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The Key Determinants to Quality of Life in Parkinson's Disease Patients: Results from the Parkinson's Disease Biomarker Program (PDBP)

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Ethical approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Written informed consent was obtained from all subjects at each study site, with local Institutional Review Board (IRBs) approval. The consent form clearly states that the collected data would be stored in the PDBP database and de-identified data shared with PDBP Consortium researchers and/or other investigators.

Conflict of interest

All authors have read and approved the submitted manuscript. The authors have no conflict of interest to report.

Authors' contributions

All authors contributed to the study design, data interpretation, and critical revision of the manuscript (LH, EL, NS, LK, ML, GD, PE, XH). LH provided the first draft of the manuscript. ML and XH also contributed to final editing of the manuscript, and XH supervised the progress of the project. LH and XH take full responsibility for the accuracy of the data analysis. All authors read and approved the submitted copy of the manuscript.

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Abstract

Background—To determine the impact of motor and non-motor symptoms on health-related quality of life (HRQOL) in Parkinson's disease (PD), the study explored a large cohort of 645 patients from the PD Biomarker Program.

Methods—The PD Questionnaire-39 (PDQ-39) measured HRQOL, whereas the Unified PD Rating Scale (UPDRS) assessed motor and non-motor symptoms. Determinants of HRQOL in PD patients were identified by stepwise linear regression analysis. The relationship between the PDQ-39 and UPDRS subscale scores then was explored through structural equation modeling.

Results—The mean disease duration was 6.8 years and the mean PDQ-39 summary index (PDQ-39SI) was 18.4. UPDRS-I (non-motor function) and UPDRS-II (motor questionnaire) scores demonstrated the strongest correlations with PDQ-39SI ($r > 0.4$, $P < 0.05$), whereas UPDRS-III (motor exam) and UPDRS-IV (motor complications) scores were correlated moderately with PDQ-39SI ($0.3 < r < 0.4$, $P < 0.05$). Multiple linear stepwise regression analyses showed that age ($\beta = -0.13$, $P < 0.001$), education ($\beta = -0.07$, $P = 0.008$), UPDRS-I ($\beta = 0.32$, $P = 0.000$), and UPDRS-II ($\beta = 0.44$, $P < 0.001$) significantly contributed to HRQOL, and cumulatively accounted for 69.1% of the PDQ-39SI variance. UPDRS-II score was the primary predictor of PDQ-39SI, accounting for 57.3% of the variance, whereas UPDRS-I score accounted for 7.5%. UPDRS-III and -IV and other factors measured did not survive step regression. Structural equation modeling confirmed the association of UPDRS-II ($\beta = 0.67$, $P < 0.001$) and UPDRS-I ($\beta = 0.35$, $P < 0.001$) with the PDQ-39SI.

Conclusion—Both motor and non-motor function assessed by the UPDRS-I and -II scores impacted significantly HRQOL in PD. UPDRS-III, however, has limited contributions to HRQOL although it is used as a main outcome in many clinical trials.

Keywords

Parkinson's disease; Quality of life; Motor symptoms; Non-motor symptoms; Structural equation modeling; Unified Parkinson's disease Rating Scales

Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disorder that is marked clinically by resting tremor, rigidity, and bradykinesia resulting primarily from loss of dopamine neurons in the substantia nigra, but the importance of non-motor symptoms including cognitive, mood changes, and fatigue has received increasing attention [1–3]. As a chronic and progressive disease, PD impacts the physical, mental, and social health of patients, and there is increasing need to understand the impact of different PD symptomatology on the ability of patients to perform activities of daily life, fulfill social roles, and their psychological well-being.

