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Severity of depressive and motor symptoms impacts quality of life in Parkinson's disease patients at an academic movement clinic: A cross-sectional study

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ABSTRACT

Introduction: Parkinson's disease (PD) is a neurodegenerative disease with motor and non-motor manifestations that have been previously reported to affect patient quality of life (QoL). Our objective is to investigate the factors that contribute to QoL in a cohort of PD patients receiving care at a major academic institution.

Methods: In this cross-sectional study of 124 participants (71.77% male, mean age 65.20, mean UPDRS-III score 11.25), we analyzed if certain clinical features such as UPDRS-III, QIDS-C, and total disease duration contributed to QoL as measured by two different metrics (PDQ-39 and EQ-5D) in PD patients at a university Movement Disorders Clinic.

Results: Motor symptoms of PD, with the exception of tremor, as well as depression and specific depressive symptoms were significantly and positively correlated with lower QoL metrics for patients with Parkinson's, with total depressive symptom severity (QIDS-C_{16} Total score) contributing most to QoL scores. Of the specific depressive and motor symptoms, anhedonia and rigidity contributed the most to QoL. Disease duration was significantly correlated with lower QoL for participants with Parkinson's according to the QoL metric PDQ-39 but not ED-5D. Parkinson's patients with access to high-quality healthcare are at risk for having diminished QoL due to both depressive and motor symptoms.

Conclusion: While severity of motor symptoms certainly impacted QoL in our cohort, our findings suggest that depressive symptoms contribute more to impaired QoL than severe motor symptoms do. This phenomenon suggests that concomitant depression in PD as well as one's psychological adjustment to disability may have a greater impact on QoL than severe motor symptoms.

1. Introduction

Parkinson's disease (PD) is an incurable neurodegenerative disease affecting 572 out of 100,000 adults over 45 years old [1]. The disease not only alters motor function, causing gait difficulties, tremors, rigidity, and bradykinesia but is also associated with many non-motor issues, including depression, autonomic dysfunction, sleep disturbances, fatigue, cognitive impairment, and pain. As such, this disorder can significantly impact patients' quality of life (QoL) [2]. Indeed, as with other chronic diseases, several studies have found that PD patients' QoL is worse than that of healthy controls [3–5]. With modern drug therapy, PD patients may sustain a relatively normal life expectancy, [6] so understanding the variables that impact the QoL of PD patients and addressing them promptly with medical and social interventions is important in improving PD patients' well-being.

Several clinical and demographic characteristics have been identified as contributory to how PD patients perceive their well-being and functioning, including PD duration, depression, and motor symptom severity. In comparing QoL between PD patients with shorter versus longer disease durations, Visser et al. (2008) found that pain and difficulties with ADLs significantly contributed to poor QoL only in the shorter disease duration group [7]. Depression is a common non-motor manifestation in PD; the etiology of depression in PD is likely multifactorial and has been hypothesized to be secondary to PD pathophysiology, psychosocial stress, and adverse effects of medications [8–10]. Depression can be difficult to diagnose in PD given the high prevalence of concentration difficulties, sleep disruptions, and lethargy in this population [9,11,12]. Depression has been found to significantly

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correlate with worse QoL scores in PD patients [5,13–18]. Motor symptom severity, indicated by UPDRS-III or Hoehn-Yahr stage, has been unanimously reported to be significantly correlated with QoL, as measured by both PDQ-39 and EQ-5D [3,4,6,7,13–15,19–21].

There is evidence that social support, education level, and employment status may influence QoL in PD patients [3,11,15,19,20,22]. However, it was unclear if these participants in these studies were exclusively treated at a large tertiary care center. Therefore, we were interested in determining if the other clinical features that have well-established associations with QoL – for instance, disease duration, depressive symptoms, and motor symptom severity – would still contribute to QoL in a well-supported cohort being treated exclusively by movement disorder specialists at a large academic center. We were also interested in discovering which motor and depressive symptoms were most common in a well-resourced cohort and which contributed most to the functioning and well-being of PD patients. Lastly, given that there are relatively few reports on PDQ-39 subdomains in the literature, we were interested in determining the extent of a possible relationship between depressive and motor symptoms on QoL by investigating which and how many PDQ-39 subdomains are impacted by depressive versus motor symptoms. We hypothesized that access to high-quality healthcare would be protective against impaired QoL in PD patients and would modify the relationship between prolonged disease duration, severe depressive symptoms, and severe motor symptoms and impaired QoL such that there would be no statistically significant relationship.

