CHAPTER 4

Quality of life and depressive symptoms in early-onset dementia

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Submitted
Abstract

Background: Although studies on quality of life and depressive symptoms in early-onset dementia (EOD) are important, studies focusing on quality of life (QOL) in EOD are scarce.

Objective: To study: 1) QOL and depression in patients with EOD; 2) whether QOL is lower and depressive symptoms more frequent in patients with EOD compared to controls; 3) which demographic, clinical, and lifestyle factors contribute to QOL and depressive symptoms.

Method: We studied 61 patients with EOD [age: 61.9 (4.9)y, 41 (67%) men] and 67 controls [age 61.6 (4.6)y, 28 (42%) men]. QOL was assessed with the Dementia Quality of Life scale and depressive symptoms with the Center for Epidemiologic Studies Depression scale.

Results: Patients with EOD reported overall ‘good’ QOL, controls reported ‘very good’ QOL ($p < .001$). Patients with EOD reported more depressive symptoms ($p < .001$). Depressive symptoms were associated with a more fragmented rest-activity rhythm ($\beta = .22, p = .01$). Better QOL was associated with less depressive symptoms ($\beta = -.46, p < .001$) and being female ($\beta = .20, p = .02$).

Conclusion: Although patients with EOD had lower QOL and more depressive symptoms in comparison to controls, surprisingly, overall QOL was good. A more fragmented rest-activity rhythm was related to more depressive symptoms, which in turn were related to lower QOL in patients with EOD.
Since no cure for dementia is available, studies investigating quality of life (QOL) in dementia are relevant. QOL is a multidimensional construct and has been defined in dementia as: (quote) ‘the multidimensional evaluation of the person-environment system of the individual, in terms of adaptation to the perceived consequences of the dementia’. Interestingly, in a study investigating QOL in patients with late onset dementia (LOD), QOL was found to be lower in younger patients. Studies investigating QOL in patients with early-onset dementia (EOD) specifically are scarce. One recent study focused on the relationship between health-related QOL and unmet needs in EOD, for instance the need for suitable daytime activities at the day care center. In this study, health-related QOL was not related to unmet needs, but health-related QOL was lower in patients with higher levels of depression, a finding that is consistent with studies in LOD. Depressive symptoms are one of the most common neuropsychiatric symptoms in LOD. In EOD, a large variation in point-prevalence of depression has been reported when results from multiple studies are combined: 17–66 %. It has been suggested that this variation may be caused by the different depression scales and cut-off scores used.

Several factors have been found to be related to QOL and depressive symptoms. Longitudinal studies show that older people with more cardiovascular risk factors, such as hypertension, have a higher risk of developing depressive symptoms. Circadian theories of depression suggest that the brain’s biological clock, the suprachiasmatic nucleus, may be misaligned with daily activity patterns in individuals with depression. For instance, depressed adults may be less active during the day and more active during the night than nondepressed adults, resulting in a lower amplitude of the rest-activity rhythm, meaning that the rest-activity is less strong. In older women with dementia, a less stable rest-activity rhythm over multiple days was related to more depressive symptoms. Concerning lifestyle factors, it is known that cognitively intact individuals who are physically active are less prone to
depression than physically inactive individuals. Physical activity is also related to QOL in cognitively intact older people. Studies investigating the relationship between QOL and depressive symptoms and physical activity in dementia are scarce. A review, summarizing the findings of intervention studies, showed that the effect of physical activity programs on depressive symptoms and QOL was inconsistent in older people with dementia. The reason for this inconsistency was that the measures in the studies described were disparate. Studies focusing on the relationship between clinical and lifestyle factors and QOL and depressive symptoms in EOD are even more scarce. This is unfortunate because emotional wellbeing might be low in young patients with dementia because of age specific problems. For instance, patients with EOD may lose their job because of the disease, while being at the height of their career. The aim of the present study is to provide more insight in emotional wellbeing, that is, QOL and depressive symptoms, in patients with EOD, by studying 1) the level of QOL and depression in patients with EOD; 2) whether QOL is lower and depressive symptoms are more frequent in patients with EOD compared to cognitively intact adults of the same age; and 3) which demographic, clinical, and lifestyle factors contribute to QOL and depressive symptoms in patients with EOD.