There is a growing body of literature that has established the negative impact PD has on health-related quality of life (HRQOL), an outcome index from the viewpoint of patients [1–4]. Using Unified PD Rating Scale (UPDRS) subscores, some studies have reported that non-motor symptoms are major predictors of deteriorating HRQOL [1–3], whereas others suggest motor symptoms and complications were determinants of worse HRQOL [1, 4–9]. The impact of both motor (UPDRS-II) and non-motor symptoms (UPDRS-I) on QOL for PD patients has been the subject of several studies [9–12]. One systematic review by Post et al. [13] explored factors that predicted changes in motor impairment, disability, and QOL over the disease course. Another review evaluated demographic (age, sex, and employment status) and clinical factors (disease severity, disease duration, and motor and non-motor PD symptoms) that contribute to HRQOL in PD patients [7]. Despite the existing literature, a comprehensive study that includes these and other relevant factors (such as education, sleep, anxiety, et al.) is lacking. In addition, the relative contributions of different PD symptoms to HRQOL have not been investigated thoroughly.

The objectives of the present study were: (1) to explore comprehensively the predictors of HRQOL in PD, including demographic and clinical measures, with the hypothesis that the severity of motor and non-motor symptoms may contribute differentially to HRQOL in PD patients; and (2) to determine the contribution of symptoms or signs of PD measured by UPDRS subscales to HRQOL using structural equation modeling.

Methods

Data

The data in the study was downloaded from the PD Biomarkers Program (PDBP) established by the National Institute of Neurological Disorders and Stroke (NINDS). The PDBP comprises seven research projects located at different institutions that all collect the same common data elements (CDEs) from several domains (see https://commondataelements.ninds.nih.gov/pd.aspx#tab=Data_Standards). Written informed consent was obtained from all subjects at each study site, with local Institutional Review Board (IRBs) approval. The consent form clearly states that the collected data would be stored in the PDBP database and de-identified data shared with PDBP Consortium researchers and/or other investigators.

Records were downloaded from 645 PD subjects who were recruited from Brigham and Women's Hospital (n=16, 2.5%), Johns Hopkins University (n=76, 11.8%), the Pennsylvania State University (Hershey, n=137, 21.2%), the University of Alabama at Birmingham (n=223, 34.6%), the University of Washington (n=2, 0.3%), and UT-Southwestern Medical Center (n=191, 29.6%). Of these 645 records, 508 documented the age of diagnosis and disease duration.

Measures

HRQOL is a subjective, patient-reported outcome that may be influenced by physical, cognitive, and/or psychological factors. We chose the 39-item PD Questionnaire (PDQ-39) [14] as an indicator of quality of life [1–4, 7, 10, 15]. It has eight domains: Mobility; Activities of Daily Life (ADL); Emotional Well-Being; Stigma; Social Support; Cognition; Communication; and Bodily Discomfort. A summary index (SI) score and the mean of the eight dimension scores were used for analysis. The SI score ranges from “0=no difficulties” to “100=maximum level of difficulty.” Higher scores indicate poorer HRQOL.

The UPDRS [16] has four subscales and was used to evaluate non-motor (UPDRS-I), motor symptoms as judged by the subject (UPDRS-II), motor symptoms assessed by an evaluator trained via standard video (website) (UPDRS-III), and motor complications (UPDRS-IV). UPDRS-III scores were evaluated while patients were taking their prescribed PD medications ('on' medication). Hoehn & Yahr staging (H-Y stage) also was used to measure motor severity in PD [6, 12, 17].

Sleepiness was assessed using the Epworth Sleepiness Scale (ESS) [18], depression by the Hamilton Depression Rating Scale (HAM-D) [19] and anxiety by the Hamilton Anxiety Rating Scale (HAM-A) [19]. General cognition was evaluated using the Montreal Cognitive Assessment (MoCA) [20], overall activities of daily living by the Schwab and England ADL scale (SEAS) [21], and olfaction using the University of Pennsylvania Smell Identification Test (UPSIT) [22].

Statistical analyses

A general description of the patients was obtained by performing descriptive analyses. Continuous variables are presented as the mean (M) $\pm$ standard deviation (SD) and categorical variables are presented as percentages (%). First, the associations between the PDQ-39SI and other clinical factors were obtained via Pearson (for normally distributed data) and Spearman Rank (for non-normally distributed data) correlation coefficients. Correlation strength was interpreted as follows: $r \geq 0.4$ as an obviously strong correlation, $0.3 \leq r < 0.4$ as a moderate correlation, and $r < 0.3$ as a weak correlation [17]. We considered $P < 0.05$ as statistically significant.