2. Materials and methods

Participants consisted of 124 patients with PD who were being followed by a movement disorders specialist at the Clinical Center for Movement Disorders at UT Southwestern. The patients were invited to participate during their routine clinic visits from February 2010 to April 2011. Patients provided written informed consent to participate, and the investigation was approved by the UT Southwestern Institutional Review Board. All participants had to be 90 years old or younger, identify English as their primary language, and be clinically diagnosed with PD, as defined by the diagnostic criteria described by Hughes, Daniel, Kilford and Lees [23]. Exclusion criteria were any other known or suspected cause of parkinsonism, significant features suggesting atypical parkinsonism, lifetime Diagnostic and Statistical Manual of Mental Disorders, 4th Ed., text revision Axis I psychiatric diagnosis other than major depressive disorder, alcohol abuse or dependence within the past 6 months, substance abuse or dependence within the past 6 months, any unstable or clinically significant condition that could impair the person's ability to comply with study procedures, history of mental retardation, or current diagnosis of delirium.

We performed a clinical neurologic exam to establish that the participant had at least 2 of the 3 cardinal features of PD, and, by history, had responded to dopaminergic medication. We obtained the Unified Parkinson Disease Rating Scale (UPDRS) motor score (Domain III) [24] at the baseline clinical visit to determine disease severity. The UPDRS assesses the severity of symptoms in four domains, including: 1) Mental abilities and mood; 2) Activities of daily living; 3) Motor abilities and 4) On and off fluctuations. Only Domain III — Motor scale of the UPDRS was utilized in this study. The majority of participants were on dopaminergic medications during this assessment. Information regarding disease duration and demographics (e.g., age, gender, race, educational attainment, occupation type) was obtained during a clinical interview. We calculated disease duration as the year of study enrollment minus the year of symptom onset that the patients had reported in the history of present illness.

Clinicians completed the Quick Inventory of Depressive Symptoms - Clinician Rated (QIDS-C_{16}), and participants completed the Parkinson's Disease Questionnaire-39 (PDQ-39) and the EuroQoL (EQ-5D) at the 2nd clinical visit, 1 month after the baseline visits. The QIDS-C_{16} is a 16-item clinician-reported questionnaire used for measuring the severity of depressive symptoms [25].

The PDQ-39 is a self-report questionnaire assessing health-related quality of life specific to Parkinson's disease. The questionnaire addresses how often patients experience difficulty in the 8 dimensions of quality of life: mobility, ADLs, emotional well-being, stigma, social support, cognition, communication, and bodily discomfort. Summary indices and the PDQ-39 Summary Index (PDQ-39SI) were calculated according to scoring guidelines [26]. The lowest possible PDQ-39SI is 20 and indicates less time spent experiencing difficulty in functioning and well-being and therefore better health-related quality of life. The highest possible PDQ-39SI is 100 and signifies poor health-related quality of life.

The EQ-5D is a brief self-complete health-status measure assessing the degree to which participants encounter difficulties with mobility, self-care, usual activities, pain/discomfort, and anxiety/depression [27]. EQ-5D indices were calculated according to values of health states in the United States described by Shaw et al. (2005) [27]. Health states are 5-digit profiles that represent the unique combinations of item responses, and each health state has a single corresponding index value. The index value reflects how good or bad the health state is in the context of the region/country in which the individual is responding. An index value of 1 indicates the fewest health and function issues and therefore better QoL whereas an index of 0 indicates poor QoL.

Preceding statistical analyses, composite scores were formed from the QIDS-C_{16} for Sleep (items 1–4), Appetite/Weight (items 6–9), Anhedonia (items 5, 11, and 13), and Somatic symptoms (items 14–16). Since Suicidal Ideation and Concentration were each measured by one specific item in the QIDS-C_{16}, no composite scores were formed for these depressive symptoms. We combined rest and action tremor scores from the UPDRS-III to form a composite Tremor score. Similarly, we combined scores on rigidity in each extremity and neck from the UPDRS-III to form a composite Rigidity score. Since Bradykinesia was measured by one specific item in the UPDRS-III, no composite score was formed for this motor symptom. We excluded data from 7 participants out of 124, who were missing data from PDQ-39, UPDRS-III, and/or disease duration.

The RStudio statistical computer package (version 1.4.1103; PBC, USA) was used for all statistical analyses. Normality of the data was analyzed using the Shapiro-Wilk test. None of the variables exhibited normal distributions. Thus, we used the non-parametric Spearman correlation. For all analyses, $p < 0.05$ was considered statistically significant.

