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Quality of life in a German cohort of Parkinson's patients assessed with three different measures

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Summary

Background: Parkinson's Disease (PD) is characterized by severe motor and non-motor symptoms reducing patients' quality of life (QoL). Instruments have been well-established for QoL assessments in PD, including the EuroQol (EQ-5D), the Parkinson's Disease questionnaire (PDQ-39), or rather uncommon, like the WHOQOL-100. So far, the impact of variables has been investigated for each of these measures separately in different study populations, limiting the comparability of the results. Thus, this study compared the EQ-5D, PDQ-39, and the WHOQOL-100 (with its short form WHOQOL-BREF) in the same study population.

Methods: Seventy-five PD outpatients were assessed in a prospective study, including disease severity according to Hoehn and Yahr stage (HY) and Unified Parkinson Disease Rating Scale (UPDRS). The Geriatric Depression Scale (GDS-15) screened for depression.

Results: Decreased QoL was found with all three instruments. In multivariate models, sex and treatment complications had an impact on QoL according to all three measures, while duration of PD and HY were not associated with QoL in any of them. Depression was relevant for the WHOQOL-100/WHOQOL-BREF and the PDQ-39, but not for the EQ-5D. The total variances explained by the WHOQOL-100, WHOQOL-BREF, PDQ-39, and the EQ-5D were .27, .34, .70, and .50, respectively.

Conclusions: The associations between clinical aspects of PD and QoL vary substantially among all three measures. Importantly, depression as a frequent comorbidity in PD is underestimated by the EQ-5D, but not by the PDQ-39 and the WHOQOL-100/WHOQOL-BREF. In turn, motor impairments are underestimated by the latter and associated strongest with QoL in the EQ-5D.

Keywords: Quality of life, Parkinson's disease, cohort study, WHOQOL-100, DEMPARK/LANDSCAPE study

Introduction

Parkinson's disease (PD) ranks second among neurodegenerative disorders with an incidence that rises with age and a lifetime risk of 1.5% [1]. It is clinically characterized by rigidity, tremor, bradykinesia, and impaired postural reflexes. Additionally, non-motor symptoms such as psychiatric symptoms, autonomic disturbances, and sleep disorders frequently complicate the course of the disease. Since there is no curative treatment for PD and symptom load often increases over the course of the disease, patient-reported outcomes and especially the patients' QoL become increasingly important. This holds particularly true in later stages, when problems such as treatment-related complications, falls, depression, and dementia can occur and may negatively impact the patients' health-related quality of life (HrQoL) more than the motor symptoms of PD [2, 3].

The Constitution of the World Health Organization (WHO) defines health as "a state of complete physical, mental, and social well-being, not merely the absence of disease" and quality of life (QoL) as an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards, and concerns [4]. However, as is the case for many psychological constructs, the one true definition of QoL does not exist. Concepts may rather vary, depending on the context in which they were developed. Consequently, various measures and assessments for QoL are applicable. During the past two decades, numerous studies have investigated QoL in patients with PD, mostly using the generic EuroQoL instrument (EQ-5D), which rather depicts an individual’s health state rather than his or her well-being, or the disease-specific Parkinson’s Disease Questionnaire (PDQ-39) to assess participants' QoL.

Despite their different conceptual approaches, both measures have been well-established and frequently used in research on PD, and the impact of sociodemographic and clinical variables on QoL has been previously described in great detail [5]. Compared to these two commonly used measures, the generic WHOQOL-100 instrument as well as it short form WHOQOL-BREF have been used only in few studies on PD patients so far [6-10]. Moreover, the utility of each of these measures has only been separately investigated in different study populations [5], and little is known about how these three measures differ regarding the impact of different variables when assessing the same study population. Studies which have investigated the comparability of these instruments by using one common sample of PD patients are still lacking. Such data could be helpful for the decision whether certain QoL measures should be favored for specific PD populations (e.g., with and without depression).

Therefore, the aims of this study were twofold: (1) To compare QoL as assessed by the EQ-5D, the PDQ-39 and the WHOQOL-100 in PD outpatients of a prospective, observational

study (DEMPARK/LANDSCAPE), (2) to assess the feasibility of the short-version of the WHOQOL-100 ("WHOQOL-BREF") in this population.

Patients and Methods

Study design

The ongoing DEMPARK/LANDSCAPE trial was designed as a multicenter prospective, observational cohort study that included more than 700 patients with a diagnosis of idiopathic PD according to the UK Brain Bank Criteria [11] and with or without dementia in Germany. The patients were recruited in nine specialized movement disorder clinics and most of them had follow-up visits for more than 48 months. At baseline and yearly follow-ups, well-established standardized questionnaires/tests were applied for detailed neurological and neuropsychological assessment of the patients. The clinical examination was performed in the clinical "on" state. The detailed study protocol of the DEMPARK/LANDSCAPE study has been published elsewhere [12]. For the analyses presented in this paper, only patients from the Marburg study center (n=92) were considered.

