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Mapping of the PDQ-39 to EQ-5D scores in patients with Parkinson's disease

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Abstract
Purpose The EuroQoL (EQ-5D) is ideal to compare quality of life across conditions. However, the Parkinson's Disease Questionnaire (PDQ-39) is often the only quality-of-life instrument used in Parkinson's disease research. We aimed to identify associations between PDQ-39 domains and EQ-5D domains, and compare different methods of developing a function to map the PDQ-39 to EQ-5D scores.
Methods Adults with Parkinson's disease self-completed both instruments. Ordinal regression identified associations between PDQ-39 domain scores and each EQ-5D domain. Modeling ($n = 80$) and validation sets ($n = 16$) were randomly generated. Overall performance of four methods of mapping the PDQ-39 to EQ-5D scores (using PDQ-39 domains and total score in ordinal and linear regression) was assessed with the validation set, followed by assessing the equivalence of observed and predicted EQ-5D scores on the full dataset controlling for sociodemographic factors.
Results Different sets of PDQ-39 domains were associated with each EQ-5D domain. For example, PDQ-39 "Activities of Daily Living" and "Social Support" were associated with EQ-5D "Personal Care," while PDQ-39 "Emotional Well-being" was associated with EQ-5D "Anxiety/Depression." Over one-third (37.5 %) of predictions from ordinal regressions had an error <0.01 % (compared to 6.3 % for linear regressions). The EQ-5D scores predicted with ordinal regression using PDQ-39 domains were similar in distribution and association with sociodemographic factors to the observed EQ-5D scores.
Conclusions Of the four methods tested, using PDQ-39 domains in ordinal regression was superior for mapping EQ-5D scores. The function reported here may prove particularly useful for cost-utility analyses comparing Parkinson's disease with other conditions.

Keywords Quality of life · PDQ-39 · EQ-5D · Parkinson's disease · Economic evaluation

Abbreviations

CLAD	Censored least absolute deviations
DBS-STN	Deep brain stimulation
EM	Expectation–maximization
EQ-5D	EuroQoL utility index
IQR	Interquartile range
MAD	Mean absolute deviation
MAR	Missing at random
MCAR	Missing completely at random
OLS	Ordinary least squares
PDQ	Parkinson's Disease Questionnaire
QPP	Queensland Parkinson's disease Project
RMSE	Root mean squared error
SPSS	Statistical Package for the Social Sciences
UK	United Kingdom
VAS	Visual analogue scale

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Introduction

Parkinson's disease is a chronic and incurable neurodegenerative condition of unknown origin that results in significant morbidity including gait and fine motor disturbance, insomnia, fatigue, urinary incontinence, gastrointestinal dysfunction, and mental disorders [1]. The disease impacts significantly on the sufferer's psychological well-being and their occupational and social roles as well as their physical abilities [2]. Thus, measuring health-related quality of life, rather than, or in addition to, physical functioning is important for clinical trials and economic analyses of therapies for the disease.

Health-related quality of life may be measured using disease-specific or generic instruments. The Parkinson's Disease Questionnaire (PDQ-39) is a quality-of-life scale specific to Parkinson's disease [3]. It is a valid and reliable instrument. It has been translated and validated in a number of different languages. It is widely used in Parkinson's disease research, and much of the research involving Parkinson's disease sufferers utilizes the PDQ-39 as the only measure of quality of life (see [4–6] as examples). However, the EuroQoL utility index (EQ-5D) is also commonly used in Parkinson's disease research and utilized more broadly among health researchers. The EQ-5D is also a valid and reliable instrument that uses preference-based valuations of health states to construct an index of quality of life that has the maximum value of 1.0 (full health). Although negative values are possible, an index score of 0.0 is "dead." This instrument allows quality of life to be compared across a wide spectrum of health conditions, including for Parkinson's disease sufferers [7, 8].