Two-tailed Spearman correlations were determined between each of the QoL metrics (PDQ-39SI and EQ-5D Index) and 1) the total QIDS-C_{16} score, 2) each of the composite depressive symptoms (Sleep, Appetite/Weight, Anhedonia, Somatic, Suicidal Ideation, Concentration), 3) the total UPDRS-III score, 4) each of the composite motor symptoms (Tremor, Rigidity, Bradykinesia), and 5) disease duration. To determine if participants scored disproportionately higher or lower on any of the QIDS-C_{16} components or any of the UPDRS-III components, non-parametric repeated measures ANOVA's were performed. The Nemanyi test was used for post-hoc analysis when the initial test was statistically significant. Finally, two-tailed Spearman correlations were determined between each PDQ-39 subdomain and 1) the total QIDS-C_{16} score, 2) the total UPDRS-III score, and 3) disease duration.

3. Results

Data from 124 participants, who had provided written informed consent and completed the baseline neurologic exam, were used. Seven participants were excluded from analysis due to incomplete data. Thirty-five participants (28.23 %) were taking antidepressants at the time of interview. Further, most participants (99.19 %) were on Parkinson's medication(s). The majority of participants was male (71.77 %), white (89.52 %), college-educated (66.13 %), and in professional industry (73.39 %). By comparison, Dallas County residents are less college-educated (31.5 %), less male (49.3 %), and less white (66.6 %) than

our study cohort [28].

Table 1 lists clinical information for our cohort, along with the percentage of participants taking Parkinson's medications. The mean age of our participants was 65.20 ± 10.66 years with an average duration of PD of 6.53 ± 4.81 years. The average QIDS-C_{16} total score was 3.93 ± 4.00. Of all of the QIDS-C_{16} components, participants scored highest on sleep symptoms with a mean of 0.602. Non-parametric repeated measures ANOVA revealed that scores on some of the components were significantly different from others (Friedman chi-squared = 187.71, df = 5, p-value < 2.2e-16). Post-hoc Nemenyi test showed that scores on sleep were significantly higher than scores on all of the other components.

The average UPDRS-III total score from the motor examination at the baseline visits was 11.65 ± 8.65. Of the 3 UPDRS-III components analyzed in this study, participants scored highest on rigidity with a mean of 0.6023. Non-parametric repeated measures ANOVA revealed that scores on some of the components were significantly different from others (Friedman chi-squared = 15.105, df = 2, p-value = 0.0005248). Post-hoc Nemenyi test showed that scores on rigidity severity were significantly higher than scores on tremor (0.602 vs 0.2458, p-value = 0.0017) but not on bradykinesia (0.602 vs 0.500, p-value = 0.0631). The average PDQ-39SI was 36.05 ± 10.47, and the average EQ-5D Index was 0.796 ± 0.156.

Fig. 1 shows the relative strengths of associations of each clinical feature (i.e., disease duration, UPDRS-III total score, UPDRS-III components, QIDS-C_{16} total score, and QIDS-C_{16} components) with PDQ-39SI. While UPDRS-III scores are derived from data collected at the baseline visits, QIDS-C_{16} and PDQ-39 scores are from participants' visits 1 month later. Higher summary indices on PDQ-39 indicate a worse QoL, and higher scores on UPDRS-III and QIDS-C_{16} represent more severe motor and depressive symptoms, respectively. All clinical characteristics correlated positively and significantly with QoL except for UPDRS-III Average Tremor Score, which correlated negatively and significantly with QoL, and QIDS-C_{16} Suicidal Ideation score, which correlated positively and non-significantly. Of the motor symptom subtypes, rigidity contributed the most to QoL. Total depressive symptom severity (QIDS-C_{16} Total score) contributed the most to PDQ-39SI. Of the depressive symptom subtypes, anhedonia contributed the most and suicidal ideation contributed the least to PDQ-39SI.

Fig. 2 shows the relative strengths of associations of each clinical feature with EQ-5D Index. Higher indices on EQ-5D indicate a better QoL. All clinical characteristics correlated negatively and significantly with QoL except for UPDRS-III Average Tremor Score, which correlated negatively and non-significantly with QoL, and disease duration, which correlated positively and non-significantly. Of the motor symptom subtypes, rigidity contributed the most to QoL. Total depressive symptom severity (QIDS-C_{16} Total score) contributed the most to EQ-5D Index. Of the depressive symptom subtypes, anhedonia contributed the most and suicidal ideation contributed the least to EQ-5D Index.