Clinical outcome measures

The severity of PD was assessed with the original five-stage version of the Hoehn and Yahr scale (HY), which defines broad categories of symptom and disability progress (i.e., disease severity) in PD. Lower HY stages (I-III) represent low to moderate impairment, while stages IV and V indicate severe impairment [13]. For more detailed assessments, the Unified Parkinson's Disease Rating Scale (UPDRS) part III was used for motor symptoms and the UPDRS part IV for complications of therapy [14].

Global cognitive impairment was assessed with the Mini Mental State Examination (MMSE) in all patients [15] and the Parkinson Neuropsychometric Assessment (PANDA) [16]. Using a comprehensive neuropsychological test battery, all patients were tested for deficits in the cognitive domains of memory, language, executive functions, visuospatial orientation, and attention (for a full description of all included scales and corresponding references please see [12]). Cognitive dysfunction was defined as scores ≤ -1.5 standard deviations below the mean in at least one neuropsychological test score. Patients without cognitive dysfunction were categorized as PD without cognitive impairment (PD). The presence of mild cognitive impairment (PD-MCI) was operationalized according to Petersen et al. [17]. Parkinson's disease with dementia (PDD) was operationalized according to Emre et al. [18].

Depressive symptoms were assessed with the short form of the Geriatric Depression Scale (GDS-15) [19]. The short form of the GDS is a self-rating instrument for the detection of depressive symptoms especially in the elderly. Following recommendations, a score of ≥5 out of 15 points maximum was used as an indicator for clinical depression [20].

Quality of life measures

The QoL was assessed in all participating patients at all nine centers with the EuroQol instrument and the PDQ-39 [21, 22]. Additionally, the WHOQOL-100 was used to assess QoL in the study participants in Marburg only.

The QoL was assessed with the generic EuroQol instrument, comprising the EQ-5D questionnaire and a visual analogue scale (EQ VAS) for patients to indicate their perception of their actual state of health. The EQ VAS ranges from 0 to 100 points with higher scores indicating a better QoL. The EQ-5D has five domains relating to mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each of these domains can be endorsed at three levels (0 = no problems, 1 = some problems, and 2 = severe problems) and, as a result, allows for the definition of 3^5 (= 243) different health states. A composite utility index was calculated according to the algorithm published by Greiner and colleagues [23].

The Parkinson's Disease Questionnaire (PDQ-39) is a PD-specific measure of QoL, consisting of 39 questions covering eight dimensions (mobility, activities of daily living, emotional well-being, stigma, social support, cognition, communication, and bodily discomfort). A summary index is calculated as the mean of the total sum score of the dimensions divided by the number of dimensions [22, 24]. The sum of all items yields a score between 0 and 100 with higher scores indicating lower QoL.

The generic WHOQOL-100 assesses QoL in 24 facets across six broad domains (physical health, psychological health, level of independence, social relations, environment, and spirituality/religion/personal beliefs) as well as general items covering subjective overall QoL and health with a total of 100 items [25]. All items are rated on a five-point scale (1-5) with higher scores reflecting higher QoL, except for the facets pain and discomfort, negative feelings, and dependence on medication or treatments [26]. The WHOQOL-100 has been shown to display good discriminant validity, content validity, and test-retest reliability. We additionally assessed the short form of the WHOQOL-100 (“WHOQOL-BREF”) which can be generated based on 26 out of the 100 items of the original WHOQOL-100, merging domains 1 and 3, and also domains 2 and 6, to yield a four-domain structure (covering physical health, psychological health, social relations, and environment (see Suppl. Table 1)).

Statistical Analysis

All data are presented as means with standard deviation (SD) or number of cases (percentages) where appropriate. Group differences were tested by t-test for symmetrically distributed metric variables and Mann-Whitney U-test or Kruskal-Wallis-test otherwise. Correlations between QoL measures were calculated based on Pearson's *r*. Linear regression analyses were conducted to investigate potential predictor variables for the three QoL measures WHOQOL-100, PDQ-39, and EQ-5D index. The standardized regression coefficient (β_{ST}) was reported in addition to the common regression coefficient (β) and can be categorized into a small (β_{ST} <0.1), medium (0.1≤ β_{ST} ≤0.3), and large effect (β_{ST} >0.3) for continuously distributed variables. Accordingly, categorical variables are classified as small (β_{ST} <0.3), medium (0.3≤ β_{ST}≤.0.8), and large (β_{ST} >0.8) [27]. The predictors for the regression analyses were chosen according to previously published findings [7, 9], depending on data availability.

The significance level was α = 0.05. All statistical analyses were conducted with SAS 9.3 (SAS Institute Inc., Cary, NC).