Current cost-utility analyses of the aspects of Parkinson's disease treatment use other Parkinson's disease treatments as comparators [9–12], and many quality-of-life studies of Parkinson's disease have not compared Parkinson's disease to other conditions [1, 13–17]. When considering broad questions of the population burden of disease, or the comparative effectiveness of a model of care for Parkinson's disease sufferers, being able to compare quality of life across conditions is fundamental. For undertaking cost-utility analyses, a measure of utility is needed, and this is not readily provided by the PDQ-39. In these instances, a formula to convert existing PDQ-39 scores from specific study populations to comparable EQ-5D utilities would be particularly useful. Cheung et al. [18] mapped the PDQ-8 to the EQ-5D, but did not utilize the full complement of PDQ-39 responses. We aimed to identify PDQ-39 domains that were associated with each of the five EQ-5D domains and compare different methods of developing a function to map the PDQ-39 to EQ-5D utilities in our population.

Methods

Study design

This study utilizes the demographic details and the quality-of-life measures (the EQ-5D, visual analogue scale (VAS), and the PDQ-39) collected as part of a cross-sectional survey of adults with Parkinson's disease undertaken in 2007 for a pilot study on the cost-utility of deep brain stimulation (DBS-STN). The questionnaire also included service usage and costs.

Participants

Participants recruited to the pilot study had either previously undergone DBS-STN, were on the waiting list for DBS-STN, or had been diagnosed with Parkinson's disease and attended a public neurology outpatients department at one of two major hospitals in Brisbane. All potential participants from the Queensland Parkinson's disease Project (QPP), an existing research study register of over 3000 community-dwelling subjects recruited since 2005 who have agreed to participate in research into Parkinson's disease and related disorders, and who met these criteria were posted a letter explaining the study, and a questionnaire. Consent was indicated by return of the questionnaire by post. The study was approved by the Griffith University and Uniting Healthcare Ethics Committees.

The response rate was 53 % (96 of 182 questionnaires returned). Sixty-four percent of respondents were male and 7 % were currently employed. The mean age of participants was 65 years and ranged from 34 to 87 years (Table 1). The median observed EQ-5D index score was 0.59, with interquartile range (IQR) of 0.21. The median observed total PDQ-39 score was 33.3, with an IQR of 27.5.

Respondents to the questionnaire were younger (mean difference 5.95 years $p < 0.001$), had an earlier age of diagnosis of Parkinson's disease (mean difference 13.18 years $p < 0.001$), and were more likely to have had neurosurgical intervention (66.7 vs. 0 % < 0.001) than those who did not respond to the questionnaire. There were no gender differences between participants and non-participants ($p = 0.4$).

Instruments

PDQ-39

The PDQ-39 was scored and interpreted according to the instruments' instructions [19]. This instrument consists of 39 questions on a range of aspects of health and functioning associated with Parkinson's disease with answers

Table 1 Demographic characteristics of participants with Parkinson's disease

Characteristics	Frequency (%) or mean (SD)
Age in years	64.90 (7.9)
Gender (male)	61 (63.5 %)
Employment In employment or self-employed	7 (7.4 %)
Retired	73 (76.8 %)
Housework	13 (13.7 %)
Other	2 (2.1 %)
Education (continue after the minimum school leaving age)	52 (54.2 %)
Higher education (degree or equivalent)	33 (34.7 %)
Income	
Up to $25,000	35 (38.9 %)
$25,001–$50,000	32 (35.6 %)
$50,001–$75,000	12 (13.3 %)
$75,001–$100,000	5 (5.6 %)
$100,001 plus	6 (6.7 %)
Private hospital cover	72 (76.6 %)
Private extras cover	62 (68.1 %)
Live on his/her own	12 (12.5 %)
Deep brain stimulation	64 (66.7 %)

of "never," "occasionally," "sometimes," "often," and "always." Responses are allocated a value from 0 to 4, and subsets of questions require specific calculations to compute domain scores. These are then averaged to obtain the total score [19].

EQ-5D

The EQ-5D was scored and interpreted according to the instruments' instructions [20]. The EQ-5D consists of five questions, each on a different aspect of health or functioning. The answer to each question corresponds to either "no problems," "some problems," or "extreme problems." Each answer is allocated a domain score of 1–3. An individual's EQ-5D index is then calculated by weighting each domain score, based on health state valuations derived from a general population, and summing the results. The weights used vary according to the population from which the scoring algorithm was derived. For our study, the United Kingdom (UK) scoring algorithm was used [21].

