Association between non-motor symptoms and health-related quality of life for patients with Parkinson's disease: Evidence from a smartphone-based survey

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Abstract

Background

This study aims to explore the association between the total number of non-motor symptoms and the Parkinson's disease (PD) patients' health-related quality of life quantitatively, using data from one of the largest smartphone-powered studies and a simplified version of 8-item Parkinson's disease Quality of life Questionnaire (PDQ-8).

Methods

The data used for analysis constitutes one part of a dataset derived from the project named '100 for Parkinson's', an initiative of uMotif in conjunction with the Cure Parkinson's Trust, Parkinson's UK and the European Parkinson's Disease Association. 1246 patients were included in the baseline survey. The 30-item Non-Motor Symptom (NMS-30) Questionnaire and PDQ-8 Summary Index (PDQ-8 SI) were used to measure health-related quality of life and a generalized linear model was used to analyze the association of the non-motor symptoms and quality of life.

Results

The mean number of NMS per patient was 11.81 ± 5.53 . For patients with limited ability to work: the key symptoms were urgency (77.4%), sad or blue (71.05%) and difficulty getting to sleep or staying asleep (70.90%). After controlling for the life-style determinants and psychological symptoms prior PD diagnosis determinants, GLM presented the total sum of NMS-30 questions had the strongest positive influence on health-related quality of life as measured by the PDQ-8 SI. Where the sum of NMS scores increases by 1 point, the PDQ-8 SI will increase by 1.33 points (95%CI: 1.13, 1.52; $P < 0.001$). For patients without limited ability to work: urgency (62.45%), difficulty getting to sleep or staying asleep (59.81%) and getting up regularly at night to pass urine (55.09%) were the most frequent symptoms. GLM showed that where the total sum of NMS scores increases by 1 point, the PDQ-8 SI will increase by 1.56 points (95%CI: 1.37, 1.76; $P < 0.001$) after controlling for other confounders.

Conclusions

This smartphone-based study finds a higher total number of non-motor symptoms is related to a lower health-related quality of life for PD patients. It provides useful evidence for the PDQ-8 instrument and is helpful for a multidisciplinary approach to patient care and facilitate the provision of more comprehensive education for patients and caregivers.

Background

Parkinson's disease (PD) is a slowly progressive neurological disorder and manifests with a broad range of symptoms, both motor and non-motor [1]. It is the second most common neurodegenerative disease in the world, and its incidence and prevalence are shifted by demographic changes [2]. Compared with 2.5 million in 1990, there are 6.1 million people with PD globally in 2016 [3]. In addition to typical motor symptoms, patients also suffer from various non-motor symptoms, such as depression, psychosis, falls, anxiety and sleep disturbance that seriously affect quality of life [1, 4–6]. Non-motor symptoms are correlated with advancing age and disease severity, which are often poorly recognised and inadequately treated [7]. The non-motor symptoms mainly included six aspects: neuropsychiatric symptoms, sleep disorders, autonomic symptoms, gastrointestinal symptoms, sensory symptoms and other symptoms include Fatigue, Diplopia, Blurred vision and so on [7, 8].

Health-related Quality of Life has become an important endpoint in the evaluation of public policy. The World Health Organization's Quality of Life Group defines quality of life as individual's perception of his or her life status within the context of the culture and value system in which individual lives and concerns[9]. Quality of life is one of the most important concepts and indicators for studying management of chronic disease such as PD [10]. Most studies evaluated health-related quality of life for people with PD through the 39-item Parkinson's disease Quality of life Questionnaire (PDQ-39) [11–13]. PDQ-39 includes 39 items in a single questionnaire, which can be time consuming for respondents to complete. An 8-item Parkinson's Disease Quality of life Questionnaire (PDQ-8) is a shorter

version of PDQ-39 and has been proven to be a valid and reliable instrument to assess quality of life in a PD population, while reducing respondent burden[14].

According to previous studies, non-motor symptoms such as cognitive impairment, autonomic dysfunction and sleep disorders have become major determinants of health-related quality of life [7, 15]. Fewer population-based researches report specific data on the magnitude of the correlation between total number of non-motor symptoms and the health-related quality of life measured by the PDQ-8. In this study, we use a large smartphone-based prospective study named '100 for Parkinson's' to capture data and explore the relationship of the total number of non-motor symptoms and the health-related quality of life for people with Parkinson's quantitatively. Smartphone-based studies have been proved to provide equivalent results to other traditional methods (such as fieldwork done with paper and pencil), but with added advantages such as lessening the burden of data entry [16, 17].