Second, statistically significant variables in the correlation analysis were entered into a stepwise regression analysis. PDQ-39SI and its eight domain scores acted as the dependent variable. Entry and removal of independent variables at each step was set at a p value = 0.05 and 0.1, respectively. The R² (proportion of variance explained by the model) and adjusted R² (adjusted for the number of variables included in the final model) were calculated to assess the impact of all factors on the PDQ-39SI. SPSS 15.0 was used for these analyses.

Third, structural equation modeling (SEM) was applied to test the relationship between the PDQ-39 and the four subscales of the UPDRS using the LISREL 8.7 software. Compared with multiple linear regression models, SEM is a multivariate technique that can estimate a set of regression models simultaneously. In addition, it can handle latent variables that represent different constructs that cannot be assessed directly and should be indexed with the relevant indicators. The overall goodness of fit was verified by the following fit indices: Root Mean Square Error of Approximation (RMSEA), Comparative Fit Index (CFI), Incremental Fit Index (IFI), and Normalized Fit Index (NFI). The models have a satisfactory goodness-of-fit when CFI = 0.95, and RFI and RMSEA = 0.1 [23]. The hypothesized SEM then was tested to examine the relationships among constructs of the UPDRS and PDQ-39SI. Estimates of path coefficients represent the strength of the relationships between two variables and were calculated using standardized regression coefficients (i.e., β values).

Results

Patient characteristics

Table 1 summarizes the demographic and clinical information from the 645 patients included in the study. The mean age of PD patients was 64.8 ± 9.4 years and 61.7% of them were male. The mean age at diagnosis of the 508 patients who had this information documented was 58.4 ± 10.7 years and the mean disease duration was 6.8 ± 5.3 years, with the mean and median H-Y stage being 2.07 and 2.00, respectively. Ninety-three percent of patients were on medicine for the treatment of PD symptoms and 85.9% of them reported a good response. The mean scores on the UPDRS and PDQ-39SI for PD patients were 51.3 ± 27.1 and 18.4 ± 14.0 , respectively. The scores from the other scales assessed are listed in Table 1.

Predictors of PDQ-39SI

The correlation results between the PDQ-39SI and other clinical assessments are listed in Table 2. Age and education showed weak correlations ($R^2=0.04$) with HRQOL for PD patients ($r<0.2$, $P<0.05$). HAM-A, MoCA, and disease duration also were weakly correlated with the PDQ-39 SI ($r<0.3$, $P<0.05$). Moderate positive correlations were found between the PDQ-39SI and ESS, UPDRS-III, UPDRS-IV, and H-Y stage ($0.3<r<0.4$, $P<0.05$). HAM-D, UPDRS-I, and UPDRS-II demonstrated strong and positive correlations with the PDQ-39SI ($r>0.4$, $P<0.05$). The SEAS was correlated negatively with the PDQ-39SI ($r=-0.58$, $p<0.01$). UPSIT, on the other hand, showed no correlation with the PDQ-39SI in PD patients. The contribution of each UPDRS subscale to the PDQ-39SI was analyzed using univariate analysis and is detailed in the supplemental Figure.

Predictors of HRQOL in PD patients were identified through multiple linear stepwise regression analysis with the PDQ-39SI as the dependent variable (Table 3). Results showed that age, gender, education, UPDRS-II, UPDRS-I, SEAS, and ESS contributed significantly to PDQ-39SI ($P<0.05$). These factors cumulatively accounted for 69.1% of the variance in the PDQ-39SI. UPDRS-II was the most powerful predictor of the PDQ-39SI, accounting for 57.3% of the variance, with the UPDRS-I accounting for 7.5% of the variance. UPDRS-III and UPDRS-IV scores did not show any significant relationship to PDQ-39SI. The other

variables accounted for only about 1% each. Disease severity (H-Y stage) and duration did not survive this regression analysis.

