of the relationship with the carer was also independently predictive, additionally accounting for a small proportion of variance.

(((Table 4 near here)))

Discussion

This study is one of few to have examined trajectories of self-rated QoL in a community-dwelling sample of people with early-stage dementia. While mean QoL score did not change over the 20-month study period, there was a degree of individual variation, with nearly one-third rating their QoL more positively and nearly one-third rating their QoL more negatively at follow-up. Changes could be considered reliable for one-quarter of the sample, based on a reliable change index of 6 points or more in either direction. Comparison of those whose scores increased, declined or stayed the same indicated that those taking AChEI medication at baseline were more likely to show a decline in QoL score, but yielded no other significant between-group differences in baseline levels.
of demographic or disease-related variables or in mood, perceived quality of relationship, or carer stress. Regression analysis indicated that PwD perceptions of quality of relationship with the carer at baseline significantly predicted QoL score at 20-month follow-up; where the relationship was evaluated more positively, this was associated with an increase in QoL score.

The first aim of the study was to examine trajectories of QoL scores over a 20-month period in a community-dwelling sample of people with early-stage dementia. We previously reported no change in mean QoL score for the whole MIDAS study sample (Clare et al., 2011) over three assessment time-points at baseline, 12 and 20 months. The present study demonstrates no change in mean score for the sub-group of participants who contributed both at baseline and at 20-month follow-up. This is consistent with the finding of no change in mean self-rated QoL scores in the most directly comparable study (Tatsumi et al., 2009). Proxy ratings made by carers of community-dwelling PwD may be more likely to decline (Tatsumi et al., 2009; Vogel et al., 2012). Our finding of a degree of individual variation in QoL trajectories was in keeping with findings of previous studies (Hoe et al., 2009; Selwood et al., 2005; Vogel et al., 2012). This study was the first to consider what constitutes reliable change, demonstrating that one-quarter of the sample showed changes in QoL score of a magnitude that was unlikely to result from simple measurement unreliability. This highlights the need to take a more individually-focused, person-centred approach to understanding the nature and trajectory of QoL in dementia and identifying the factors that support improvement in, or maintenance of, QoL, as well as the factors that undermine QoL.

The second aim of the study was to establish whether different QoL trajectories were associated with differences at baseline in key characteristics or illness-related variables. Those taking AChEI medication at baseline were more than twice as likely to show a decline in QoL scores at 20-month follow-up as those not taking AChEI medication. This pattern could not be accounted for by differences in diagnosis or by differences in QoL score at baseline between those taking and not taking AChEI medication. It contrasts with previous reports indicating that PwD taking AChEI medication rate their QoL more positively than those not taking AChEI medication.
QoL trajectories in early-stage dementia

(Hoe et al., 2007). QoL has been infrequently assessed as an outcome in trials of AChEI medication (Birks, 2006). Where effects on self-rated QoL have been evaluated, no benefits of medication have been found at 30-week study endpoints (Rogers et al., 1998; Burns et al., 1999); however, evidence on longer-term effects on self-rated QoL is lacking. The association between AChEI use and QoL trajectory requires further investigation with a larger sample.

The analyses yielded no evidence of significant differences between the groups at baseline on any other variables. Clearly these non-significant findings must be interpreted with some caution as group sizes were relatively small and cut-offs for assignment to groups were chosen in line with previous research, making it possible to achieve three groups of more or less similar size. However, the findings support the view that change in QoL score is not straightforwardly related to most basic demographic and disease-related variables (Clare et al., 2011; Missotten et al., 2007), while suggesting a potentially important association between prescription of AChEI medication and a declining QoL trajectory.