**Methods**

**DESIGN**

The present study used a cross-sectional design. The medical ethics review committee of the VU University Medical Center (VUmc) approved all study procedures. We obtained written informed consent of each participant and all caregivers of the patients with EOD.
PARTICIPANTS

We studied 61 community-dwelling patients with EOD and 67 cognitively intact individuals. Patients with EOD were recruited primarily in the VUmc Alzheimer Center in Amsterdam, the Netherlands. The patients with EOD were recruited in order to participate in an exercise intervention trial. Detailed descriptions of the diagnostic and recruitment procedures are provided elsewhere. The cognitively intact controls were recruited using printed information leaflets.

*Inclusion criteria* for patients with EOD were the following: 1) diagnosis of EOD (onset of complaints < 66 years); 2) mild to moderate stage of dementia [Mini Mental State Examination (MMSE) score > 15]; 3) presence of a primary caregiver during the study. *Exclusion criteria* for this study were the same as for the intervention study: 1) wheelchair bound; 2) diagnosis of a neurodegenerative disease that primarily results in motor impairments; 3) diagnosis of serious cardiovascular disease, such as myocardial infarction; 4) substance abuse; 5) head injury involving loss of consciousness greater than 15 minutes in the medical history; 6) severe psychiatric illness, such as schizophrenia, N.B. depressive symptoms were not an exclusion criteria; 7) severe visual problems; 8) severe hearing problems; 9) insufficient mastery of the Dutch language.

*Inclusion criteria* for cognitively intact participants were: 1) age between 55 and 70 years, 2) normal cognitive status (MMSE > 25). *Exclusion criteria* were: acute or chronic health problems and in addition exclusion criteria 1, and 4 to 9 as applied in the EOD group.

*Demographic, clinical and lifestyle factors.* Factors considered were age, gender, educational level, MMSE total score, cardiovascular comorbidities, rest-activity rhythm variables, and the level of physical activity. The educational level was recorded according to the system of Verhage. Scores ranged from 1 (less than 6 years of elementary school) through 7 (academic degree). Subsequently, patients were classified as having received...
low (Verhage score 1 through 3), medium (Verhage score 4 and 5) or high (Verhage score 6 and 7) education. The number of cardiovascular comorbidities was recorded during an interview. Cardiovascular comorbidities that were recorded included: hypertension, cardiac arrhythmia, cardiac decompensation, arteriosclerotic vascular disease, thrombosis, and peripheral artery disease. We measured the rest-activity-rhythm with wrist actigraphy [Actiwatch-4 (AW4) Cambridge Neurotechnology, Ltd., Cambridge, Great Britain]. Participants wore the actiwatch for seven consecutive days and nights. We analyzed the data using Actiwatch Sleep Analysis Software (2001, version 1.06, Cambridge, Neurotechnology, Ltd., Cambridge, Great Britain), and calculated three rest-activity rhythm variables (for a detailed description see 25): Intradaily Variability (IV), i.e. the degree of fragmentation of periods of rest and activity within 24 hours, higher values reflect a higher degree of fragmentation; Interdaily Stability (IS), i.e. the stability of the rest-activity rhythm over multiple days, higher values indicate greater stability; Relative Amplitude (RA), i.e. the normalized difference between the most active and the least active period, with higher values reflecting a larger amplitude and therefore a stronger rhythm. The level of physical activity was assessed using a pedometer (OMRON Walking Style II, OMRON Healthcare CO. Ltd. Kyoto, Japan). The pedometer was worn for seven consecutive days. Participants recorded the number of steps in a diary every evening. Patients with EOD were assisted by their caregiver when needed. We calculated the mean number of steps per day.