Eight multiple linear regression models were created, one for each of the eight domains of the PDQ-39, to explore the predictive value of UPDRS subscale scores and other patient characteristics (Table 4). UPDRS-II score was predictive of most domains of the PDQ-39 except for Social Support, with the most predictable domains being ADL, Mobility, Stigma, and Cognition. UPDRS-I scores were significantly related to Cognition, Body Discomfort, and the Emotional Well-Being domains. UPDRS-III, UPDRS-IV, other scores, and clinical characteristics had very little statistical relationship to any of the eight PDQ-39 domains. Whether using overall PDQ-39SI or domain scores as the dependent variable, UPDRS-I and UPDRS-II scores contributed to a considerable proportion of the variance in both types of models (Tables 3 and 4, Supplemental Figure).

UPDRS-II, UPDRS-I and PDQ-39 – Structural equation modeling

The SEM modeling presented in Figure 1 showed the full structural equation model with standardized coefficients and factor loadings. For the current study, UPDRS-I, UPDRS-II, UPDRS-III, UPDRS-IV, and PDQ-39 were latent variables. All of the pathway estimates (β) are reported in standardized format. In the structure model, as hypothesized, UPDRS-II scores were significantly and positively associated with the PDQ-39 in PD patients (standardized correlation coefficient $\beta = 0.67$, $t=10.55$, $P<0.001$), as were UPDRS-I scores (standardized path coefficient $\beta=0.35$, $t=6.92$, $P<0.001$), and all indices of the model indicated a considerable goodness of fit to the data (CFI=0.91; NFI=0.90; IFI=0.91; RMSEA=0.09). UPDRS-III and UPDRS-IV scores, however, did not exhibit a significant impact on the PDQ-39 ($\beta = -0.02$ and -0.03 ; $t = -0.60$ and $t = -1.07$, respectively.).

In the measurement model, the coefficients between Cognition and Hallucinations and UPDRS-I scores were 0.54, and 0.43, respectively. The coefficients between the eight subdomains and the PDQ-39 were Mobility (0.84), ADL (0.83), Emotional Well-Being (0.67), Stigma (0.46), Social Support (0.48), Cognition (0.64), Communication (0.70), and Bodily Discomfort (0.59), respectively. In summary, these coefficients indicated that the UPDRS and PDQ-39 scales were valid.

Discussion

In the current study, we explored the association and predictive value of demographic and clinical variables to HRQOL in PD patients using multiple methods. The rich dataset collected under the PDBP using NINDS common data elements allows a comprehensive and systematic evaluation of other clinically-relevant factors on HRQOL. Our results identified that age, gender, education, UPDRS-I, UPDRS-II, SEAS, and ESS were major contributors of HRQOL using multiple stepwise regression analysis. These factors cumulatively accounted for 69.1% of the variance in PDQ-39SI score. Among these factors, UPDRS-II was the most powerful determinant of PDQ-39SI, which accounted for 57.3% of the PDQ-39SI variance, followed by UPDRS-I scores that accounted for 7.5% of the variance. The SEM analysis verified that UPDRS-II and UPDRS-I, were the most robust determinants of HRQOL in PD patients. These results are consistent with previous studies [7], and

underscore the importance of motor and non-motor symptoms (to a lesser degree) in contributing to HRQOL. Interestingly, UPDRS-III has a limited contribution to HRQOL, although it is used as a main outcome measurement in many clinical trials. This result sheds doubt on the utility of UPDRS-III as a major outcome measure in future clinical practice and research [7, 24].