The third aim of the study was to investigate what predicts change in QoL score over time. The strongest predictor of QoL at 20-month follow-up was baseline QoL score. This in part attests to the reliability of the scale and the validity of the construct on which it is based. This pattern was also expected in the light of previous findings from care home samples (Lyketsos et al., 2003; Selwood et al., 2005) follow-up. In line with some previous findings from care home samples (Lyketsos et al., 2003), but in contrast to others (Hoe et al., 2009), baseline depression scores did not predict QoL at follow-up in our sample. However, uniquely, our study also showed that over and above baseline QoL, the perceived quality of relationship with the caregiver significantly predicted PwD self-ratings of QoL at follow-up, albeit explaining a modest proportion of the variance. This demonstrates the crucial importance of social and relationship factors in supporting the QoL of PwD, and highlights the value of focusing on these issues in attempting to understand QoL. Social and psychological factors influence individual appraisals of QoL (Byrne-Davis et al., 2006) and the expectations on which such appraisals are based (Ettema et al., 2005). It is likely that...
feeling well-supported in a relationship with a trusted carer facilitates more positive appraisals of one’s situation and makes it easier to adjust expectations. Carer perceptions of quality of relationship, or of the stresses associated with caregiving, were not predictive of PwD QoL. This might seem surprising in view of the previous finding that caregiver stress and perceived quality of relationship were associated with PwD well-being six months later (Burgener and Twigg, 2002), but in that study carer factors were associated with subsequent proxy ratings of PwD well-being, rather than with self-ratings by the PwD. Thus, it seems that it is the perceptions held by PwD that influence their self-ratings of QoL, while carer perceptions influence proxy ratings of PwD QoL, but not PwD self-ratings. This demonstrates the importance of seeking the perspective of the PwD wherever possible, rather than relying on proxy ratings.

As noted above, there are a number of limitations that must be taken into account in interpreting the present findings. The QoL-AD scale is a valid and reliable measure which has been described as the measure of choice when assessing QoL outcomes for PwD (Moniz-Cook et al., 2008), but it is important to acknowledge that QoL is a broad concept and that there are differing perspectives on how it should be measured (WHOQOL Group, 1994). The sample size of 51 was adequate for the regression analyses undertaken to examine predictors of QoL score at 20-month follow-up, but the size of the three sub-groups which were identified to permit comparison of scores on baseline variables was relatively small. While the group mean scores suggest that the absence of significant between-group findings in all variables except for use of AChEI medication was generally robust, the small group size may have masked effects in the quality of relationship domain. This could be explored further with a larger sample. Additionally, our no-change criterion of ± 2 points was consistent with an earlier study (Hoe et al., 2009), but may not have been large enough to rule out possible measurement unreliability and regression to the mean; with a larger sample it would be possible to make comparisons on the basis of more pronounced changes using the reliable change index, here calculated as a 6-point difference, as a cut-off. While the present study constituted a first step in considering the impact of psychological and social variables on QoL
trajectories, we were only able to consider the predictive value of a relatively limited set of variables, selected on the basis of existing evidence. Future studies could draw on a more extensive range of variables that might influence change in QoL. Generalisability is limited by the application of exclusion criteria covering major depression and past history of psychosis or other neurological disorder, and inclusion criteria requiring the involvement of a carer. In this regard it is particularly important to note that, unlike participants in the current sample, many PwD do not have a carer or other significant person in their lives to offer support and assistance, and these individuals may be at particular risk for declining QoL. Finally, the study focused on people with early-stage dementia scoring between 18 and 30 on the MMSE at baseline, and hence the findings do not offer information about QoL in people with moderate to severe dementia.

Despite these limitations, the findings contribute new information about factors influencing the trajectory of QoL in early-stage dementia, adding to the limited evidence available about change over time and providing a detailed focus on potential predictor variables. There is a need for a broader perspective if we are to understand variations in QoL among PwD (O’Connor et al., 2007). It has been suggested that domains potentially relevant to QoL in dementia include social, environmental, economic, cultural and psychological factors (Byrne-Davis et al., 2006; Katsuno, 2005; Moyle et al., 2011; Murray and Boyd, 2009; Parse, 1996; Smith et al., 2005; Venturato, 2010). The present findings raise questions about the association between taking AChEI medication and QoL, and highlight for the first time the central importance of the perceived quality of relationship with a carer as a predictor of subsequent self-ratings of QoL by PwD. Focusing on this important domain may offer a vital route to supporting the maintenance or improvement of QoL for PwD.
References