**MATERIAL AND PROCEDURE**

QOL was measured using the *Dementia Quality of Life* scale (DQOL). 26 The DQOL is a self-report questionnaire and is considered a valid instrument to assess QOL in persons with mild to moderate dementia. 26 The DQOL consists of 5 subscales: self-esteem (e.g. feelings of confidence, self-content), positive affect (e.g. feeling fortunate, happy or hopeful), negative affect (e.g. feeling embarrassed, afraid or lonely), feelings of belonging (e.g. feeling useful, loved or liked), and sense of aesthetics (enjoying beauty, nature
and the surroundings), with possible scores ranging from 1 to 5. Also, using a 5-point Likert scale, the patient was asked to evaluate his/her overall quality of life as bad, reasonable, good, very good, or excellent. We constructed a factor that represents positive QOL by converting the subscales self-esteem, positive affect, feelings of belonging, and sense of aesthetics to z-scores and calculating the mean. We left negative affect out of this factor because of overlap with the depression scale.

Depressive symptoms were measured using the Center for Epidemiologic Studies Depression scale (CESD). The CESD is a 20-item self-report questionnaire used to quantify depressive symptoms in the general population. Possible scores range from 0 to 60 with higher scores reflecting greater symptomatology of depression. The most used cut off score for an indication of depression is ≥ 16.

**STATISTICAL ANALYSIS**

In case of missing values on the questionnaires, cases were excluded from the analyses. In the pedometer data, persons with more than two days missing were excluded. For persons with one or two days missing, a corrected mean number of steps per day was calculated, by adding the values of the days that were completed and dividing this value by the number of days that were recorded. Normality was checked using Shapiro-Wilk tests, with transformations applied afterwards when appropriate. Reliability analysis (Cronbach’s Alpha) was used to examine the QOL factor. A Cronbach’s alpha of .80 or higher is indicative of a good internal consistency. Group characteristics regarding demographics, QOL, and depressive symptoms were considered using independent sample t-tests, Mann-Whitney U tests, and χ²-tests.

To study which demographic, clinical, and lifestyle factors contributed to QOL and depressive symptoms, we conducted multiple linear regression analysis, in the entire sample. The positive QOL factor (z-score) and the
CESD total score were the dependent variables (each in separate analysis). Independent variables were group, age, gender, educational level, MMSE, cardiovascular co-morbidities, IV, IS, RA, mean steps per day, and depressive symptoms (for QOL), which were entered stepwise (forward). The interaction between group and significant predictors was assessed to establish whether the found relationships were the same for the EOD group and the control group. For all regression analyses probability for entry was set at .05, and probability for removal was set at .10. For statistical analysis we used SPSS version 20.0 for Windows (SPSS Inc., Chicago, IL, USA).

Results

DATA-EXPLORATION

On the DQOL one patient with EOD and two controls had missing values, on the CESD four patients with EOD and one control had missing values; these cases were excluded from the analyses. In the pedometer data seven patients with EOD had more than two days missing and were excluded from analyses. For four patients with EOD and three controls a corrected mean number steps per day was calculated. Reliability analysis showed sufficient reliability for the QOL factor (Cronbach’s Alpha = .78).

GROUP CHARACTERISTICS

An overview of the group characteristics is given in Table 1 (p. 75). In the EOD group, 75.4% of the patients had a diagnosis of Alzheimer’s disease (AD). The MMSE score was lower in the EOD group than in the control group, $U = 231.5$, $p < .001$. Men were overrepresented in the EOD group, $\chi^2(1) = 8.31$, $p = .004$. 


QOL AND DEPRESSIVE SYMPTOMS IN PATIENTS WITH EOD COMPARED WITH COGNITIVELY INTACT ADULTS

An overview of the scores on the DQOL and the CESD in the EOD group and the control group is given in Table 2 (p. 76).

**QOL.** Patients with EOD reported an overall ‘good’ QOL, controls reported an overall ‘very good’ QOL ($U = 1286.0, p < .001$). Patients with EOD reported more often a ‘poor’, ‘reasonable’, and a ‘good’ QOL, while controls reported more often a ‘very good’ and an ‘excellent’ QOL ($\chi^2 = 16.57, p = .002$). Regarding the subscales of the DQOL, patients with EOD had a lower self-esteem ($t(124) = -4.26, p < .001$), a lower positive affect ($t(113) = -2.23, p = .03$), and a higher negative affect than controls ($t(125) = 3.40, p = .001$). No differences were found on the subscales feelings of belonging and sense of aesthetics.