Statistical analysis

As utility scores and demographic characteristics for DBS-STN and non-DBS-STN groups were not significantly different (data not shown), all cases were initially included in the analysis. Missing values in the eight PDQ-39 domain scores (3.0 %) were computed using the Expectation–Maximization (EM) algorithm [22], assuming multivariate normal distribution. In the EM algorithm, the missing values are imputed in the E-step and complete-data methods are applied on the M-step. Thus, the EM algorithm, besides providing maximum likelihood estimates of parameters, also provides estimates for the missing values [23]. The EM algorithm assumes the data are either missing completely at random (MCAR) or missing at random (MAR), where the former can be tested in the Statistical Package for the Social Sciences (SPSS) "Missing Values Imputation" procedure using a chi-square statistic [24]. There were two cases (2.1 %) with missing EQ-5D index scores and these were excluded from the analysis.

To identify associations between PDQ-39 and EQ-5D, prediction of the EQ-5D utility index was first performed by modeling the five EQ-5D domains (Mobility, self-care, Usual Activities, Pain/Discomfort, and Anxiety/Depression) separately based on the eight PDQ-39 domain scores. Functioning levels (no problems, some problems, and extreme problems) were estimated for each of the five EQ-5D domains. The estimated functioning levels were then used to calculate the EQ-5D utility index using the established equation [21].

We adopted ordinal regression to determine the model relating the functioning levels for each EQ-5D domain with the eight PDQ-39 domain scores. The Cauchit (inverse Cauchy) link function was selected as it provided a better fit for the proportional odds assumption in the ordinal regression models [25]. The latter was formally tested using the "Test of Parallel Lines" function in SPSS. More specifically, the Cauchit link function implied that the probabilities of functioning levels were defined as follows:

$$\begin{aligned}
&\text{prob}(\text{``no problems''}) = \vartheta_1 = 0.5 - \tan^{-1}(-\alpha_1 + \beta' X)/\pi \\
&\text{prob}(\text{``some problems''}) = \vartheta_2 \\
&\qquad = 0.5 - \tan^{-1}(-\alpha_2 + \beta' X)/\pi - \vartheta_1 \\
&\text{prob}(\text{``extreme problems''}) = \vartheta_3 = 1 - \vartheta_1 - \vartheta_2
\end{aligned}$$

where $\alpha_i\,(i = 1, 2)$ were the constant terms in the linear predictor for "no problems" and "some problems," respectively, and $\beta' X$ in the linear predictor related the functioning levels of an EQ-5D domain with the PDQ-39 domain scores. Based on individual pattern X, the predicted functioning level can be obtained by assigning the category with the largest estimated probability (that is, the maximum of ϑ_1, ϑ_2, and ϑ_3). The backward elimination method was used for the ordinal regression, where the elimination threshold was set at $p = 0.1$. Goodness of fit of ordinal regression models was assessed using the deviance measure comparing the observed and expected frequencies.

The strength of the association between the EQ-5D domain and the identified predictor variables was measured using the Cox and Snell R^2 statistic. The performance of the ordinal regression models was examined by the apparent misclassification error rates.

Overall performance of the methods of predicting the EQ-5D utility index was assessed and validated in two ways. Firstly, the 96 observations were split into two groups using random sampling (80 observations as a training set for the modeling and 16 observations as a validation set), allowing the estimation of the true mean absolute deviation (MAD) and root mean squared error (RMSE) as well as investigation of how well the predicted EQ-5D utility indices compared to the observed scores in the validation set based on the prediction errors and the descriptive summary of observed and predicted EQ-5D utility indices. Secondly, multiple regression analysis using the complete database of observations assessed for the equivalence of the adjusted linear trends of the observed and predicted EQ-5D utility indices in relation to the visual analogue scale (VAS) result, age, gender, household income, private health insurance, living alone, and having undergone deep brain stimulation.

For each of these validation processes, ordinal regression using PDQ-39 domain scores was compared with three other methods of developing a function to map the PDQ-39 and EQ-5D: ordinal regression using total PDQ-39 score and typical linear regression [18, 26] via ordinary least squares (OLS) using PDQ-39 domain scores and using total PDQ-39 score (final model determined using the backward elimination method).