Motor functions as predictors of quality of life in PD patients

Converging evidence from the correlation analysis ($r=0.77$), multiple stepwise regression analysis ($\beta=0.44$), and SEM modeling ($\beta=0.67$) showed that motor symptoms assessed by patients (UPDRS-II) were the strongest contributors to the PDQ-39, consistent with previous studies [1, 4, 5]. UPDRS-II affected most domains of the PDQ-39, namely ADL, Mobility, Communication, Stigma, and Cognition. This is probably because motor impairment may cause difficulty for PD patients in completing simple tasks such as using eating, using utensils, dressing, walking, and speaking. The Stigma domain also may have been affected due to impairment in the ability to dress, walk, maintain balance, and/or have freezing of gait. Subjects also might avoid public situations because of worrying about falling and drooling.

There has been controversy regarding the relationship between UPDRS-III and UPDRS-IV scores and HRQOL in PD patients. For example, one study demonstrated that UPDRS-III did not predict poorer HRQOL [1], whereas two other studies reported that UPDRS-III was a predictor of PDQ-39SI [7]. Sotirios et al. [25] provided evidence that UPDRS-II and UPDRS-III could be used to measure disease progression in early PD. In our study, UPDRS-III was correlated moderately with PDQ-39SI ($r=0.42$). Whereas UPDRS-III was a significant factor for ADL only ($\beta = 0.09$), it had almost no impact on the PDQ-39 in the SEM ($\beta = -0.02$). Similarly, UPDRS-IV had very little impact on the PDQ-39 ($\beta = -0.03$ in SEM), although it showed a moderate correlation with the PDQ-39SI ($r=0.34$). This result is consistent with previous literature [8, 15, 26].

It is worthwhile to note that both UPDRS-II and III are measuring motor function. UPDRS-II assesses motor function over the past seven days via subject recall, whereas UPDRS-III is obtained as a five-minute exam rated by an examiner. UPDRS-II focuses on the impact of symptoms, whereas UPDRS-III focuses on the presence and severity of symptoms [16]. Despite the subjective nature of the UPDRS-II, it had a greater impact on HRQOL in patients than the UPDRS-III. This finding is not expected because UPDRS-III is most often used as an outcome measurement for clinical trials. It is not surprising, however, because the reliability of the UPDRS-III between the raters was less than ideal [27] and motor symptoms may change over the course of the day depending on the activity and spirit of subjects. These results suggest that UPDRS-II scores may be more relevant to overall HRQOL in PD patients and be used as an outcome measure in clinical and research settings.

Non-motor function as a predictor of quality of life in PD patients

Some literature has reported that non-motor symptoms are major predictors of HRQOL deterioration [1–3]. In our study, however, UPDRS-I was the second best predictor of HRQOL in PD patients, a conclusion supported by different methods of analysis, including

correlation analysis ($r=0.721$), multiple stepwise regression analysis ($\beta=0.316$), and the SEM model ($\beta=0.35$). In addition, UPDRS-I had a major impact on three domains of the PDQ-39: Cognition, Body Discomfort, and Emotional Well-Being. This result is consistent with a study showing high-moderate correlations between UPDRS-I scores and each PDQ-39 domain [2].

A recent systematic review assessing contributors to HRQOL in PD [7] confirmed the importance of depression on this measure. Although most previous studies identified depression symptoms from the UPDRS-I, depression was assessed in the current study by both the HAM-D and UPDRS-I. The correlation coefficient between depression (HAM-D) and PDQ-39SI was strong ($R=0.46$). HAM-D, however, did not contribute significantly to PDQ-39SI, which may be due to the co-linearity of the HAM-D and UPDRS-I ($r=0.57$).

Lower MoCA scores ($r=-0.25$, standard $\beta=-0.08$) resulted in poorer HRQOL in PD. This finding is consistent with a previous study [28]. Increased anxiety also was related to lower QOL in PD patients ($r=0.28$) and mainly influenced the Social Support domain (standard $\beta=0.13$), consistent with a previous study [4]. Olfaction (UPSIT) was not a predictor of QOL in PD patients.