There are two key strengths for this study. Firstly, the data were drawn from one of the largest smartphone- supported studies that enabled symptom tracking for patients with PD. Secondly, it is the first study in UK to use the PDQ-8 to show the specific association of non-motor symptoms and the health-related quality of life for patients with PD.

Methods

Participants

The data used for analysis derived from a part of the data from the project named '100 for Parkinson's', an initiative of uMotif in conjunction with the Cure Parkinson's Trust, Parkinson's UK and the European Parkinson's Disease Association. The details of the project can be seen from the previous research [18] and open website (<http://www.100forparkinsons.com>). Patients with PD were diagnosed before the survey and collected by using the uMotif app on their own Android or iOS mobile phones and/or tablets to record a range of data including: demographic characteristics, questionnaires (PDQ-8, NMS-30, EQ-5D et al), medications and so on. There were no exclusion criteria applied. 1246 patients with PD consented to take part in this project and completed both the NMS-30 questionnaire and PDQ-8 questionnaire.

Non-Motor Symptom

The Non-Motor Symptom Questionnaire is used to screen and evaluate non-motor symptoms of Parkinson's [19]. It is a 30-item self-completed questionnaire consisting of 6 domains that cover symptoms ranging from gastrointestinal symptoms to sensory symptoms. Each item of a domain is listed in the form of chief complaints; thus, the patients can easily understand the question and provide simple "yes," "no," and "don't know" responses to each question [20]. The total number of non-motor symptoms means the number of "yes" for items of the NMS-30. The NMS in PD are diverse and range from cognitive problems, such as apathy, depression, anxiety disorders, and hallucinations, to sleep disorders, sexual dysfunction, bowel problems, and dribbling of saliva. In this study, the NMS of PD is divided into 6 kinds: neuropsychiatric symptoms, sleep disorders, autonomic symptoms, gastrointestinal symptoms, sensory symptoms, other symptoms according to previous study [7] (Additional file 1).

Health-Related Quality of Life

The health-related quality of life of PD patients was evaluated using the 8-item Parkinson's disease Questionnaire (PDQ-8). The scale has been validated and measured by eight dimensions of quality of life related specifically to PD: mobility, activities of daily living, emotional wellbeing, stigma, social support, cognition, communication and bodily discomfort [21]. The PDQ-8 summary index (PDQ-8 SI) is calculated from the following items of the PDQ-39: Q7, Q12, Q17, Q25, Q27, Q31, Q35 and Q37 with each item derived from one dimension [22, 23]. The health-related quality of life gets worse when the PDQ-8 SI is higher (range: 0 -100) [21, 24]. The total score of the PDQ-8 SI is used to report outcomes. All questions on the PDQ-8 are coded in the same way. The data is entered using the following codes: 0 = Never; 1 = Occasionally; 2 = Sometimes; 3 = Often; 4 = Always. Formula for the PDQ-8 Summary Index is as following:

$$PDQ-8 SI = \frac{T_s}{4 \times 8} \times 100 \quad (1)$$

T_s means sum of scores of each questionnaire for each people with PD, 4 means the maximum score of per question, 8 means the total number of questions. The health-related quality of life gets worse when the PDQ-8 SI is higher.

Statistical Analysis

Considering the fact that motor characteristic of patients with PD (with and without limited ability to work) having different quality of life, data analysis was divided into two group of participants: patients with limited ability to work and without limited ability to work. Differences in variables between PDQ-8 questions and motor characteristic were compared using Chi-square tests. The generalized linear model (GLM) was employed to analyze the influence of total number of non-motor symptoms on the health-related quality of life for people with PD and explore the potential determinants of quality of life quantitatively when controlling for confounding factors (including socio-economic factors, lifestyle factors and psychological symptoms prior PD diagnosis). The PDQ-8 SI score is the outcome variable; the sum of NMS-30 questions is the main determinant. The statistical analyses were performed using STATA statistical software version 12.0 (StataCorp LP, College station 77845, USA), related figures were made using Excel 2016. All p values were 2-sided and values of less than 0.05 were considered statistically significant.