Results

Ascertainment and characteristics of the study sample

At baseline, 77 out of 92 recruited DEMPARK/LANDSCAPE patients (85.9%) in Marburg filled out all three QoL questionnaires. Two of these patients had to be excluded from the analyses due to a change of the initial diagnosis from PD to Dementia with Lewy bodies, resulting in a total of n=75 patients considered for the analyses (see table 1). Hereof, 69.3% were male. The average age of the participants was 65.5±8.3 years, and overall, more than 80% lived in a stable relationship, but significantly more women than men were either divorced, separated or widowed (17 vs 4%, respectively). Regarding the clinical status, the average age at PD onset was 58.4±7.8 with a mean disease duration of 7.0±5.0 years; there were no significant differences between the sexes. More than 40 percent of the patients were categorized as HY stage II. No patient was in HY stage IV and only one in V, who was considered in descriptive analyses only. There were no sex differences concerning disease severity. Patients scored 25-30 (mean 28.8) points in the MMSE and 9-30 (mean: 23.7) points in the PANDA. No patient showed dementia at baseline. The mean score of the GDS was 2.9±2.5, and 22.7% of the patients had depression (GDS score ≥5). Depressed patients did not differ from non-depressed patients regarding the variables as shown in Table 1 with

the exception of significantly higher scores on the UPDRS subscales I (4.0 vs 2.1, p<.001) and III (25.4 vs. 18.4, p<.05). We also found a trend (p=.05) of more advanced HY stages among depressed than non-depressed subjects (stages I+II: 70.6% vs. 88%, stage III: 23.5% vs. 12.1%, data not shown).

Quality of life measures

Table 2 shows the mean scores on the PDQ-39, EQ-5D (including the VAS), and the WHOQOL-100. QoL deteriorates with increasing disease severity as reflected by the HY stage of the patients. We tested the differences between the subgroups for significance after the exclusion of the single patient with HY stage V (data not shown). On the WHOQOL-100, females scored significantly worse (p<.001) on each scale with the exception of social relations (p=.119). No difference was detected between patients from the younger (≤ 65 years) and older (≥ 66 years) age groups on any scale. Regarding PD duration, there were only significant (p<.001) differences on the level of independence between patients with a shorter and a longer disease duration. With regard to the HY stage, significant differences were only detected for physical health and the level of independence, here, the HY stages I, II, and III differed from each other on a level of p<.01.

For the PDQ-39, we found significant differences between male and female patients in terms of higher values for women on the subdomains mobility, emotional well-being, bodily discomfort (p<.01 each), and stigma (p<.05). Older patients scored significantly lower than younger patients on the domains stigma and social support. Patients with a shorter disease duration differed from patients with a longer duration only concerning the mobility domain (p<.01). Patients from HY stages I to III differed significantly from each other (p<.01) on all PDQ-39 domains except stigma, social support, and bodily discomfort. The PDQ-39 index score was significantly higher in women than in men (p<.01). There was also a significant difference between HY stages I, II, and III (p<.001): The QoL decreased with disease progression and severity of symptoms. The PDQ-39 score was not associated with age (p=.598) or PD duration (p=.147).

The same results were found for the EQ-5D index score, which was significantly different between men and women (p<.01), between all three HY stages (p<.01), and between patients with shorter or longer PD duration (p<.05). The EQ VAS decreased significantly with increasing disease severity (HY) but was not associated with sex (p=.280), age (p=.598) or PD duration (p=.147). When we examined the single dimensions of the EQ-5D (see table 3), we found significant differences associated with age, where older patients (≥66 years) reported more problems with self-care than younger patients, and with disease duration,

where more problems in the dimension usual activities were associated with a disease duration of more than five years. Higher HY stages were associated with more problems in each dimension. Females reported more severe problems than males in all dimensions; all reported differences were significant except for those in the dimension self-care and mobility, as all patients reported mobility impairments.

We next analyzed associations of selected sociodemographic and clinical variables with the total scores of the WHOQOL-100, WHOQOL-BREF, PDQ-39, and the EQ-5D index score, respectively (see table 4). There were differences between the WHOQOL-100, PDQ-39, and the EQ-5D regarding the explained variance in the multivariable models. The clinical variables resulted in a higher R^2 value for the disease-specific PDQ-39 (R^2=0.70), in contrast to the multivariable model for WHOQOL-100 (R^2=0.27) and WHOQOL-BREF (R^2=0.34). Consistently, sex, depression (GDS score), and treatment complications (UPDRS IV) were significant predictors for QoL across all four measures. The GDS score showed a medium association for EQ-5D index and WHOQOL-100/WHOQOL-BREF and a large association for PDQ-39. UPDRS III had a large effect on PDQ-39 and EQ-5D index. HY stage was not significantly associated with the outcome in any of these.

In the total sample, significant correlations were found between the EQ-5D and the PDQ-39 (r=-.65, p<.001), between the EQ-5D and the WHOQOL-100 (r=.41, p<.001), and between the PDQ-39 and the WHOQOL-100 (r=-.45, p<.0001), respectively. These correlations were only slightly reduced in patients with depression (r=-.63, p<.001; r=.44, p<.001; r=.-45, p<.001). Correlations between domains of the WHOQOL-100 and their counterparts in the WHOQOL-BREF ranged between r=.88 (physical health, social relations) and r=.96 (psychological health). The global scores of both versions correlated at r=.90. All correlations were highly significant (p<.001).