All statistical analyses were performed using SPSS 17.0 for Windows. Statistical tests were all two-sided and conducted at a significance level of 0.05.

Results

Missing data

The proportions of missing data in the eight PDQ-39 domains were low (ranging from 1.0 to 5.2 %). There was no particular pattern of (jointly) missing data. The MCAR test was not significant ($\chi^2 = 81.35$, degrees of freedom = 72, $p = 0.211$), confirming that the data were missing completely at random.

Prediction models for the five EQ-5D domains

Table 2 presents the five prediction models (the estimates of $\alpha_i\,(i = 1, 2)$ and the parameters in the linear predictor $\beta' X$) for each of the five EQ-5D domains. For example, the first model indicates that the EQ-5D Mobility domain will score worse ("serious problem") when there are poor results in PDQ Mobility, PDQ Activities of Daily Living, and PDQ Bodily Discomfort domain scores, but better results in PDQ Social Support domain score. With this model for EQ-5D Mobility, the Cox and Snell R^2 statistic is 55.7 % and the apparent misclassification rate is 0.074. The apparent misclassification rates for the other four models corresponding to the other EQ-5D domains, however, are not small (ranging from 0.208 to 0.240).

Estimation of the EQ-5D utility index

The estimated functioning levels for each of the five EQ-5D domains were combined to calculate the EQ-5D utility index using the established equation [21]. Table 3 presents the performances of estimating the EQ-5D utility index in the validation set from four different approaches. The

Table 2 Predictors in the PDQ-39 domain scores for the five EQ-5D domains (ordinal regression)

Scores	EQ-5D Mobility coefficient (p value)	EQ-5D Personal Care coefficient (p value)	EQ-5D Usual Activities coefficient (p value)	EQ-5D Pain/ Dis-comfort coefficient (p value)	EQ-5D Anxiety/ Depression coefficient (p value)
Constant ("no problems")	11.701 (0.043)	1.985 (0.003)	1.931 (0.030)	1.079 (0.143)	2.512 (0.005)
Constant ("some problems")	68.418 (0.044)	11.111 (0.004)	13.773 (0.001)	11.032 (0.001)	24.255 (0.133)
PDQ Mobility	0.201 (0.062)		0.084 (0.022)		
PDQ Activities of Daily Living	0.447 (0.058)	0.090 (0.002)	0.113 (0.013)	0.088 (0.015)	
PDQ Emotional Well-being					0.126 (0.003)
PDQ Stigma					
PDQ Social Support	−0.455 (0.043)	−0.045 (0.024)			
PDQ Cognition			−0.044 (0.082)		
PDQ Communication				−0.048 (0.044)	
PDQ Bodily Discomfort	0.213 (0.044)			0.070 (0.016)	
Pseudo R^2	55.7 %	32.2 %	43.8 %	27.9 %	37.6 %
Misclassification rate	0.074	0.240	0.208	0.208	0.221

Table 3 Performance of regression models for estimating EQ-5D utility index (validation set, $N = 16$)

	Ordinal regression using		Linear regression using	
	PDQ-39 domain scores	PDQ-39 total	PDQ-39 domain scores	PDQ-39 total
Mean absolute deviation (MAD)	0.104	0.112	0.128	0.144
Root mean squared error (RMSE)	0.152	0.162	0.160	0.175
Absolute error (e)				
$e \leq 0.01$	6 (37.5 %)	6 (37.5 %)	1 (6.3 %)	1 (6.3 %)
$0.01 < e \leq 0.05$	1 (6.3 %)	2 (12.5 %)	3 (18.8 %)	3 (18.8 %)
$0.05 < e \leq 0.10$	1 (6.3 %)	1 (6.3 %)	1 (6.3 %)	3 (18.8 %)
$0.10 < e \leq 0.15$	3 (18.8 %)	0 (0.0 %)	6 (37.5 %)	2 (12.5 %)
$0.15 < e \leq 0.20$	2 (12.5 %)	3 (18.8 %)	2 (12.5 %)	3 (18.5 %)
$0.20 < e \leq 0.30$	1 (6.3 %)	2 (12.5 %)	2 (12.5 %)	2 (12.5 %)
$0.30 < e$	2 (12.5 %)	2 (12.5 %)	1 (6.3 %)	2 (12.5 %)