Other factors influencing quality of life in PD patients

Other clinical features (i.e. disease duration and H-Y stage) did not predict the level of overall HRQOL. These findings are consistent with several previous studies [11, 17]. Interestingly, disease duration had little impact on HRQOL, affecting the Social Support domain ($\beta=0.03$) only slightly. This data might be biased, however, because the majority of PD patients in our study had a disease duration <15 years. Indeed, only 27 (4.2%) subjects were H-Y stage IV. Further follow up on this cohort or analysis of other cohorts with longer durations of illness and more advanced stages are needed.

Interestingly, we found that current age was a weak protective factor for better HRQOL in PD patients ($r=-0.08$, $\beta=-0.13$). Female gender and higher education level also were associated with improved PDQ-39 scores ($\beta=0.08$), in agreement with previous studies [29, 30]. [17, 29]. The SEAS assesses a person's ability to perform daily activities. As expected, SEAS showed a strong negative correlation ($r=-0.58$) with PDQ-39SI, especially in the Mobility, ADL, and Social Support domains.

Strengths, limitations, and summary

The current study utilized a large sample of PD patients recruited from several movement disorder centers included in the PDBP study sponsored by NINDS. PD patients in our study reported a relatively better HRQOL according to the PDQ-39SI (18.4 ± 14.0) than that of previous studies in other cohorts documenting scores of 21.5 or 48.8 in patients with disease duration 4.4 ± 4.2 or 8.1 ± 10.6 years, respectively [1–3, 10, 15]. Multiple regression models were used to explore the relationships between predictor variables and HRQOL in PD patients. This is the first study to our knowledge to examine the relationships among UPDRS subscale scores and PDQ-39 using an SEM approach based on theoretical and empirical support. Results of these analyses supported the hypothesis that both motor and non-motor symptoms measured by UPDRS-I and II, but not UPDRS-III or IV, were key

predictors of HRQOL in PD patients. One limitation regards the UPDRS-III that is subjective and can be rater-dependent. Since we downloaded the data for our analysis, one group contributing to the data found significant between-rater variability and re-scored the recorded videos of the UPDRS-III exam once raters were trained and had an inter-rater cross correlation (ICC) of >0.9 . These data subsequently were updated in the PDBP database in Jan, 2016. We downloaded this new data and re-ran our analysis. The results for the whole group and for our site alone remained the same, underscoring the robustness of the current findings and the limitation of the UPDRS-III in gauging quality of life despite a very vigorous approach. The findings of the current study are important and may guide future selections of outcome measurements used in clinical practice and research.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

ADL	Activities of Daily Life
CFI	Comparative Fit Index
ESS	Epworth Sleepiness Scale
HAM-A	Hamilton Anxiety Rating Scale
HAM-D	Hamilton Depression Rating Scale
IRB	Institutional Review Board
HRQOL	Health-related quality of life
MoCA	Montreal Cognitive Assessment
NINDS	National Institute of Neurological Disorders and Stroke
PD	Parkinson's disease
PDBP	Parkinson's Disease Biomarkers Program
PDQ-39	39-item PD Questionnaire

PDQ -39SI	Parkinson's Disease Questionnaire summary index
RMSEA	Root Mean Square Error of Approximation
SEAS	Schwab and England ADL scale
SEM	structural equation modeling
UPDRS	Unified Parkinson's Disease Rating Scale
UPDRS-I	Non-Motor Function
UPDRS-II	Motor questionnaire
UPDRS-III	Motor Exam
UPDRS-IV	Motor Complications
UPSIT	University of Pennsylvania Smell Identification

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Figure 1.

Structural equation modeling: the relationships among constructs of the four subscales of UPDRS and PDQ-39. Latent variables: UPDRS-I: Non-Motor Function; UPDRS-II: Motor questionnaire; UPDRS-III: Motor Exam; UPDRS-IV: Motor Complications; PDQ39: 39-item PD Questionnaire. ADL: Activity of daily living; EMOTION: Emotional Well-being; SOCIALSP: Social Support; COGIMPAL: Cognition; COMMUNCA: Communication; BODYDISC: Body Discomfort.