Results

Basic characteristics

The basic demographic features of 1246 patients with PD were displayed in Table 1. As for socio-economic characteristics, there were 577 females and 615 males. The majority of patients' education were university/college/equivalent (72.64%). For the Life-style characteristics, 62.87% of patients never smoked tobacco and 15.33% of patients never consume drinks containing alcohol. 87.67% of patients live with others (including their wife, partners, children, relatives and hired carer). In the psychological symptoms prior PD diagnosis characteristics, from the sample, 261 (21.62%) patients suffered from depression prior to PD diagnosis, 225 (18.6%) had anxiety prior to PD diagnosis, and 677 (56.09%) had limited ability to work.

Table 1
Basic characteristics of patients with Parkinson's disease (n = 1246)

Variables	n	%
Socio-economic characteristics		
Gender		
Female	577	48.41
Male	615	51.59
Age of participants (years)		
≤59	561	45.03
60–69	446	35.79
≥70	239	19.18
Education		
Up to 16 years old	192	16.21
Up to 18 years old	132	11.15
University / College / Equivalent	860	72.64
Life-style characteristics		
Do you smoke tobacco?		
No, never	750	62.87
No, but used to	371	31.10
Yes	72	6.03
How often do you have a drink containing alcohol?		
Never	182	15.33
2–3 times per week	291	24.52
2–4 times per month	246	20.72
4 or more times per week	251	21.15
Monthly or less	217	18.28
Live style		
Live with others	1031	87.67
Live alone	145	12.33
Psychological symptoms prior PD diagnosis		
Depression prior PD diagnosis		
No	946	78.38
Yes	261	21.62
Anxiety prior PD diagnosis		
No	985	81.40
Yes	225	18.60
Motor characteristic		

Variables	n	%
Without limited ability to work	530	43.91
With limited ability to work	677	56.09

Distribution of NMS-30 and PDQ-8 questions

1.28% of patients had no NMS and 98.72% presented more than one symptom. The mean number of NMS per patient was 11.81 ± 5.53 . Figure 1 showed neuropsychiatric symptoms, sleep disorders, autonomic symptoms and gastrointestinal symptoms were less frequent in the patients without limitations to work than the patients with limited ability to work. The key symptoms were urgency (77.4%), feeling sad or blue (71.05%) and difficulty getting to sleep or staying asleep (70.90%) respectively for the PD patients with limited ability to work, whereas the urgency (62.45%), difficulty getting to sleep or staying asleep (59.81%) and getting up regularly at night to pass urine (55.09%) were the most frequent symptoms for the PD patients without limited ability to work. The distribution of PDQ-8 questions between patients with and without limit ability to work were shown in Table 2. Compared to those without limited ability to work, patients with limited ability to work reported more problems in always difficulty getting around (3.69% vs 0.19%), dressing (1.18% vs 0.19%), always feeling depressed (2.07% vs 0.75%), always problems with close personal relationships (2.66% vs 1.13%), always feeling unable to communicate properly (1.62% vs 0.57%), always painful muscle cramps (2.66% vs 0.75%) and always feeling embarrassed in public (2.51% vs 0.19%) except problems with concentration (13.96% vs 7.39%).

Table 2
Distribution of PDQ-8 questions between patients with and without limited ability to work (n = 1207)

PDQ-8 questions	Limited ability to work				χ^2	P
	Without (n = 530)		With (n = 677)			
	n	%	n	%		
Difficulty getting around					324.12	< 0.001
Always	1	0.19	25	3.69		
Often	343	64.72	114	16.84		
Sometimes	131	24.72	247	36.48		
Occasionally	16	3.01	141	20.83		
Never	39	7.36	150	22.16		
Difficulty dressing					193.12	< 0.001
Always	1	0.19	8	1.18		
Often	334	64.91	196	28.95		
Sometimes	160	30.19	281	41.51		
Occasionally	7	1.32	74	10.93		
Never	18	3.40	118	17.43		
Felt depressed					104.81	< 0.001
Always	4	0.75	14	2.07		
Often	239	45.09	154	22.75		
Sometimes	204	38.49	260	38.40		
Occasionally	22	4.15	115	16.99		
Never	61	11.51	134	19.79		
Problems with close personal relationships					127.65	< 0.001
Always	6	1.13	18	2.66		
Often	329	62.08	219	32.35		
Sometimes	147	27.74	240	35.45		
Occasionally	18	3.40	70	10.34		
Never	30	5.66	130	19.20		
Problems with concentration					120.02	< 0.001
Always	74	13.96	50	7.39		
Often	237	44.72	162	23.93		
Sometimes	144	27.17	199	29.39		
Occasionally	32	6.04	140	20.68		
Never	43	8.11	126	18.61		
Felt unable to communicate properly					200.90	< 0.001
Always	3	0.57	11	1.62		