ordinal regression method using PDQ-39 domain scores outperformed the other models with smaller true MAD and RMSE. In particular, 37.5 % predictions have an error smaller than 0.01 (compared to only 6.3 % for both linear regression models). Table 4 shows the distribution of the observed and predicted utility indices in the validation set. The ordinal regression method using PDQ-39 domain scores again outperformed the other three models. It gave the best estimates for the mean EQ-5D utility index, the median, and the first quartile, but it slightly overestimated the third quartile. The ordinal regression model using PDQ-39 total scores considerably overestimated the mean and the third quartile, while underestimated the median of the EQ-5D utility index. The linear regression model using PDQ-39 domain scores considerably underestimated the mean, the median, and the first quartile of the EQ-5D utility index. The linear regression model using PDQ-39 total scores considerably underestimated the standard deviation and the first quartile of the EQ-5D utility index, but it overestimated the third quartile.

Table 4 Descriptive summary of observed and predicted EQ-5D utility index (validation set, $N = 16$)

	Observed	Predicted (ordinal regression) using		Predicted (linear regression) using	
		PDQ-39 domain scores	PDQ-39 total	PDQ-39 domain scores	PDQ-39 total
Mean	0.632	0.630	0.658	0.585	0.596
Standard deviation	0.195	0.187	0.198	0.188	0.177
1st quartile	0.516	0.516	0.516	0.459	0.428
Median	0.604	0.604	0.516	0.569	0.584
3rd quartile	0.718	0.739	0.835	0.717	0.760

Table 5 presents the results of multiple regression of observed and predicted EQ-5D utility indices on several risk factors. The final model of predicted EQ-5D utility indices using the ordinal regression method with PDQ-39 domain scores is equivalent to that of the observed EQ-5D. The latter model implies that the EQ-5D utility index will increase by about 0.072 per 10 points increase in VAS. The final models obtained for predicted EQ-5D using ordinal regression on PDQ-39 total scores and the linear regression methods are, however, different from that of the observed EQ-5D utility indices.

Table 5 Multiple regression—association of observed and predicted EQ-5D utility index in relation to visual analogue scale (VAS), age, gender, income, private health insurance, living alone, and having undergone deep brain stimulation ($N = 96$)

	Observed	Predicted (ordinal regression) using		Predicted (linear regression) using	
		PDQ-39 domain scores	PDQ-39 total	PDQ-39 domain scores	PDQ-39 total
VAS (per 10 points)	0.072*	0.077*	0.036*	0.065*	0.045*
Age (per 10 years)	NS	NS	NS	NS	NS
Gender	NS	NS	NS	NS	NS
Income	NS	NS	0.032*	0.026*	0.024*
Private hospital	NS	NS	NS	NS	NS
Private extra	NS	NS	NS	NS	NS
Live alone	NS	NS	NS	NS	NS
Deep brain stimulation	NS	NS	NS	NS	NS

NS association not significant (eliminated from the final model)

* significant at 5 % level

Discussion

We compared several methods of mapping PDQ-39 scores to EQ-5D utilities. In this population from southeast Queensland and northern New South Wales with Parkinson's disease, we found the most reliable and effective method was utilizing PDQ-39 domain scores to predict EQ-5D domain scores by ordinal regression. As described above, each EQ-5D domain was predicted to be either (1) no problems, (2) some problems, or (3) extreme problems, depending on which estimated probability (given PDQ-39 domain scores) (ϑ_1, ϑ_2, and ϑ_3, respectively) was the largest. On the basis of the results given in Table 2, the predicted functioning levels of the EQ-5D domains are i ($i = 1, 2,$ or 3):