Table 1

Demographic and clinical characteristics of the participants

	Mean	SD
Age (y)	64.8	9.4
Gender: Male number (%)	398 (61.7%)	
PD duration (y) (N=508)	6.8	5.3
< 5 y	227	
5~10 y	158	
10~15 y	84	
15 y	39	
Hoehn Yahr Stage	2.07	0.76
Age of Diagnosis (y)	58.4	10.7
Medication (YES)	602 (93.2%)	
Clinical State (ON)	559 (85.9%)	
ESS	8.4	5.0
HAM-A	5.3	5.4
HAM-D	4.5	4.2
MoCA	24.7	4.2
SEAS	83%	17%
PDQ-39SI	18.4	14.0
Mobility	20.4	18.6
ADL	21.8	20.3
Emotional	16.7	17.0
Stigma	15.7	19.2
Social Support	7.2	13.5
Cognition	20.6	17.7
Communication	18.1	20.9
Body Discomfort	26.9	22.2
UPDRS Score	51.3	27.1
UPDRS-I	11.7	8.7
UPDRS-II	9.9	6.3
UPDRS-III	28.7	16.6
UPDRS-IV	2.2	3.3
UPSIT	19.9	7.9

ESS: Epworth Sleepiness Scale; HAM-A: Hamilton Anxiety Rating Scale; HAM-D: Hamilton Depression Rating Scale; MoCA: Montreal Cognitive Assessment; SEAS: Schwab and England ADL scale; PDQ -39SI: Parkinson's Disease Questionnaire summary index; ADL: Activities of Daily Life; UPDRS: Unified Parkinson's Disease Rating Scale; UPDRS-I: Non-Motor Function; UPDRS-II: motor questionnaire; UPDRS-III: Motor Exam; UPDRS-IV: Motor Complications; UPSIT: University of Pennsylvania Smell Identification.

Table 2

The correlation (r or R2?) matrix between PDQ-39SI and the demographic, clinical characteristics, and relevant scale scores

	PDQ-39SI	Age	Education	ESS	HAM-A	HAM-D	MoCA	SEAS	UPSIT	UPDRS-I	UPDRS-II	UPDRS-III	UPDRS-IV	H-Y Stage
PDQ-39SI	1.00													
Age	-0.08 [*]	1.00												
Education	-0.16 ^{**}	0.06	1.00											
ESS	0.36 ^{**}	-0.03	-0.04	1.00										
HAM-A	0.28 ^{**}	0.01	-0.05	0.08 [*]	1.00									
HAM-D	0.42 ^{**}	0.00	-0.04	0.13 ^{**}	0.75 ^{**}	1.00								
MoCA	-0.25 ^{**}	-0.30 ^{**}	0.19 ^{**}	-0.10 [*]	-0.09 [*]	-0.16 ^{**}	1.00							
SEAS	-0.58 ^{**}	-0.17 ^{**}	0.06	-0.21 ^{**}	-0.18 ^{**}	-0.29 ^{**}	0.37 ^{**}	1.00						
UPSIT	-0.03	-0.26 ^{**}	-0.04	-0.09 [*]	0.01	-0.02 ^{**}	0.22	0.07	1.00					
UPDRS-I	0.72 ^{**}	0.03	-0.04	0.42 ^{**}	0.39 ^{**}	0.57 ^{**}	-0.25 ^{**}	-0.45 ^{**}	-0.10 [*]	1.00				
UPDRS-II	0.77 ^{**}	0.04	-0.12 ^{**}	0.31 ^{**}	0.18 ^{**}	0.33 ^{**}	-0.33 ^{**}	-0.65 ^{**}	-0.10 [*]	0.64 ^{**}	1.00			
UPDRS-III	0.42 ^{**}	0.18 ^{**}	-0.07	0.16 ^{**}	0.19 ^{**}	0.22 ^{**}	-0.30 ^{**}	-0.50 ^{**}	-0.16 ^{**}	0.33 ^{**}	0.57 ^{**}	1.00		
UPDRS-IV	0.34 ^{**}	-0.05	-0.02	0.11 ^{**}	0.28 ^{**}	0.30 ^{**}	-0.06	-0.28 ^{**}	-0.08 [*]	0.31 ^{**}	0.33 ^{**}	0.25 ^{**}	1.00	
H-Y Stage	0.42 ^{**}	0.23 ^{**}	-0.08 [*]	0.09 [*]	0.20 ^{**}	0.24 ^{**}	-0.23 ^{**}	-0.54 ^{**}	-0.13 ^{**}	0.36 ^{**}	0.54 ^{**}	0.65 ^{**}	0.24 ^{**}	1.00
Duration	0.30 ^{**}	0.02	-0.10	0.21 ^{**}	-0.01	0.07	-0.15 ^{**}	-0.28 ^{**}	-0.10 ^{**}	0.19 ^{**}	0.27 ^{**}	0.19 ^{**}	0.33 ^{**}	0.25 ^{**}