Fig. 3 indicates the correlation coefficients between each of the PDQ-39 subdomains and QIDS-C_{16} total score, UPDRS-III total score, and disease duration. Of all the PDQ-39 subdomains, emotional well-being and mobility correlated most strongly with total QIDS-C_{16} score. Disease duration correlated most strongly with the mobility subdomain, and total UPDRS-III score correlated most strongly with the activities of daily living subdomain. Overall, depressive symptoms as indicated by the total QIDS-C_{16} score contributed the greatest to the QoL subdomains of emotional well-being, stigma, social support, and cognitive impairment. Motor symptoms as indicated by the UPDRS-III score contributed the greatest to the QoL subdomains of mobility, activities of daily living, and communication. Disease duration did not contribute the greatest to any QoL subdomain.

Table 1
Basic clinical information and scores on depression inventory, motor exam, PDQ-39, and EQ-5D. Age and disease duration are expressed in years. UPDRS-III, Unified Parkinson's Disease Rating Scale Part III; QIDS-C_{16}, Quick Inventory of Depressive Symptoms - Clinician Rated; PDQ-39SI, Parkinson's Disease Questionnaire Summary Index; EQ-5D, EuroQoL.

	Mean (SD)
Age	65.060 (10.662)
Disease Duration	6.405 (4.688)
UPDRS-III Score	11.624 (8.705)
QIDS-C_{16} Total Score	4.222 (4.075)
PDQ-39SI	36.225 (10.437)
EQ-5D Index	0.796 (0.159)
Number of participants on Parkinson's medications	123 (99.19 %)

4. Discussion

We hypothesized that among our cohort of PD patients treated at an academic movement clinic, prolonged disease duration, severe depressive symptoms, and severe motor symptoms would not significantly correlate with diminished QoL. This was not supported by our data. Our analyses showed that most clinical characteristics significantly affected QoL.

Multiple components of the rating scale used in this study to assess depressive symptoms (QIDS-C_{16}), including anhedonia, somatic symptoms, appetite/weight, concentration, and sleep quality, had a statistically significant correlation with lower QoL on both QoL metrics. This suggests that the negative impact of depression on patient health is the result of the totality of the psychiatric symptoms present in depression in contrast to a specific set of symptoms. The relatively low contribution of suicidal ideation to impairment of patient QoL (i.e., in comparison to the other depressive symptoms) could be the result of the extreme infrequency (<2%) with which participants in this study group reported having suicidal ideation. Our findings on depression severity and PDQ-39 score agree with the literature on clinician-rated and self-rated scales that determined depression significantly correlated with worse PDQ-39 scores in PD patients [5,13–18]. Monitoring and improving depressive symptoms thus could be an important component of care in patients with Parkinson's and reflects the need to assess a broad array of a patient's neurological and psychiatric state to effectively manage PD.

Severity of motor symptoms, specifically bradykinesia and rigidity, was significantly correlated with lower QoL metrics for patients with PD. Other researchers have reported that gait difficulties and limb akinesia were associated with significantly poorer QoL while tremor did not significantly correlate to worse QoL scores [16,22]. The correlation between tremor and QoL not being statistically significant could illustrate that the medication regimens for patients in this study group are more effective at managing tremor symptoms than bradykinesia and rigidity. Alternatively, the unique demographics of this study group could suggest differences in quality of care between our study and others assessing the connection between Parkinson's motor symptom severity and patient QoL. Analysis on the subdomains of the QoL metric PDQ-39 unsurprisingly revealed that more severe motor symptoms correlated most strongly with impaired mobility and activities of daily living. Providers' assessments of ADL performance should shape medication management and overall care for patients with PD.

Disease duration was not statistically significantly associated with worse EQ-5D scores in this study group but was significantly associated with worse PDQ-39 scores, owing potentially to the specific demographics of study participants. EQ-5D is a general QoL assessment metric, while PDQ-39 is a QoL assessment metric for patients with Parkinson's. The results of EQ-5D thus could be more generalizable in assessing overall QoL of the study group in contrast to PDQ-39. Given that patients participating in this study were disproportionately college-educated, white professionals compared to the general population as a whole, this study group likely had greater access to high-quality home care and medication. Access to these resources may mitigate the negative impact of certain factors and symptoms of Parkinson's on QoL over a prolonged duration. Indeed, Grosset et al. (2005) described that optimal