EQ-5D Mobility $= i$ if $\vartheta_i \geq \vartheta_h$ ($h = 1, 2, 3$), where

$$\vartheta_1 = 0.5 - \tan^{-1}\big(-11.7 + 0.2 \times \text{PDQ\_Mob} + 0.447 \times \text{PDQ\_Act} - 0.455 \times \text{PDQ\_Soc} + 0.213 \times \text{PDQ\_Disc}\big)/\pi$$

$$\vartheta_2 = 0.5 - \tan^{-1}(-68.418 + 0.2 \times \text{PDQ\_Mob} + 0.447 \times \text{PDQ\_Act} - 0.455 \times \text{PDQ\_Soc} + 0.213 \times \text{PDQ\_Disc})/\pi - \vartheta_1$$

$$\vartheta_3 = 1 - \vartheta_1 - \vartheta_2$$

EQ-5D Personal Care $= i$ if $\vartheta_i \geq \vartheta_h$ ($h = 1, 2, 3$), where

$$\vartheta_1 = 0.5 - \tan^{-1}(-1.985 + 0.09 \times \text{PDQ\_Act} - 0.045 \times \text{PDQ\_Soc})/\pi$$

$$\vartheta_2 = 0.5 - \tan^{-1}(-11.111 + 0.09 \times \text{PDQ\_Act} - 0.045 \times \text{PDQ\_Soc})/\pi - \vartheta_1$$

$$\vartheta_3 = 1 - \vartheta_1 - \vartheta_2$$

EQ-5D Usual Activities $= i$ if $\vartheta_i \geq \vartheta_h$ ($h = 1, 2, 3$), where

$$\vartheta_1 = 0.5 - \tan^{-1}(-1.931 + 0.084 \times \text{PDQ\_Mob} + 0.113 \times \text{PDQ\_Act} - 0.044 \times \text{PDQ\_Cog})/\pi$$

$$\vartheta_2 = 0.5 - \tan^{-1}(-13.773 + 0.084 \times \text{PDQ\_Mob} + 0.113 \times \text{PDQ\_Act} - 0.044 \times \text{PDQ\_Cog})/\pi - \vartheta_1$$

$$\vartheta_3 = 1 - \vartheta_1 - \vartheta_2$$

EQ-5D Pain/Discomfort $= i$ if $\vartheta_i \geq \vartheta_h$ ($h = 1, 2, 3$), where

$$\vartheta_1 = 0.5 - \tan^{-1}(-1.079 + 0.088 \times \text{PDQ\_Act} - 0.048 \times \text{PDQ\_Comm} + 0.07 \times \text{PDQ\_Disc})/\pi$$

$$\vartheta_2 = 0.5 - \tan^{-1}(-11.032 + 0.088 \times \text{PDQ\_Act} - 0.048 \times \text{PDQ\_Comm} + 0.07 \times \text{PDQ\_Disc})/\pi - \vartheta_1$$

$$\vartheta_3 = 1 - \vartheta_1 - \vartheta_2$$

EQ-5D Anxiety/Depression $= i$ if $\vartheta_i \geq \vartheta_h$ ($h = 1, 2, 3$), where

$$\vartheta_1 = 0.5 - \tan^{-1}(-2.512 + 0.126 \times \text{PDQ\_Emotion})/\pi$$

$$\vartheta_2 = 0.5 - \tan^{-1}(-24.255 + 0.126 \times \text{PDQ\_Emotion})/\pi - \vartheta_1$$

$$\vartheta_3 = 1 - \vartheta_1 - \vartheta_2$$

Finally, the EQ-5D utility index is calculated based on these predicted functioning levels of EQ-5D domains, using the established equation for EQ-5D [21].

Compared to using PDQ-39 total scores, this method resulted in lower misclassification rates and better prediction in terms of the distribution of the predicted EQ-5D utility indices. Compared to using linear regression, this method resulted in lower MAD and RMSE, and greater alignment between observed and predicted values in terms of the absolute errors and the distribution of the predicted EQ-5D utility indices.

We adopted ordinal regression to determine the five prediction models relating the functioning levels for each EQ-5D domain with the eight PDQ-39 domain scores. The EQ-5D Personal Care domain score was associated with the PDQ-39 Activities of Daily Living and Social Support domain scores, the EQ-5D Usual Activities domain score was associated with the PDQ-39 Mobility, Activities of Daily Living, and Cognition domain scores, the EQ-5D Pain/Discomfort domain score was associated with the PDQ-39 Activities of Daily Living and Communication domain scores, and the EQ-5D Anxiety/Depression domain score was associated with the PDQ-39 Emotional Well-being domain score.