PDQ-8 questions	Limited ability to work				χ^2	<i>P</i>
	Without (n = 530)		With (n = 677)			
	n	%	n	%		
Often	257	48.49	120	17.73		
Sometimes	214	40.38	267	39.44		
Occasionally	11	2.08	127	18.76		
Never	45	8.49	152	22.45		
Painful muscle cramps or spasm					75.45	< 0.001
Always	4	0.75	18	2.66		
Often	148	27.92	108	15.95		
Sometimes	226	42.64	214	31.61		
Occasionally	69	13.02	199	29.39		
Never	83	15.66	138	20.38		
Felt embarrassed in public					107.02	< 0.001
Always	1	0.19	17	2.51		
Often	272	51.32	188	27.77		
Sometimes	188	35.47	245	36.19		
Occasionally	23	4.34	101	14.92		
Never	46	8.68	126	18.61		

The association of NMS-30 and PDQ-8 SI

For patients with limited ability to work (Table 3), GLM presented the sum of NMS-30 questions had the strongest positive influence on the health-related quality of life as measured by the PDQ-8 SI score, among the factors analyzed in this study. When controlling socioeconomic characteristic in model 1, the estimates of the association of NMS and PDQ-8 SI is 1.33 (95%CI: 1.13, 1.52; $P < 0.001$). After controlling the life-style determinants and psychological symptoms prior to PD diagnosis determinants, the results in model 3 are still statistically significant ($P < 0.001$), indicating that where the sum of NMS increases by 1 point, the PDQ-8 SI would increase by 1.33 points, meaning the quality of life will decrease. Besides, the GLM indicated that depression prior to PD diagnosis ($\beta = 3.08$, 95%CI: 0.14, 6.02; $P = 0.040$) is also the potential determinant of worse quality of life of PD patients. However, age of 60–69 ($\beta = -2.87$, 95%CI: -5.20, -0.54; $P = 0.016$) and education of up to 18 years old ($\beta = -4.19$, 95%CI: -8.18, -0.21; $P = 0.039$) were the potential determinants of better health-related quality of life, compared to age ≤ 59 and education of up to 16 years old, respectively.

Table 3

The multivariate analysis of the correlation of total number of Non-Motor Symptoms on PDQ-8 Single index by generalized linear model analysis for patients with limited ability to work (n = 677)

Variables	Model 1				Model 2				Model 3			
	Estimates	<i>P</i>	95%CI		Estimates	<i>P</i>	95%CI		Estimates	<i>P</i>	95%CI	
Main determinants												
Sum of NMS-30 questions	1.33	< 0.001	1.13	1.52	1.30	< 0.001	1.10	1.50	1.33	< 0.001	1.12	1.54
Socio-economic determinants												
Gender												
Female	Reference				Reference				Reference			
Male	-0.15	0.886	-2.18	1.88	-0.001	0.999	-2.16	2.16	-0.21	0.854	-2.41	2.00
Age of participants (years)												
≤59	Reference				Reference				Reference			
60–69	-3.44	0.002	-5.65	-1.24	-2.83	0.016	-5.13	-0.54	-2.87	0.016	-5.20	-0.54
≥70	-2.42	0.121	-5.48	0.64	-1.73	0.283	-4.89	1.43	-2.52	0.129	-5.79	0.74
Education												
Up to 16 years old	Reference				Reference				Reference			
Up to 18 years old	-3.46	0.080	-7.34	0.42	-3.90	0.052	-7.85	0.04	-4.19	0.039	-8.18	-0.21
University / College / Equivalent	-1.33	0.353	-4.14	1.48	-1.59	0.280	-4.46	1.29	-1.83	0.221	-4.76	1.10
Life-style determinants												
Do you smoke tobacco?												
No, never					Reference				Reference			
No, but used to					-0.35	0.764	-2.65	1.94	-0.59	0.624	-2.93	1.76
Yes					3.62	0.086	-0.52	7.76	3.35	0.117	-0.84	7.55
How often do you have a drink containing alcohol?												
Never					Reference				Reference			
2–3 times per week					-0.02	0.991	-3.41	3.37	0.14	0.938	-3.31	3.58