Discussion

Chronic conditions have been repeatedly shown to be associated with decreased QoL [28, 29]. This finding has also been reproduced in PD patients by various studies [30], yet by using different measures for QoL in different study populations, leading to unclarity about the comparability of these measures when assessing PD patients. This was the first study to compare the QoL according to two generic and one PD-specific QoL measures in the very same population.

We found a reduced QoL in patients with PD and the reduction was associated with higher disease severity and longer disease duration as well as the occurrence of depressive

symptoms. The generic EuroQol instrument underestimated the impact of depression on PD patients' QoL in comparison to the WHOQOL-100, which should (in its shortened version) be considered as an alternative assessment tool also for PD patients. To our best knowledge, there are only two publications using the WHOQOL-100 to assess QoL in PD patients. Valeikiene et al. [10] compared patients with osteoarthritis, patients with PD, and a control group. Overall, QoL in PD patients did not differ significantly from the other two groups while the scores for mobility, activities of daily living, and working capacity of the level-of-independence domain were significantly poorer in PD patients. PD patients tended to score lower on all facets of the WHOQOL-100 except for social support of the social relations domain and positive feeling of the psychological health domain. Chen et al. [6] compared the acupuncture treatment in 33 PD patients who additionally received Western medicine as compared to patients who received Western medicine only and found significant improvements in QoL as assessed with the WHOQOL-100 in the former patient group. The utility of the short form WHOQOL-BREF in PD patients has been described in few studies as well. Hendred and Foster [7] investigated the WHOQOL-BREF in a sample of 96 patients with mild to moderate PD and found acceptable psychometric properties and a good discrimination between PD patients and healthy controls. Two Brazilian publications reported data on the WHOQOL-BREF in PD outpatients [8, 9], underscoring the good psychometric properties of this instrument when used in this population. However, due to the limited sample sizes, further stratifications of the results (eg. to patients' sex) were restricted. Moreover, Lucas-Carrasco et al. [31] investigated the utility of the Disability Module (WHOQOL-DIS) with the WHOQOL-BREF in 65 PD patients, and found acceptable internal consistency and validity. Because of logistical reasons, however, this instrument could not be implemented in our study.

Due to the nature of a disease-specific instrument, the PDQ-39 cannot be compared to a standard population, but the two generic instruments used, the EuroQol instrument and the WHOQOL-100, were compared to EQ-5D data on German reference populations as published by Koenig et al. [32]. In their 2005 study, females reported significantly more problems than males, especially in the dimensions self-care and pain/discomfort. In our cohort, we found that female participants reported more problems in all dimensions, with a significant difference in all dimensions except self-care. The most obvious difference was found in the anxiety/depression dimension: In the German population of 2005, 4.3% of the participants reported problems, in our cohort, 28.4% reported either some or severe problems. In our cohort, all patients reported problems with mobility, 73% with pain/discomfort, 37.9% with usual activities, 28.4% with self-care, and 28.4% with anxiety/depression (data not shown). In comparison, Koenig et al. found much lower values for all dimensions. Concerning age and health status, they found a decrease of the EQ VAS

values with age and a low of 60.5 in the oldest (>75 years) participants. In our cohort, we found no difference in EQ VAS in association with age, and the mean EQ VAS value of the participants was higher (65.7±17.3) than that found in the German population of 2005 (see table 2). When comparing these findings however, it is necessary to keep two aspects in mind. First, as Koenig et al. reported data from the general population, different results can be expected in a population of subjects suffering from a severe, chronic disease. Second, female patients in our cohort were less likely to live in a relationship than male patients, and Koenig et al [32] found in their study that persons living in a relationship reported less frequently problems in the EQ-5D. In a study with 124 PD patients in London, Schrag et al. [33] found an EQ VAS of 64.8±22.8 and a PDQ-39 summary index of 30.0±19.3 compared to our 65.7±17.3 and 25.0±16.0, respectively; both values are similar to those found in our cohort.

Although disease-specific QoL measures (e.g., here the PDQ-39) reflect disease-specific impact in more detail, for the comparison of QoL across different diseases and with control populations, generic instruments are preferable. But in our patient sample, one of the most common non-motor symptoms in PD, depression, was underestimated by the generic EuroQoL instrument, but not by the WHOQOL-100 or the WHOQOL-BREF. Thus, in further studies, especially in cohorts where depression might be an issue, the WHOQOL-100 should be considered as an alternative assessment for QoL. Yet, the filling of the 100 questions of the WHOQOL-100 is time-consuming and sometimes exceeds the concentration limit of the patients, which might result in cancellation of further data collection. Given the very similar associations between clinical outcomes and either the WHOQOL-100 or the WHOQOL-BREF in our study, the shorter version of the instrument should be used. As our data have shown, the short version of the WHOQOL also estimates the impact of depression on QoL in PD patients better than the EuroQol instrument.