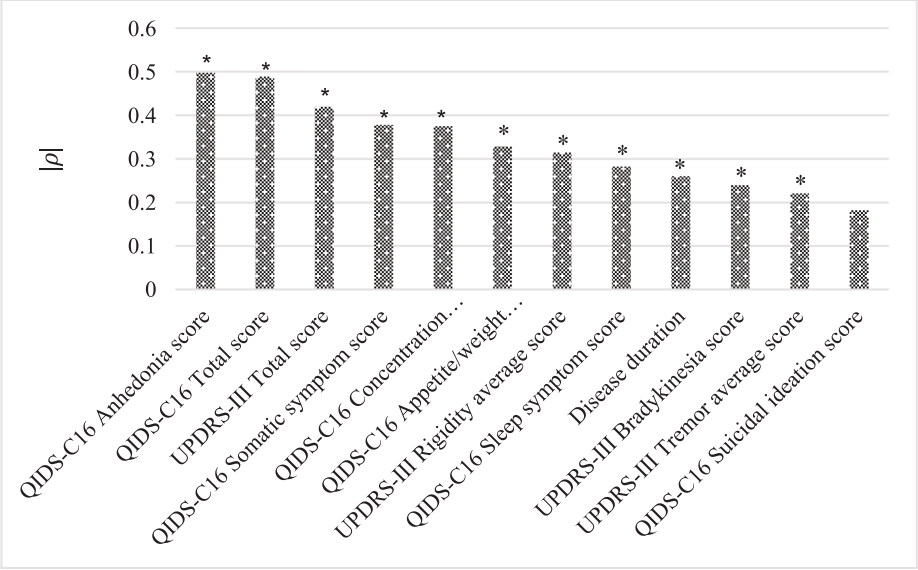

Fig. 1. Factors contributing to Parkinson's Disease Questionnaire-39 (PDQ-39) Summary Index. X-axis represents the clinical features of interest, including QIDS and UPDRS composites and disease duration. *p-value < 0.05. ρ, Spearman correlation coefficient; UPDRS-III, Unified Parkinson's Disease Rating Scale Part III; QIDS-C_{16}, Quick Inventory of Depressive Symptoms - Clinician Rated.

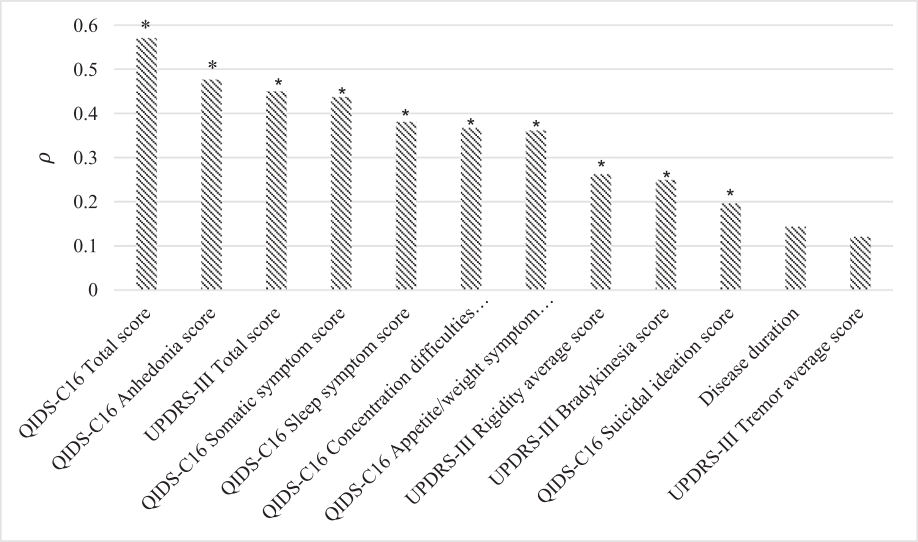

Fig. 2. Factors contributing to EuroQoL (EQ-5D) Index. X-axis represents the clinical features of interest, including QIDS and UPDRS composites and disease duration. *p-value < 0.05. ρ, Spearman correlation coefficient; UPDRS-III, Unified Parkinson's Disease Rating Scale Part III; QIDS-C_{16}, Quick Inventory of Depressive Symptoms - Clinician Rated.

medication adherence is protective against poor QoL in PD patients and that those who had higher adherence were more likely to have social support [22]. Especially with chronic diseases like Parkinson's, health-care access could play a significant role in shaping long-term patient well-being and symptom severity.