Model 1 is a model controlling the main determinants and socio-economic determinants including gender, age and education; model 2 is a model adding life-style characteristics (e.g. smoking status, drinking status and live style) as covariates into model 1; model 3 is a model controlling the main determinants, socio-economic determinants, life-style characteristics and psychological symptoms prior PD diagnosis (e.g. depression prior PD diagnosis and anxiety prior PD diagnosis).

Variables	Model 1			Model 2			Model 3		
	Estimates	<i>P</i>	95%CI	Estimates	<i>P</i>	95%CI	Estimates	<i>P</i>	95%CI
2–4 times per month				1.73	0.312	-1.63 5.09	1.59	0.365	-1.85 5.04
4 or more times per week				-0.81	0.641	-4.22 2.60	-0.33	0.852	-3.84 3.17
Monthly or less				-0.65	0.694	-3.91 2.61	-0.87	0.610	-4.20 2.47
Live style									
Live with others				Reference			Reference		
Live alone				0.92	0.566	-2.22 4.06	1.11	0.496	-2.09 4.32
Psychological symptoms prior PD diagnosis									
Depression prior PD diagnosis									
No							Reference		
Yes							3.08	0.040	0.14 6.02
Anxiety prior PD diagnosis									
No							Reference		
Yes							-2.26	0.157	-5.39 0.87
Model 1 is a model controlling the main determinants and socio-economic determinants including gender, age and education; model 2 is a model adding life-style characteristics (e.g. smoking status, drinking status and live style) as covariates into model 1; model 3 is a model controlling the main determinants, socio-economic determinants, life-style characteristics and psychological symptoms prior PD diagnosis (e.g. depression prior PD diagnosis and anxiety prior PD diagnosis).									

For patients without limited ability to work - after controlling for the socio-economic determinants (Table 4), life-style and psychological symptoms prior to PD diagnosis determinants in model 3 – where the total sum of NMS increases by 1 point, the PDQ-8 SI score will increase by 1.56 points (95%CI: 1.37, 1.76; $P < 0.001$). In other words, where the non-motor symptoms are more, the health-related quality of life of PD patients without limited ability to work was worse. The GLM also indicated that depression prior to PD diagnosis ($\beta = 4.06$, 95%CI: 1.03, 7.09; $P = 0.009$) was also the potential determinant of worse quality of life than no depression prior to PD diagnosis; while age of 60–69 ($\beta = -2.84$, 95%CI: -4.85, -0.82; $P = 0.006$) was the potential determinant of better health-related quality of life of PD patients, compared to age ≤ 59 and education of up to 16 years old, respectively.

Table 4

The multivariate analysis of the correlation of total number of Non-Motor Symptoms on PDQ-8 Single index by generalized linear model analysis for patients without limited ability to work (n = 530)