The present study has several limitations. A fundamental problem is the general comparability of the three measures of QoL since in the end they all differ more or less in their underlying conceptualization, such as a more patient-focused perspective of the PDQ-39 versus the general target population of the WHOQOL-100/WHOQOL-BREF. One could also argue that, strictly speaking, the EuroQol instrument (and as its part, the EQ-5D) does not assess QoL at all but rather an individual's health state (which is composed, however, of domains that are used for the assessment of QoL according to the two other measures). While this argument is comprehensible, the EQ-5D indubitably has been commonly used for the assessment of QoL in many different patient populations, including PD patients [34-36] and it is reasonable that this instrument will also be used frequently in future studies, not least because of its simplicity and brevity [37]. Due to this, a direct comparison of the EQ-5D

with the PDQ-39 and WHOQOL-100/WHOQOL-BREF seemed appropriate to us, as it accounts for the daily practice. However, any differences between all three measures as depicted in our data should also interpreted as potentially being caused by underlying differences in concepts of QoL. Further limitations refer to the methodology of the study. First, the study design was cross-sectional, which does not allow for conclusions in terms of causality. Therefore, the described relationships between QoL and sociodemographic or clinical variables can only be understood as associations and have to be interpreted cautiously. To ascertain the causative direction, further longitudinal studies are needed. Second, the patient sample we analyzed is a clinical as well as a convenience sample and not necessarily representative for patients with PD in Germany or generalizable to other countries. Baseline analyses of patients' characteristics show that the patients of the study center Marburg are not representative for the whole DEMPARK/LANDSCAPE study population: At the time of inclusion, patients in Marburg were younger, in lower HY stages, and less cognitively impaired than participants in the other study centers. Because of our recruitment method and the characteristics of the rural surroundings of Marburg, Hessen, more severe disease stages (i.e., HY stages IV and V) are underrepresented, leading to a selection bias towards less impaired patients. Therefore, future studies should also include patients with more progressed PD, e.g., by offering home visits, and should also be designed longitudinally to analyze the causative direction of associations. Though the sample size of 75 PD patients seems small, it exceeds the number of recruited patients in all but one other published study data [6-10]. It should be noted, however, that due to the sample size more sophisticated analyses of the WHOQOL facets could not be conducted with sufficient statistical power. Finally, some variables that have been reported to be predictors for QoL (e. g. fatigue) could not considered for our regression analyses since corresponding data were not available in the study. Yet, despite these limitations, our work makes valuable scientific contributions, as it provides further evidence on the feasibility of the WHOQOL-100/WHOQOL-BREF in PD outpatients, which can still be regarded understudied. As it compares three different measures of QoL based on one single study population, it might aid clinicians in gauging which instrument to use for a specific patient, premised on additional information they already have about this patient (e. g. presence of depression). This study also provides evidence on the equivalence of the WHOQOL-100 and the WHOQOL-BREF and is also – to our best knowledge – the first study to evaluate the German version of the WHOQOL-100/WHOQOL-BREF in PD patients.

Ethical standards

The DEMPARK/LANDSCAPE study was approved by the Ethics Committee of Philipps University of Marburg (approval numbers 178/07 and 25/11) and subsequently by the local ethics committees of the participating centers. Written informed consent was obtained from all participants before study entry.

Conflicts of interest

All authors declare that they have no conflicts of interests.

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Table 1. Characteristics of the study population.

Variable	Males	Females	p-Value	Total
Sociodemographics				
N[#]	52	23	--	75
Male : Female Ratio (%)	--	--	--	69.3 : 30.7
Age, years				
Mean ± SD	66.3 ± 8.1	63.5 ± 8.6	0.172	65.5 ± 8.3
Minimum; Maximum	44; 77	45; 81		44; 81
Marital status (%)				
Married / Partnership	90.4	60.9	<.001	81.3
Divorced / Separated	3.9	17.4		8.0
Widowed	3.9	17.4		8.0
Single	1.9	4.3		2.7
Clinical status				
Age at PD onset, years				
Mean ± SD	59.4 ± 8.0	56.2 ± 6.9	0.094	58.4 ± 7.8
Minimum; Maximum	43; 73	42; 70		42; 73
Duration of PD, years				
Mean ± SD	6.9 ± 5.4	7.3 ± 4.2	0.742	7.0 ± 5.0
Minimum; Maximum	0; 25	1; 16		0; 25
Hoehn & Yahr stage, n (%)				
I	16 (30.8)	6 (26.1)	0.486	22 (29.3)
II	29 (55.8)	12 (52.2)		41 (54.7)
III	7 (13.5)	4 (17.4)		11 (14.7)
IV	0 (0.0)	0 (0.0)		0 (0.0)
V	0 (0.0)	1 (4.4)		1 (1.3)
UPDRS Score (mean±sd)				
I: Mentation, Behavior, Mood	2.3 ± 2.1	3.0 ± 1.9	0.129	2.5 ± 2.0
III: Motor examination	19.7 ± 11.1	20.7 ± 11.0	0.706	20.0 ± 11.0
IV: Complications of therapy	2.4 ± 3.1	3.3 ± 3.2	0.235	2.7 ± 3.1
Cognitive group (%)				
PD	32.7	30.4	0.848	32.0
PD-MCI	67.3	69.6		68.0
PDD	0	0		0
MMSE Score				
Mean ± SD	29.0 ± 1.2	28.7 ± 1.3	0.430	28.9 ± 1.3
Minimum; Maximum	25; 30	25; 30		25; 30
PANDA Score				
Mean ± SD	24 ± 5.4	23.0 ± 5.5	0.443	23.7 ± 5.4
Minimum; Maximum	11; 30	9; 30		9; 30
GDS 15-Score				
Mean ± SD	2.7 ± 2.5	3.3 ± 2.6	0.320	2.9 ± 2.5
Minimum; Maximum	0; 11	0; 10		0; 11
≥5 (%)	21.1	26.1	0.640	22.7