An alternative explanation for the equivocal results on disease duration and QoL could be that because the average disease duration for this cohort was 6 years, a disproportionate amount of the cohort may be fairly well-controlled with medications, as is typical for early stages of PD. Our participants simply may not be at the stage at which disease duration would significantly worsen QoL. In our analysis of the QoL subdomains, disease duration was most strongly correlated with poor mobility scores. If this cohort was in the later stages of the PD when medications may not be as efficacious and therefore mobility and QoL would be impaired, disease duration and QoL may be more meaningfully connected. More research is needed on a cohort with a wider range of disease duration and severity to determine how QoL changes with increasing duration of illness and medication efficacy and adherence.

We determined that severe motor symptoms certainly impact QoL in PD patients, mainly by impairing patients' ability to perform ADLs. However, given the larger correlation coefficient of depressive symptoms versus motor symptoms and that motor symptoms contributed the greatest to only three subdomains of QoL while depressive symptoms contributed the greatest to four subdomains of QoL, our findings suggest that depressive symptoms contribute more to impaired QoL than severe motor symptoms do. These findings from an academic movement clinic align with studies with unclear care setting and suggest that one's psychological adjustment to disability may have a greater impact on QoL than motor disability itself [6,7,14–18,29].

A future area of research could focus on the impact socioeconomic

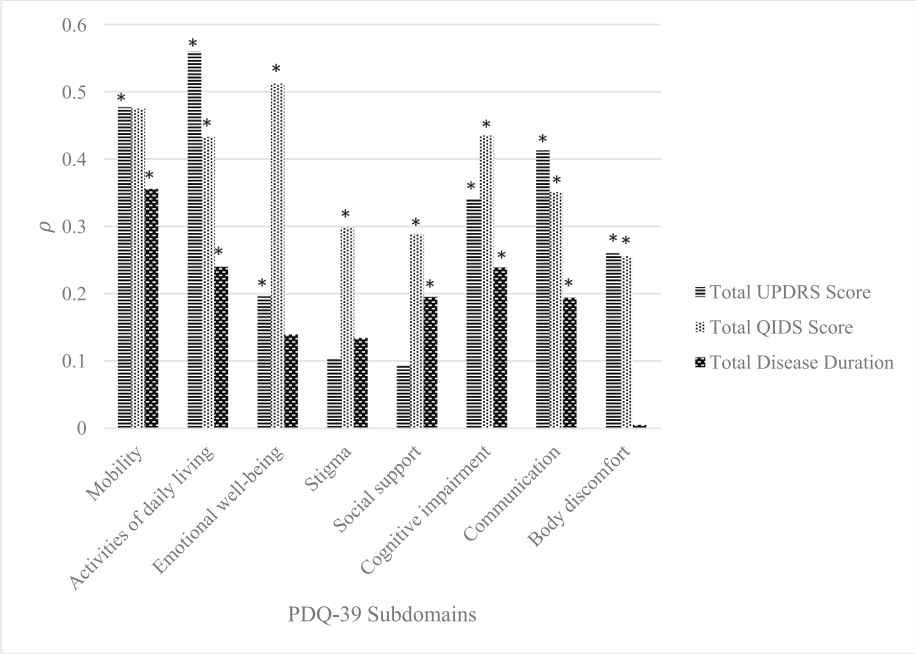

Fig. 3. Correlation coefficients between PDQ-39 subdomains and depressive symptoms, motor symptoms, and disease duration. *p-value < 0.05. UPDRS-III, Unified Parkinson's Disease Rating Scale Part III; QIDS-C_{16}, Quick Inventory of Depressive Symptoms - Clinician Rated; PDQ-39, Parkinson's Disease Questionnaire-39.

status has on QoL of PD patients, for instance to assess if patients with lower socioeconomic status are at higher risk than patients with higher socioeconomic status to have lower QoL and if access to best care practices for managing depressive and motor symptoms is meaningfully impacted by patient socioeconomic status. Research should also be conducted to determine which aspects of Parkinson's care management, including screening, follow-ups, medication, and home care, help to mitigate the impact of Parkinson's symptoms on QoL.