**Depressive symptoms.** Patients with EOD experienced more depressive symptoms compared to controls ($U = 966.0, p < .001$). The mean CESD score was in both groups below the cut-off score of 16 points. In the EOD group 21.1% of the patients was depressed, whereas in the control group 7.6% of the persons was depressed ($\chi^2 = 4.66, p = .03$).

ASSOCIATIONS BETWEEN QOL AND DEPRESSIVE SYMPTOMS AND DEMOGRAPHIC, CLINICAL, AND LIFESTYLE FACTORS

An overview of the regression coefficients ($B$), standard errors ($SE$), 95% confidence intervals ($CI 95\%$), standardized regression coefficients ($Beta$) and the proportions explained variance, is given in Table 3 (p. 77).

The model predicting QOL by group, age, gender, educational level, MMSE, IV, IS, RA, mean steps per day, and depressive symptoms, showed that a higher QOL was associated with less symptoms of depression and being female, which accounted for 28.7 % of the variance ($F(2,111) = 22.38, p < .001$).
Concerning depressive symptoms, independent factors considered were group, age, gender, educational level, MMSE, cardiovascular disorders, IV, IS, RA, and mean steps per day. More symptoms of depression were associated with a higher IV, meaning a more fragmented rest-activity rhythm within 24 hours, and by group. The model explained 21.7% of the variance (F(2,112) = 15.48, p < .001). None of the other factors contributed to QOL or depressive symptoms. No interactions between group and the main predictors were present in either analysis, therefore the associations were the same for the EOD group as for the control group.

**Discussion**

The main results of this study are that patients with EOD reported an overall ‘good’ QOL, while controls reported a ‘very good’ QOL. Further, patients with EOD reported more depressive symptoms. Twenty-one percent of the patients with EOD and eight percent of the controls were depressed. Depressive symptoms were associated with a more fragmented rest-activity rhythm. Better QOL was associated with less depressive symptoms and being female.

It is quite remarkable that after receiving a diagnosis of dementia at a young age and the additional consequences, the reported overall QOL can still be good. This intriguing finding might be partly explained by the nature of our sample. The patients in this study were willing to participate in an exercise intervention and hence may have better health and be more active than patients with EOD who did not participate. As a result, the patients in the current study might have better QOL than those who were not willing to participate; regardless, an EOD diagnosis does not necessarily result in poor QOL. When comparing our results to studies that used the DQOL in patients with LOD, mean overall DQOL values were similar, that is, a score of 3.0 indicating ‘good’ QOL. The scores on the subscales of the DQOL were 0.3 to 0.5 points higher (on a scale ranging from 1 to 5) in our study.
than in the studies assessing QOL in LOD. The largest differences were on the subscales feelings of belonging (0.4 point higher) and sense of aesthetics (0.5 points higher). In the present study, feelings of belonging and sense of aesthetics were at the same level for patients with EOD and cognitively intact adults. This means that patients with EOD feel safe, secure and loved to the same degree as the control group.26 Also, they enjoy nature and beautiful things just as much as controls do. This encourages activities such as taking a walk, visiting a museum, or listening to music. Activities that the patient enjoyed premorbidly may be a good basis for activities that can still be enjoyed. Further, positive affect was lower and negative affect was higher in patients with EOD than in controls. These findings are not surprising, since we also found that depressive symptoms were more frequent in patients with EOD than in cognitively intact adults, which is in agreement with studies in LOD.6 Self-esteem was lower in the EOD group compared to the control group, which is in accordance with previous work in EOD.37 The EOD group as a whole did not score above the CESD cut-off of 16 points, meaning that they did not reach the criteria of depression. Of the EOD group a relatively small portion (21%) did reach the threshold for depression. This percentage is in agreement with the study of van Vliet (2012) who reported a point prevalence of depression of 17% in patients with EOD, as measured with the neuropsychiatric inventory.7 Other studies have reported higher numbers of depression among patients with EOD.8,10 This difference may be explained by the nature of our sample. The present sample may be relatively physically active, which is related to a lower risk of developing depressive symptoms.17 The difference in prevalence may also be caused by the depression scales and cut-off scores used in the different studies.8