PD = Parkinson's Disease, UPDRS=Unified Parkinson's Disease Rating Scale; MMSE = Mini-Mental-State Exam; PANDA = Parkinson Neuropsychometric Dementia Assessment; GDS=Geriatric Depression Rating Scale

Table 2. Mean scorings on the WHOQOL-100, the PDQ-39 and the EQ-5D in the study sample (Values are expressed as means±standard deviations; bold values indicate significant differences with a=p<.01, and b=p<.05).

	Sex		Age, years		PD duration, years		Hoehn & Yahr stage				All
	Male	Female	≤65	≥66	≤5	≥6	I	II	III	V	
N	52	23	29	46	38	37	22	41	11	1	75
WHOQOL-100:											
Physical Health	**62.9± 19.7**	**45.6±15.1**[a]	55.0±20.0	58.8±20.0	56.9±20.2	56.7±20.0	**64.3±19.9**	**58.7±19.1**	**40.0±13.2**[b]	37.5	57.3±20.0
Psychological Health	**66.2±15.1**	**55.2±13.5**[a]	62.0±14.8	63.3±16.0	63.3±14.6	62.3±16.4	66.3±13.6	63.2±16.9	57.0±10.0	36.3	62.8±15.4
Level of independence	**56.1±18.2**	**45.2±10.7**[a]	54.2± 16.6	51.9±17.4	**57.3±18.0**	**48.1±14.6**[b]	**62.2±19.9**	**52.1±12.9**	**37.8±12.8**[a]	34.4	52.8±17.0
Social relation	66.9±12.3	61.9±13.1	63.9±13.7	66.2±12.1	64.6±13.6	66.1±11.9	66.4±16.0	65.9±11.3	61.1±11.2	65.6	65.3±12.7
Environment	**74.4±12.7**	**64.4±13.2**[a]	68.2±14.1	73.3±13.0	70.5±13.9	72.1±13.3	72.2±14.9	71.9±13.0	67.6±13.9	68.0	71.3±13.6
Spirituality/religion/ personal beliefs	**69.8±18.2**	**56.8±24.0**[a]	64.7±19.9	66.2±21.9	65.1±20.0	66.0±22.3	66.8±20.9	68.4±19.6	56.3±22.7	25.0	65.6±21.0
Global	**63.1±12.8**	**50.8±15.6**[a]	58.2±13.5	59.9±15.6	60.7±14.6	57.9±15.0	59.43±15.3	60.6±14.7	56.3±14.0	37.5	59.3±14.8
PDQ-39:											
Mobility	**20.6±21.3**	**42.0±24.0**[a]	24.9±22.6	28.2±25.2	**20.1±20.7**	**34.1±25.6**[a]	**13.8±17.3**	**26.7±22.0**	**49.4±22.5**[a]	80.0	26.9±24.1
ADL	25.5±26.5	30.3±20.5	22.8±17.9	29.6±28.1	22.1±19.3	32.0±28.8	**11.4±11.9**	**27.5±22.8**	**52.5±26.9**[a]	70.0	27.0±24.8
Emot.well-being	**21.8±18.2**	**37.0±18.9**[a]	31.1±18.3	23.6±20.0	26.7±19.3	26.3±20.2	**21.6±15.2**	**24.6±20.3**	**42.0±18.9**[b]	38,0	26.5±19.6
Stigma	**13.3±16.9**	**21.2±16.1**[b]	**20.9±19.7**	**12.4±14.2**[b]	14.5±16.2	16.9±17.8	10.0±12.2	17.5±19.0	18.6±15.1	37.0	15.7±16.9
Social support	14.7±18.2	15.1±20.4	**21.7±21.8**	**10.5±15.3**[b]	15.1±20.0	14.5±17.7	9.7±14.7	16.9±20.3	18.8±19.6	0.0	14.8±18.8
Cognition	31.6±22.4	32.0±19.3	31.7±23.9	31.8±19.9	32.0±21.4	31.5±21.7	**21.6±14.2**	**31.6±21.9**	**52.7±18.4**[a]	31.0	31.7±21.4
Communication	17.3±15.1	21.3±19.4	22.2±17.3	16.2±15.7	17.6±17.3	19.4±15.8	**11.2±11.3**	**18.7±15.7**	**30.5±20.8**[a]	41.0	18.5±16.5
Bod. discomfort	**28.8±23.8**	**49.0±24.7**[a]	38.7±28.7	32.6±23.6	33.5±28.5	36.4±22.8	32.2±27.1	32.4±24.4	52.6±22.6	8.0	35.0±25.7
Index Score	**21.6±15.7**	**32.7±14.1**[a]	26.3±16.2	24.3±16.0	22.4±16.1	27.8±15.6	**15.7±9.6**	**24.8±15.7**	**42.4±11.8**[a]	48.1	25.0±16.0
EQ-5D:											
Index Score	**59.8±32.9**	**27.7±31.2**[a]	57.6±33.3	45.8±36.3	**60.6±32.6**	**39.9±35.5**[b]	**69.4±27.8**	**48.9±36.9**	**21.6±19.7**[a]	18.7	50.2±35.4
VAS Score	67.1±18.3	62.4±14.4	65.3±17.5	65.9±17.3	66.4±18.0	64.8±16.8	**71.4±16.4**	**66.1±16.2**	**51.4±16.6**[a]	80.0	65.7±17.3