QoL trajectories in early-stage dementia


Table 1. Sample characteristics

<table>
<thead>
<tr>
<th>Key characteristic</th>
<th>Frequency or mean score (sd; range)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PwD</strong></td>
<td></td>
</tr>
<tr>
<td>Gender - Female : Male</td>
<td>26 : 25</td>
</tr>
<tr>
<td>Age at baseline</td>
<td>76.75 (7.88; 55 - 91)</td>
</tr>
<tr>
<td>Years of education</td>
<td>11.76 (2.42; 8 - 17)</td>
</tr>
<tr>
<td>Diagnosis - Alzheimer’s : Vascular dementia : Mixed</td>
<td>31 : 11 : 9</td>
</tr>
<tr>
<td>Acetylcholinesterase-inhibiting medication - Yes : No</td>
<td>30 : 21</td>
</tr>
<tr>
<td>MMSE score at baseline</td>
<td>24.5 (2.80; 18 - 30)</td>
</tr>
<tr>
<td>MMSE score at 20-month follow-up</td>
<td>21.61 (5.35; 6 - 30)</td>
</tr>
<tr>
<td><strong>Carer</strong></td>
<td></td>
</tr>
<tr>
<td>Gender - Female : Male</td>
<td>35 : 16</td>
</tr>
<tr>
<td>Age</td>
<td>65.06 (14.50; 33 - 89)</td>
</tr>
<tr>
<td>Relationship to PwD - Spouse : Child : Other relative : Friend</td>
<td>29 : 16 : 4 : 2</td>
</tr>
<tr>
<td>Residing with PwD - Yes : No</td>
<td>32 : 19</td>
</tr>
</tbody>
</table>

Note: Mini-Mental State Examination (MMSE)
Table 2. Mean scores (sds; ranges) for the whole sample and for the three sub-groups at baseline and 20-month follow-up

<table>
<thead>
<tr>
<th>Quality of Life rating</th>
<th>Total sample n = 51</th>
<th>Increased ≥ 3 pts n = 15</th>
<th>Did not change n = 20</th>
<th>Decreased ≥ 3 pts n = 16</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>36.96 (5.09; 24 - 48)</td>
<td>35.00 (4.47; 24 - 43)</td>
<td>36.70 (5.55; 27 - 48)</td>
<td>39.13 (4.43; 33 - 48)</td>
</tr>
<tr>
<td>20-month follow-up</td>
<td>36.84 (5.78; 24 - 48)</td>
<td>40.60 (3.16; 37 - 46)</td>
<td>36.60 (5.68; 25 - 48)</td>
<td>33.63 (6.00; 24 - 45)</td>
</tr>
</tbody>
</table>
Table 3. Baseline mean scores (sds; ranges) or frequencies for key variables in each QoL group, and statistical comparisons