* P<0.05

** P<0.01

ESS: Epworth Sleepiness Scale; HAM-A: Hamilton Anxiety Rating Scale; HAM-D: Hamilton Depression Rating Scale; MoCA: Montreal Cognitive Assessment; SEAS: Schwab and England ADL scale; UPSIT: University of Pennsylvania Smell Identification; UPDRS-I: Non-Motor Function; UPDRS-II: Motor questionnaire; UPDRS-III: Motor Exam; UPDRS-IV: Motor Complications.

A summary of the linear stepwise regression analyses. The PDQ-39SI was used as the dependent variable and the demographic characteristics, the four subscale scores of the UPDRS, and the other relevant scale score as the independent variables.

Table 3

	β	Std. Error	Standardized β	t	P	Modified R Squared	Adjusted R Squared
UPDRS-II	0.75	0.07	0.44	10.95	0.000	0.573	0.572
UPDRS-I	0.74	0.08	0.32	9.03	0.000	0.075	0.646
Age	-0.21	0.04	-0.13	-5.09	0.000	0.013	0.659
SEAS	-14.91	3.20	-0.16	-4.67	0.000	0.015	0.673
Female	2.35	0.78	0.08	3.02	0.003	0.007	0.680
Education	-0.77	0.29	-0.07	-2.65	0.008	0.005	0.684
ESS	0.17	0.08	0.06	2.11	0.035	0.003	0.686

UPDRS-I: Non-Motor Function; UPDRS-II: Motor questionnaire; SEAS: Schwab and England ADL scale; ESS: Epworth Sleepiness Scale;

Table 4

Standard β of the independent factors in each linear stepwise regression analysis with all of the domains scores of the PDQ-39 as the dependent variable.

	UPDRS-I	UPDRS-II	UPDRS-III	UPDRS-IV	Age	SEAS	Gender	Education	HAM-A	HAM-D	Duration	MoCA
Mobility	0.12	0.44	--	--	--	-0.35	0.11	-0.11	--	--	--	--
ADL	--	0.66	0.09	-0.08	-0.10	-0.15	--	--	--	--	--	--
Emotional	0.37	0.21	--	--	-0.13	--	0.95	--	--	0.18	--	--
Stigma	--	0.35	--	--	.086	--	1.60	--	--	--	--	--
Socialsupport	0.21	--	--	--	-0.18	-0.14	--	-0.09	0.13	--	0.03	--
Cognition	0.50	0.34	--	--	--	--	--	--	--	--	--	-0.08
Communication	0.16	0.44	--	--	-0.10	-0.13	--	--	--	--	--	--
Bodydiscomfort	0.38	0.23	--	--	--	--	0.13	-0.12	--	--	--	--

Abbreviations: ADL: Activities of Daily Life; UPDRS-I: Non-Motor Function; UPDRS-II: Motor questionnaire; UPDRS-III: Motor Exam Scale; UPDRS-IV: Motor Complications SEAS; Schwab and England ADL scale; HAM-A: Hamilton Anxiety Rating Scale; HAM-D: Hamilton Depression Rating Scale; MoCA: Montreal Cognitive Assessment.