Table 3. Proportions of patients with and without impairments in the EQ-5D dimensions (in %, bold values indicate significant differences with a=p<.01, and b=p<.05).

	Sex		Age, years		PD duration, years		Hoehn & Yahr stage				All
	Male	Female	≤65	≥66	≤5	≥6	I	II	III	V	
Mobility											
No Impairment	0	0	0	0	0	0	0	0	0	0	0
Impairment	100	100	100	100	100	100	100	100	100	100	100
Self Care											
No Impairment	76.9	59.1	**89.3**	**60.9**[a]	**86.5**	**56.8**[a]	**90.5**	**70.7**	**45.5**[b]	0	71.6
Impairment	23.1	40.9	**10.7**	**39.1**	**13.5**	**43.2**	**9.5**	**29.3**	**54.5**	100	28.4
Usual Activities											
No Impairment	**73.1**	**36.4**[a]	71.4	56.5	**75.7**	**48.6**[a]	**81.0**	**63.4**	**27.3a**	0	62.2
Impairment	**62.9**	**63.6**	28.6	43.5	**24.3**	**51.4**	**19.0**	**36.6**	**72.7**	100	37.8
Pain											
None	**32.7**	**13.6**[b]	28.6	26.1	32.4	21.6	**42.9**	**24.4**	**0**[b]	100	27.0
Present	**67.3**	**82.4**	71.4	73.9	67.6	78.4	**57.1**	**75.6**	**100**	0	73
Anxiety / Depression											
None	**78.8**	**54.5**[b]	60.7	78.3	67.6	75.7	76.2	75.6	45.5	100	71.6
Present	**21.2**	**45.5**	39.3	21.7	32.4	24.3	23.8	24.4	54.5	0	28.4

Table 4. Effects of sociodemographic and clinical variables on the QoL as assessed in univariate and multivariable regression analyses.

	Univariate Models					Multivariable Models				
	β	95%CI	p	β_{ST}	R^2	β	95%CI	p	β_{ST}	R^2
WHOQOL-100 GLOBAL:										
Sociodemographic										
Sex	**-12.25**	-19.09 ; -5.40	0.001	**-0.39**	0.14	**-10.38**	-16.99 ; -3.78	0.003	**-0.33**	0.27
Age, years	0.23	-0.19 ; 0.64	0.278	0.13	0.01	0.05	-0.41 ; 0.51	0.833	0.03	
Depression										
GDS Score	**-2.20**	-3.47 ; -0.93	0.001	**-0.38**	0.13	**-1.49**	-2.86 ; -0.13	0.033	**-0.25**	
PD Status										
UPDRS III score	-0.29	-0.60 ; 0.01	0.060	-0.22	0.03	-0.24	-0.67 ; 0.19	0.261	-0.18	
UPDRS IV score	**-1.75**	-2.77 ; -0.74	0.001	**-0.37**	0.13	**-1.19**	-2.18 ; -0.21	0.019	**-0.25**	
Disease duration, years	-0.29	-0.97 ; 0.39	0.394	-0.10	0.01	0.07	-0.65 ; 0.80	0.839	0.03	
Hoehn & Yahr stage	-2.44	-7.02 ; 2.14	0.291	-0.12	0.01	2.59	-3.19 ; 8.37	0.375	0.13	
WHOQOL-BREF:										
Sociodemographic										
Sex	**-15.49**	-23.40 ; -7.58	<0.001	**-0.42**	0.39	**-14.15**	-21.91 ; -6.38	0.001	**-0.38**	0.34
Age, years	0.39	-0.09 ; 0.87	0.110	0.19	0.03	-0.01	-0.54 ; 0.54	0.999	0.01	
Depression										
GDS Score	**-2.24**	-3.75 ; -0.72	0.005	**-0.32**	0.11	**-1.68**	-3.28 ; -0.07	0.041	**-0.24**	
PD Status										
UPDRS III score	-0.17	-0.54 ; 0.20	0.358	-0.11	0.01	-0.27	-0.78 ; 0.23	0.282	-0.17	
UPDRS IV score	**-1.86**	-3.07 ; -0.65	0.003	**-0.34**	0.11	**-1.34**	-2.50 ; -0.18	0.024	**-0.24**	
Disease duration, years	0.08	-0.72 ; 0.88	0.845	0.02	0.01	0.42	-0.43 ; 1.27	0.325	0.12	
Hoehn & Yahr stage	-0.32	-5.73 ; 5.10	0.908	-0.01	0.01	4.99	-1.81 ; 11.79	0.148	0.21	