In our study a better QOL was associated with less depressive symptoms and by being female. The relationship between QOL and depressive symptoms has been described before in LOD.5 However, the finding that women have better QOL than men, is in contrast with findings in the general population.38 Why QOL is lower in men than in women with EOD remains speculative and could be explored in future studies. One possible explanation may be that men of middle age, who were the main provider in their family and who
lost their job because of the EOD, have a larger decrease in QOL than persons, perhaps more often women, who were not the head of income in their family on time of diagnosis. Depressive symptoms were associated with higher IV, that is, a more fragmented rest-activity rhythm within 24 hours. A previous study showed, that adults with a major depression were less active during the day and more active during the night compared to controls. These activity patterns could translate into a higher IV. In contrast to our findings, in older women with dementia, more depressive symptoms were related to a lower stability of the rest-activity rhythm over days (IS). That study population differed however from our population in view of age (older) and gender (only women). Whether age and gender influence the relationship between depressive symptoms and rest-activity variables may be explored in future research endeavors.

Several limitations have to be considered. The present study is cross-sectional in nature precluding inferences on causation. QOL and depressive symptoms were assessed using self-report questionnaires. Whether it is best to use self-reports or proxy reports in patients with dementia is a matter of debate. We chose self-report questionnaires because our patients with EOD had mild to moderate stages of dementia, and hence we believed that insight would be relatively intact. Further, self-report measures are generally considered as the gold standard, since proxies may have different appraisal of emotional wellbeing than the patients themselves. Finally, the results of our study cannot be generalized to all patients with EOD. The present population was mild to moderately affected and recruited in order to participate in an intervention study, which could have led to a more active study population.

To conclude, although patients with EOD had lower QOL and more depressive symptoms in comparison to cognitively intact adults, overall QOL was good. A more fragmented rest-activity rhythm was related to depressive symptoms, which in turn was related to QOL in patients with EOD. The present findings give an indication of emotional wellbeing in patients with EOD and may be replicated in future studies.
ACKNOWLEDGEMENTS
We would like to acknowledge the contributions of the participants of this study.

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References


Table 1. Group characteristics of patients with early-onset dementia and cognitively intact adults

|                          | **EOD**  
|--------------------------|----------|
|                          | \(n = 61\) | **Controls**  
|                          |          \(n = 67\) | **p** |
| Age, mean (SD)           | 61.9 (4.9) | 61.6 (4.6) | .774\(^a\) |
| MMSE, median (range)     | 25 (16-30) | 30 (26-30) | <.001\(^b\) |
| Gender, men (%)          | 41 (67.2)  | 28 (41.8)  | .004\(^c\) |
| Educational level, median (range) |          |          | .235\(^c\) |
| Low                      | 4 (6.6)    | 1 (1.5)    |          |
| Medium                   | 25 (41.0)  | 34 (50.7)  |          |
| High                     | 32 (52.5)  | 32 (47.8)  |          |
| Diagnosis, n (%)         | n.a.       | n.a.       |          |
| AD                       | 46 (75.4)  |          |          |
| VaD                      | 5 (8.2)    |          |          |
| DLB                      | 7 (11.5)   |          |          |
| FTD                      | 2 (3.3)    |          |          |
| Dem nao                  | 1 (1.6)    |          |          |
| Cardiovascular comorbidities, n (%) | 15 (24.6)| 18 (26.9) | .769\(^c\) |

Notes:
\(^a\) Independent sample \(t\)-test; 
\(^b\) Mann-Whitney \(U\) test; 
\(^c\) \(\chi^2\)-test 
\(^d\) Level of education is assessed with Verhage’s education classification (Verhage, 1964).