Variables	Model 1				Model 2				Model 3			
	Estimates	<i>P</i>	95%CI		Estimates	<i>P</i>	95%CI		Estimates	<i>P</i>	95%CI	
Main determinants												
Sum of NMS-30 questions	1.59	< 0.001	1.41	1.78	1.60	< 0.001	1.41	1.79	1.56	< 0.001	1.37	1.76
Socio-economic determinants												
Gender												
Female	Reference				Reference				Reference			
Male	-0.35	0.696	-2.09	1.40	-0.15	0.871	-1.99	1.68	0.10	0.918	-1.75	1.94
Age of participants (years)												
≤59	Reference				Reference				Reference			
60–69	-3.02	0.002	-4.94	-1.10	-2.75	0.007	-4.76	-0.74	-2.84	0.006	-4.85	-0.82
≥70	-1.52	0.225	-3.98	0.94	-1.27	0.335	-3.84	1.31	-1.42	0.282	-4.00	1.17
Education												
Up to 16 years old	Reference				Reference				Reference			
Up to 18 years old	0.35	0.845	-3.12	3.81	0.41	0.821	-3.16	3.98	0.37	0.837	-3.19	3.94
University / College / Equivalent	-2.06	0.092	-4.45	0.34	-2.13	0.088	-4.57	0.31	-2.24	0.075	-4.71	0.22
Life-style determinants												
Do you smoke tobacco?												
No, never					Reference				Reference			
No, but used to					-0.44	0.672	-2.45	1.58	-0.31	0.764	-2.33	1.71
Yes					3.77	0.084	-0.51	8.05	3.50	0.107	-0.75	7.74
How often do you have a drink containing alcohol?												
Never					Reference				Reference			
2–3 times per week					-2.02	0.222	-5.26	1.22	-1.43	0.395	-4.71	1.86

Model 1 is a model controlling the main determinants and socio-economic determinants including gender, age and education; model 2 is a model adding life-style characteristics (e.g. smoking status, drinking status and live style) as covariates into model 1; model 3 is a model controlling the main determinants, socio-economic determinants, life-style characteristics and psychological symptoms prior PD diagnosis (e.g. depression prior PD diagnosis and anxiety prior PD diagnosis).

Variables	Model 1			Model 2			Model 3		
	Estimates	<i>P</i>	95%CI	Estimates	<i>P</i>	95%CI	Estimates	<i>P</i>	95%CI
2–4 times per month				-2.37	0.166	-5.72 0.98	-1.66	0.339	-5.05 1.74
4 or more times per week				-3.40	0.048	-6.78 -0.03	-2.19	0.213	-5.63 1.25
Monthly or less				-2.29	0.218	-5.94 1.35	-1.72	0.361	-5.42 1.97
Live style									
Live with others				Reference			Reference		
Live alone				-0.28	0.843	-3.02 2.47	0.06	0.966	-2.72 2.84
Psychological symptoms prior PD diagnosis									
Depression prior PD diagnosis									
No							Reference		
Yes							4.06	0.009	1.03 7.09
Anxiety prior PD diagnosis									
No							Reference		
Yes							-1.10	0.479	-4.16 1.95
Model 1 is a model controlling the main determinants and socio-economic determinants including gender, age and education; model 2 is a model adding life-style characteristics (e.g. smoking status, drinking status and live style) as covariates into model 1; model 3 is a model controlling the main determinants, socio-economic determinants, life-style characteristics and psychological symptoms prior PD diagnosis (e.g. depression prior PD diagnosis and anxiety prior PD diagnosis).									

Discussion

This is the first report of a comprehensive exploration of the association of total number of non-motor symptoms and the quality of life for patients with PD quantitatively using a large smartphone-based prospective study to capture data in the UK. Non-motor symptoms have been recognized as an important part of PD, and appropriate therapy can considerably improve quality of life [25]. Many researchers have explored how some items of the NMS independently have impact on the health-related quality of life, such as depression, sleep, mood and attention [13, 26], less studied are the associations of the total number of non-motor symptoms and health-related quality of life. In this study, we explored the relationship between total number of non-motor symptoms and health-related quality of life for patients with PD and found that where the sum of NMS-30 questions is higher, PD patients' health-related quality of life is worse. The NMS could be related to degeneration of different brain structures and could exert a stronger influence on severe disability, impaired health-related quality of life and shortened life expectancy, which should be taken in account regarding treatment options [7].

Our study reveals that almost every patient with PD presented with more than one symptom. The relative NMS occurrence, as assessed by NMS-30, agrees with several other studies, showing sleep (difficulty getting to sleep or staying asleep), mood/cognition (sad or blue), memory/attention and urination (urgency, getting up regularly at night to pass urine) as the most prevalent symptoms both for PD patients with and without limited ability to work [27–29]. However, the absolute occurrence of the most frequent symptoms is lower than Paulo Bugalho's study (Sleep/fatigue, affect/cognition, attention/memory were above 80%) [30], but higher than in most studies that used this same scale [28, 29], in which above 60% are rare, while in our sample sleep disturbances reached

70.90%, and urgency reached around 80%. This difference of results could be caused by cultural, geographic or pattern of health care particularities in our sample and deserves further investigation to verify.