In contrast to the methods that estimate the EQ-5D utility index by regressing it directly on independent variables [18, 27, 28], our method avoids the bounded nature (a ceiling effect) and the skewed distribution of EQ-5D index scores, which may result in biased and inconsistent estimates [26, 29, 30]. Moreover, our method provides separate estimated functioning levels for each of the five EQ-5D domains, which are thus more informative compared to the single estimated EQ-5D utility index.

Cheung et al. [18] are the only other authors we are aware of who have attempted to map PDQ data to EQ-5D utilities. Their study mapped PDQ-8 rather than PDQ-39 and used the censored least absolute deviations (CLAD) and OLS linear regression methods to obtain functions for EQ-5D utilities. We chose not to consider the CLAD estimation method as studies have demonstrated that the CLAD method did not provide better prediction of the EQ-5D utility index than the OLS method using various scales in different disciplines [18, 26, 31]. Cheung et al. [18] excluded participants who indicated "never" on seven or more of the PDQ-8 questions from the mapping processes presumably to limit the impact of the ceiling effect using the OLS method. They conclude that the OLS method is the most useful for mapping PDQ-8 to EQ-5D utilities

and provide a recommended function. The mean absolute deviation for this function was 0.096 in their validation sample. In our population, estimating EQ-5D domains from PDQ-39 data by OLS in our small validation sample was inferior to ordinal regression with MAD of 0.128–0.144 compared to 0.102.

We observed in this self-completed questionnaire that some individuals seemed to give inconsistent responses across the PDQ-39 and EQ-5D. This may have been an issue of interpretation of questions in either the PDQ-39 or EQ-5D. Hagell et al. [32] found ambiguity in the "occasionally" and "sometimes" response categories of the PDQ-39 that may limit its ability to detect differences among people with less severe disease. This may be applicable to our population. Indeed, Cheung et al. also found not all their participants with EQ-5D results of "full health" reported the equivalent on PDQ-8 [18].

There are some limitations in our study. Firstly, potential study participants were selected based on criteria for a cost-utility analysis of deep brain stimulation, and two-thirds of respondents had neurosurgical intervention (compared to none of the non-respondents). Further, respondents included few patients on the waiting list for DBS-STN. We therefore suspect the self-completed nature of the questionnaire lead to an overrepresentation of people with higher levels of utility and functioning. Thus, our results may not be applicable for Parkinson's disease patients with more severe disease. Certainly, the ordinal regression prediction models require sufficient serious cases in order to consistently estimate the probability of "extreme problems." Participants in the Cheung et al. [18] study were also recruited from outpatient clinics and self-completed both quality-of-life measures. These authors also caution use of their results in populations of very poor health or functional status.

Secondly, while we utilized part of our dataset for the purpose of validation, an independent dataset was not available and sample size was small. Small sample size likely contributed to large apparent misclassification rates for four of the five EQ-5D domain prediction models. Replication of our methods in other populations is therefore suggested. Consideration should also be given to examining the prevalence of cases with inconsistent responses to each of the study instruments and studying the effect of removing cases with inconsistent responses.

We have presented methods for mapping PDQ-39 responses to EQ-5D utilities and recommend using PDQ-39 domains to predict EQ-5D domains via ordinal regression as the method of choice. Replication and further exploration of these methods in other populations with Parkinson's disease will prove valuable in ultimately obtaining a reliable and accurate function to calculate EQ-5D utilities from existing PDQ-39 responses. Such a function would be useful to compare the utility of different Parkinson's disease interventions when only PDQ-39 data are available. The PDQ-39 is extensively used in Parkinson's disease, and the EQ-5D is the most widely used multi-attribute utility instrument. Mapping the PDQ-39 to the EQ-5D also allows the quality of life attributable to Parkinson's disease to be directly compared with other diseases. The conversion of PDQ-39 scores to EQ-5D utility indices is thus useful to researchers, especially those undertaking cost-utility analysis to inform decision makers on funding new interventions for Parkinson's disease. Hence, it is important to have a reliable and accurate mapping function for comparative effectiveness. The functions produced here are the best fit we obtained and may prove particularly useful for cost-utility analyses in these circumstances.

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