Abbreviations: AD = Alzheimer’s Disease; Dem nao = dementia not otherwise specified; DLB = Lewy body dementia; EOD = early-onset dementia; FTD = frontotemporal dementia; MMSE = Mini-Mental State Examination; N.a. = not applicable; VaD = vascular dementia.
### Table 2. Quality of life and depressive symptoms compared between patients with early-onset dementia and cognitively intact adults

<table>
<thead>
<tr>
<th></th>
<th>EOD (n = 60)</th>
<th>Controls (n = 65)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall QOL, median (range)</td>
<td>3 (1-5)</td>
<td>4 (2-5)</td>
<td>&lt;.001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Overall QOL, n (%)</td>
<td></td>
<td></td>
<td>.002&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Poor</td>
<td>1 (1.6)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Reasonable</td>
<td>13 (21.3)</td>
<td>4 (6.1)</td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>33 (54.1)</td>
<td>26 (39.4)</td>
<td></td>
</tr>
<tr>
<td>Very good</td>
<td>9 (14.8)</td>
<td>27 (40.9)</td>
<td></td>
</tr>
<tr>
<td>Excellent</td>
<td>5 (8.2)</td>
<td>9 (13.6)</td>
<td></td>
</tr>
<tr>
<td>DQOL subscales, mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self-esteem</td>
<td>13.9 (2.4)</td>
<td>15.7 (2.1)</td>
<td>&lt;.001&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Positive affect</td>
<td>21.6 (3.5)</td>
<td>22.9 (2.7)</td>
<td>.028&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Negative affect</td>
<td>26.2 (6.5)</td>
<td>22.6 (5.2)</td>
<td>.001&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Feelings of belonging</td>
<td>11.3 (1.8)</td>
<td>11.5 (1.5)</td>
<td>.587&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Sense of aesthetics</td>
<td>18.1 (3.5)</td>
<td>18.2 (3.9)</td>
<td>.845&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>CESD total score, median (range)</td>
<td>8.5 (1-35)</td>
<td>4.0 (0-19)</td>
<td>&lt;.001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Depressed personsd, n (%)</td>
<td>12 (21.1%)</td>
<td>5 (7.6%)</td>
<td>.031&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

**Notes:**

<sup>a</sup> Mann-Whitney U test.
<sup>b</sup> χ²-test.
<sup>c</sup> Independent sample T test.
<sup>d</sup> Cut off CESD total score ≥ 16.

*Abbreviations: CESD = Center for Epidemiologic Studies Depression scale; DQOL = Dementia Quality of Life scale; EOD = early-onset dementia.*
Table 3. Associations between quality of life (QOL) and depressive symptoms and demographic, clinical and lifestyle factors in patients with early-onset dementia (EOD) and cognitively intact adults

<table>
<thead>
<tr>
<th></th>
<th>QOL (n = 114)</th>
<th></th>
<th>Depressive symptoms (n = 115)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B (SE)</td>
<td>CI 95%</td>
<td>B (SE)</td>
</tr>
<tr>
<td>Group</td>
<td>ns</td>
<td>ns</td>
<td>-0.82 (.20)***</td>
</tr>
<tr>
<td>Age</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td>Gender</td>
<td>0.30 (.13)*</td>
<td>0.05 – 0.55</td>
<td>- .36</td>
</tr>
<tr>
<td>MMSE</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td>Cardiovascular comorbidities</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
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<tr>
<td>IV</td>
<td>ns</td>
<td>ns</td>
<td>1.91 (.74)*</td>
</tr>
<tr>
<td>IS</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td>RA</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td>Mean steps per day</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td>Depressive symptoms</td>
<td>-0.32 (.06)***</td>
<td>-1.41 – 0.78</td>
<td>- .46</td>
</tr>
<tr>
<td>( R^2 )</td>
<td>.29***</td>
<td></td>
<td></td>
</tr>
<tr>
<td>( F )</td>
<td>22.38</td>
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</tbody>
</table>

**Notes:**
Associations were assessed using multiple linear regression analysis (stepwise). Only significant associations are displayed. \( R^2 \) and \( F \) of the model that best predicted the dependent variable.

\*\*\*p < .001; \*\*p < .01; \*p < .05; ns = regression coefficient not significant, excluded from the model;

Abbreviations: IV = Intradiaily Variability; IS = Interdaily Stability; MMSE = Mini-Mental State Examination; QOL = quality of life factor (mean z-score) of subscales self-esteem, positive affect, feelings of belonging, and sense of aesthetics; RA = Relative Amplitude.