Depression in PD is believed to be a common complication ranging in prevalence between 2.7% and 70% but is under self-reported[31]. Depression can precede the development of PD and has a major impact on a patient’s quality of life [31–34]. In our study, depression is one of the most prevalent symptoms both for patients with and without limited ability to work. Depression prior PD diagnosis was also a potential determinant of worse quality of life.

Age and education were found to be correlated with health-related quality of life of PD patients significantly. It is well known that age is the greatest risk factor for the development of PD. A previous study showed age-specific incidence rates of PD increased sharply beginning at age 60 years and peaking after 80 years [35]. In our study, patients aged 60–69 years had better quality of life than patients aged less than 59 years, which is inconsistent with previous research, further investigation is needed to verify. Compared with patients educated up to 16 years old, patients educated up to 18 years old is a potential determinant of better quality of life, which is consistent with the conclusion that higher education is associated with better health-related quality of life [36, 37].

Limitations

Our study presents some limitations. Firstly, the determinants of health-related quality of life are limited by the pre-specified questions in the surveys. There could be some potential unobserved confounding factors (such as individual exercise, occupation, income level or marital status) we did not control for in the generalised linear model. Secondly, this study conducted a brief question on whether patients’ motor symptoms limited their ability to work and divided the characteristic of motor symptoms into with or without limited ability to work, but lacked a detailed evaluation of Parkinson's patients' motor symptoms. More detailed study are needed to verify the association between non-motor symptoms and health-related quality of life for patients with Parkinson’s disease after controlling for their motor symptoms. A final limitation is our study is an observational study and reports the association between non-motor symptoms and health-related quality of life for patients with PD based on a quantitative study, more evidence based on qualitative studies and randomized controlled trials are needed to clarify the causal association in future research.

Conclusions

Non-motor symptoms are a key determinant of health-related quality of life and societal cost of PD and are often less appreciated than motor symptoms but are important sources of disability for PD patients. In this study, we find a reversed relationship between total numbers of non-motor symptoms with health-related quality of life for PD patients; the more the total number of non-motor symptoms, the worse of the health-related quality of life. Improved awareness and understanding of the relationship between NMS and quality of life will encourage a multidisciplinary approach to patient care and facilitate the provision of more comprehensive education for patients and caregivers.

Abbreviations

Generalized Linear Model	GLM
30-item Non-Motor Symptom	NMS-30
Parkinson’s disease	PD
8-item Parkinson’s Disease Quality of life Questionnaire	PDQ-8
39-item Parkinson’s Disease Quality of life Questionnaire	PDQ-39
PDQ-8 Summary Index	PDQ-8 SI
Participant Centered Consent	PCC

Declarations

Ethics approval and consent to participate

The '100 for Parkinson's' project was conducted in accordance with the Declaration of Helsinki and received ethical approval from the Liverpool School of Tropical Medicine (No.15–050) and an ethics exemption from the New England IRB for participants from the USA (No.16–042). Consent was obtained by adapting E-Consent, a Participant Centered Consent (PCC) Toolkit developed by Sage Bionetworks. The process is similar to the standard consent process with the only difference being that a wet signature is not collected. All participants signed e-consent for their de-identified data to be used in any future research projects that have been approved by the '100 for Parkinson's Data Access Committee'.

Consent for publication

Not applicable.

Availability of data and materials

Researchers who want to use these data should contact Bruce Hellman (bruce@umotif.com).

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

DW and BH was responsible for overall design of this study. BH and BJ were responsible for the field working including data collection and management. XF, YZ and DW were responsible for the statistical analysis plan. XF, YZ and DW performed the statistical analysis. The manuscript was prepared by XF, YZ, HL, BJ, BH and DW. All authors critically reviewed and approved the final manuscript.

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Figures

Figure 1

Neuropsychiatric symptoms

Sleep disorders

Figure 2

Sleep disorders

Autonomic symptoms

Figure 3

Autonomic symptoms

Gastrointestinal symptoms

Figure 4

Gastrointestinal symptoms

Sensory symptoms

Figure 5

Sensory symptoms

Figure 6

Other symptoms

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