CRediT authorship contribution statement

Brianne Lacy: Conceptualization, Methodology, Formal analysis, Writing – original draft, Writing – review & editing, Visualization, Project administration. **Hien J. Piotrowski:** Conceptualization, Methodology, Writing – original draft, Writing – review & editing, Visualization. **Richard B. Dewey:** Investigation, Resources, Data curation, Writing – review & editing, Supervision, Funding acquisition. **Mustafa M. Husain:** Writing – review & editing, Supervision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

[1] C. Marras, J.C. Beck, J.H. Bower, E. Roberts, B. Ritz, G.W. Ross, R.D. Abbott, R. Savica, S.K. Van Den Eeden, A.W. Willis, C.M. Tanner, P.G. Parkinson's Foundation, Prevalence of Parkinson's disease across North America, NPJ Parkinsons Dis. 4 (2018), 21-21.

[2] A. Berardi, E. Regoli, M. Tofani, D. Valente, G. Fabbrini, A. Fabbrini, M. Ruggieri, F. Panuccio, G. Galeoto, Tools to assess the quality of life in patients with Parkinson's disease: a systematic review, Expert Rev. Pharmacoecon. Outcomes Res. 21 (1) (2021) 55–68.

[3] N. Zhao, Y. Yang, L. Zhang, Q. Zhang, L. Balbuena, G.S. Ungvari, Y.F. Zang, Y. T. Xiang, Quality of life in Parkinson's disease: A systematic review and meta-analysis of comparative studies, CNS Neurosci. Ther. 27 (3) (2021) 270–279.

[4] M. Kasten, L. Kertelge, V. Tadic, N. Bruggemann, A. Schmidt, J. van der Vegt, H. Siebner, C. Buhmann, R. Lencer, K.R. Kumar, K. Lohmann, J. Hagenah, C. Klein, Depression and quality of life in monogenic compared to idiopathic, early-onset Parkinson's disease, Mov. Disord. 27 (6) (2012) 754–759.

[5] D. Santos-García, T. de Deus Fonticoba, E. Suárez Castro, A. Aneiros Díaz, C. Cores Bartolomé, M.J. Feal Panceiras, J.M. Paz González, L. Valdés Aymerich, J. M. García Moreno, M. Blázquez Estrada, S. Jesús, P. Mir, M. Aguilar, L.L. Planellas, J. García Caldentey, N. Caballol, I. Legarda, I. Cabo López, L. López Manzanares, M.A. Ávila Rivera, M.J. Catalán, L.M. López Díaz, C. Borrué, M. Álvarez Sauco, L. Vela, E. Cubo, J.C. Martínez Castrillo, P. Sánchez Alonso, M.G. Alonso Losada, N. López Ariztegui, I. Gastón, B. Pascual-Sedano, M. Seijo, J. Ruíz Martínez, C. Valero, M. Kurtis, J. González Ardura, C. Prieto Jurczynska, P. Martinez-Martin, Quality of life and non-motor symptoms in Parkinson's disease patients with subthreshold depression, J. Neurol. Sci. 418 (2020), 117109.

[6] C. Global Parkinson's Disease Survey Steering, Factors impacting on quality of life in Parkinson's disease: results from an international survey, Mov Disord 17(1) (2002) 60-7.

[7] M. Visser, S.M. van Rooden, D. Verbaan, J. Marinus, A.M. Stiggelbout, J.J. van Hilten, A comprehensive model of health-related quality of life in Parkinson's disease, J. Neurol. 255 (10) (2008) 1580–1587.

[8] Y.-P. Chang, M.-S. Lee, D.-W. Wu, J.-H. Tsai, P.-S. Ho, C.-H.-R. Lin, H.-Y. Chuang, Risk factors for depression in patients with Parkinson's disease: A nationwide nested case-control study, PLoS One 15 (7) (2020) 1–11.

[9] E. Edwards, C. Kitt, E. Oliver, J. Finkelstein, M. Wagster, W.M. McDonald, Depression and Parkinson's disease: a new look at an old problem, Depress. Anxiety 16 (1) (2002) 39–48.

[10] S.E. Starkstein, G. Petracca, E. Chemerinski, A. Teson, L. Sabe, M. Merello, R. Leiguarda, Depression in Clinic Versus Akinetic-Rigid Parkinson's Disesae, Mov. Disord. 13 (1) (1998) 29–33.

[11] C.A. Jones, S.L. Pohar, S.B. Patten, Major depression and health-related quality of life in Parkinson's disease, Gen. Hosp. Psychiatry 31 (4) (2009) 334–340.

[12] J. Koerts, K.L. Leenders, M. Koning, A. Bouma, M. van Beilen, The assessment of depression in Parkinson's disease, Eur. J. Neurol. 15 (5) (2008) 487–492.