<table>
<thead>
<tr>
<th>QoL rating</th>
<th>Increased</th>
<th>Did not change</th>
<th>Decreased</th>
<th>Statistical comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>PwD N = 15</td>
<td>N = 20</td>
<td>N = 16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>76.00 (10.01; 57-87)</td>
<td>77.40 (6.95; 66-91)</td>
<td>76.06 (7.13; 55-84)</td>
<td>$F_{2,48} = .13, p = .88$</td>
</tr>
<tr>
<td>Years of education</td>
<td>12.20 (2.48; 9-17)</td>
<td>11.35 (2.64; 8-17)</td>
<td>11.88 (2.13; 9-17)</td>
<td>$F_{2,48} = .54, p = .59$</td>
</tr>
<tr>
<td>Diagnosis AD:VaD:Mixed</td>
<td>8:3:4</td>
<td>12:7:1</td>
<td>11:1:4</td>
<td>Chi-square $df_4 = 6.73, p = .15$</td>
</tr>
<tr>
<td>AChEI Yes:No</td>
<td>5:10</td>
<td>9:11</td>
<td>11:5</td>
<td>Mantel-Haenszel $df_1 = 3.84, p = .05$</td>
</tr>
<tr>
<td>MMSE score~</td>
<td>25.07 (3.53; 18-30)</td>
<td>24.50 (2.54; 19-29)</td>
<td>24.00 (2.39; 20-28)</td>
<td>$F_{2,48} = .55, p = .58$</td>
</tr>
<tr>
<td>FAQ carer-rated°</td>
<td>12.07 (7.69; 0 – 24)</td>
<td>18.10 (7.81; 3 – 30)</td>
<td>16.88 (6.84; 7 – 28)</td>
<td>$F_{2,48} = 2.97, p = .061$</td>
</tr>
<tr>
<td>NPI-Q no of symptoms°</td>
<td>4.07 (3.13; 0-9)</td>
<td>4.90 (2.00; 1-9)</td>
<td>4.63 (2.63; 0-8)</td>
<td>$F_{2,48} = .46, p = .64$</td>
</tr>
<tr>
<td>NPI-Q severity°</td>
<td>8.00 (7.29; 0-20)</td>
<td>9.30 (4.96; 0-20)</td>
<td>7.88 (5.75; 0-20)</td>
<td>$F_{2,48} = .32, p = .73$</td>
</tr>
<tr>
<td>Depression°</td>
<td>5.60 (3.50; 0-14)</td>
<td>4.05 (3.25; 0-12)</td>
<td>4.38 (3.69; 0-12)</td>
<td>$F_{2,48} = .91, p = .41$</td>
</tr>
<tr>
<td>Quality of relationship~</td>
<td>24.2 (2.73; 20-29)</td>
<td>23.90 (4.74; 10-30)</td>
<td>23.25 (4.04; 16-30)</td>
<td>$F_{2,48} = .23, p = .80$</td>
</tr>
<tr>
<td>CARER N = 15</td>
<td>N = 20</td>
<td>N = 16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stress°</td>
<td>16.79 (11.62; 4-44)*</td>
<td>21.85 (9.23; 8-42)</td>
<td>21.31 (9.87; 6-42)</td>
<td>$F_{2,47} = 1.15, p= .32$</td>
</tr>
<tr>
<td>Quality of relationship~</td>
<td>23.87 (5.07; 14-29)</td>
<td>22.35 (3.62; 13-29)</td>
<td>21.56 (3.29; 15-27)</td>
<td>$F_{2,48} = 1.32, p = .28$</td>
</tr>
</tbody>
</table>

*n=14  
~ higher score better  
° higher score worse

Note: Quality of Life (QoL), Alzheimer’s disease (AD), vascular dementia (VaD) or mixed Alzheimer’s and vascular dementia (Mixed), acetylcholinesterase-inhibiting medication (AChEI), Mini-Mental State Examination (MMSE), Functional Activities Questionnaire (FAQ), Neuropsychiatric Inventory Questionnaire (NPI-Q). 
Mantel-Haenszel here refers to the Mantel-Haenszel test for linear-by-linear association in IBM SPSS Statistics v.20.
Table 4. Baseline predictors of QoL score at 20-month follow-up

<table>
<thead>
<tr>
<th>Model</th>
<th>Step 1 (baseline QoL only)</th>
<th>Step 2 (all variables)</th>
<th>Final analysis with significant predictors only</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>R² = .35, F₁,₄₈ = 27.25, p &lt; .001</td>
<td>R² = .38, F₅,₄₄ = 7.03, p &lt; .001</td>
<td>R² = .39, F₂,₄₈ = 16.67, p &lt; .001</td>
</tr>
<tr>
<td>Baseline variables</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PwD QoL</td>
<td>.39</td>
<td>.39</td>
<td>.45</td>
</tr>
<tr>
<td>PwD depression</td>
<td>-.01</td>
<td>.93</td>
<td></td>
</tr>
<tr>
<td>PwD quality of relationship</td>
<td>.31</td>
<td>.06</td>
<td>.28</td>
</tr>
<tr>
<td>Carer stress</td>
<td>-.20</td>
<td>.15</td>
<td></td>
</tr>
<tr>
<td>Carer quality of relationship</td>
<td>-.13</td>
<td>.89</td>
<td></td>
</tr>
</tbody>
</table>