(to be continued on the next page)

Table 4. Effects of sociodemographic and clinical variables on the QoL as assessed in univariate and multivariable regression analyses (continued).

	Univariate Models					Multivariable Models				
	β	95%CI	p	β_{ST}	R^2	β	95%CI	p	β_{ST}	R^2
PDQ-39 total score:										
Sociodemographic										
Sex	**11.11**	3.50 ; 18.72	0.005	**0.32**	0.09	**6.91**	2.33 ; 11.48	0.004	**0.20**	0.70
Age, years	0.02	-0.43 ; 0.47	0.946	0.01	0.01	-0.20	-0.52 ; 0.12	0.212	-0.10	
Depression										
GDS Score	**4.44**	3.38 ; 5.50	<0.001	**0.70**	0.48	**2.81**	1.86 ; 3.75	<0.001	**0.44**	
PD Status										
UPDRS III score	**0.90**	0.63 ; 1.17	<0.001	**0.62**	0.37	**0.59**	0.30 ; 0.89	<0.001	**0.41**	
UPDRS IV score	**1.83**	0.72 ; 2.94	0.002	**0.36**	0.12	**0.76**	0.07 ; 1.44	0.030	**0.15**	
Disease duration, years	**0.79**	0.07 ; 1.51	0.031	**0.25**	0.05	-0.20	-0.70 ; 0.30	0.426	-0.06	
Hoehn & Yahr stage	**11.29**	7.03 ; 15.54	<0.001	**0.53**	0.27	2.85	-1.16 ; 6.85	0.160	0.13	
EQ-5D Index score:										
Sociodemographic										
Sex	**-32.05**	-48.49 ; -15.61	<0.001	**-0.42**	0.16	-28.93	-42.21 ; -15.65	<0.001	**-0.38**	0.50
Age, years	-0.78	-1.79 ; 0.22	0.125	-0.18	0.02	-0.50	-1.42 ; 0.41	0.277	-0.12	
Depression										
GDS Score	**-5.66**	-8.67 ; -2.66	<0.001	**-0.40**	0.15	**-2.54**	-5.26 ; 0.19	0.067	-0.18	
PD Status										
UPDRS III score	**-1.91**	-2.52 ; -1.29	<0.001	**-0.59**	0.34	**-1.61**	-2.48 ; -0.75	<0.001	**-0.50**	
UPDRS IV score	**-4.01**	-6.61 ; -1.41	0.003	**-0.34**	0.10	**-2.15**	-4.21 ; -0.09	0.041	**-0.18**	
Disease duration, years	**-2.05**	-3.62 ; -0.48	0.011	**-0.29**	0.07	0.48	-0.97 ; 1.92	0.513	0.07	
Hoehn & Yahr stage	**-20.16**	-30.30 ; -10.02	<0.001	**-0.42**	0.17	4.28	-7.25 ; 15.81	0.461	0.09	

β = regression coefficient; β_{ST} = standardized regression coefficient; CI = confidence interval; p = p value; R^2 = proportion of explained variances

Suppl. Table 1: Domains and facets of the WHOQOL-BREF.

Domain	Facets incorporated within domains.
Physical health:	Activities of daily living Dependence on medicinal substances and medical aids Energy and fatigue Mobility Pain and discomfort Sleep and rest Work Capacity
Psychological Health:	Bodily image and appearance Negative feelings Positive feelings Self-esteem Spirituality / Religion / Personal beliefs Thinking, learning, memory and concentration
Social relations:	Personal relationships Social support Sexual activity
Environment:	Financial resources Freedom, physical safety and security Health and social care: accessibility and quality Home environment Opportunities for acquiring new information and skills Participation in and opportunities for recreation / leisure activities Physical environment (pollution / noise / traffic / climate) Transport