[13] M. Balzer-Geldsetzer, J. Klotsche, R. Dodel, O. Riedel, Quality of life in a German cohort of Parkinson's patients assessed with three different measures, J. Neurol. 265 (11) (2018) 2713–2722.

[14] W.M. Liu, R.J. Lin, R.L. Yu, C.H. Tai, C.H. Lin, R.M. Wu, The impact of nonmotor symptoms on quality of life in patients with Parkinson's disease in Taiwan, Neuropsychiatr. Dis. Treat. 11 (2015) 2865–2873.

[15] E. Cubo, A. Rojo, S. Ramos, S. Quintana, M. Gonzalez, K. Kompoliti, M. Aguilar, The importance of educational and psychological factors in Parkinson's disease quality of life, Eur. J. Neurol. 9 (6) (2002) 589–593.

[16] A. Schrag, M. Jahanshahi, N. Quinn, What contributes to quality of life in patients with Parkinson's disease? J. Neurol. Neurosurg. Psychiatry 69 (3) (2000) 308–312.

[17] W. Su, H. Liu, Y. Jiang, S. Li, Y. Jin, C. Yan, H. Chen, Correlation between depression and quality of life in patients with Parkinson's disease, Clin. Neurol. Neurosurg. 202 (2021), 106523.
[18] K.H. Karlsen, J.P. Larsen, E. Tandberg, J.G. Mæland, Influence of clinical and demographic variables on quality of life in patients with Parkinson's disease, J. Neurol. Neurosurg. Psychiatry 66 (4) (1999) 431–435.
[19] K. Takahashi, N. Kamide, M. Suzuki, M. Fukuda, Quality of life in people with Parkinson's disease: the relevance of social relationships and communication, J. Phys. Ther. Sci. 28 (2016) 541–546.
[20] K.M. Prakash, N.V. Nadkarni, W.K. Lye, M.H. Yong, E.K. Tan, The impact of non-motor symptoms on the quality of life of Parkinson's disease patients: a longitudinal study, Eur. J. Neurol. 23 (5) (2016) 854–860.
[21] P. Crispino, M. Gino, E. Barbagelata, T. Ciarambino, C. Politi, I. Ambrosino, R. Ragusa, M. Marranzano, A. Biondi, M. Vacante, Gender Differences and Quality of Life in Parkinson's Disease, Int. J. Environ. Res. Public Health 18 (1) (2020).
[22] K.A. Grosset, I. Bone, D.G. Grosset, Suboptimal medication adherence in Parkinson's disease, Mov. Disord. 20 (11) (2005) 1502–1507.
[23] A.J. Hughes, S.E. Daniel, L. Kilford, A.J. Lees, Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases, J. Neurol. Neurosurg. Psychiatry 55 (3) (1992) 181–184.
[24] S. Fahn, R.L. Elton, Unified Parkinson's disease rating scale, in: S. Fahn, C. D. Marsden, M. Goldsten, D.B. Calne (Eds.), Recent developments in Parkinson's disease, Macmillan Healthcare Information, Florham Park, NJ, 1987, pp. 153–163, 293-304.
[25] A.J. Rush, M.H. Trivedi, H.M. Ibrahim, T.J. Carmody, B. Arnow, D.N. Klein, J. C. Markowitz, P.T. Ninan, S. Kornstein, R. Manber, M.E. Thase, J.H. Kocsis, M. B. Keller, The 16-Item Quick Inventory of Depressive Symptomatology (QIDS), clinician rating (QIDS-C), and self-report (QIDS-SR): a psychometric evaluation in patients with chronic major depression, Biol. Psychiatry 54 (5) (2003) 573–583.
[26] C. Jenkinson, R. Fitzpatrick, V. Peto, R. Greenhall, N. Hyman, The Parkinson's Disease Questionnaire (PDQ-39): development and validation of a Parkinson's disease summary index score, Age Ageing 26 (5) (1997) 353–357.
[27] J.W. Shaw, J.A. Johnson, S.J. Coons, US Valuation of the EQ-5D Health States: Development and Testing of the D1 Valuation Model, Med. Care 43 (3) (2005) 203–220.
[28] QuickFacts Dallas County, Texas. https://www.census.gov/quickfacts/dallascountytexas. (Accessed December 7 2021).
[29] Y. Suzukamo, S. Ohbu, T. Kondo, J. Kohmoto, S. Fukuhara, Psychological adjustment has a greater effect on health-related quality of life than on severity of disease in Parkinson's disease, Mov. Disord. 21 (6) (2006) 761–766.