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International Multicenter Pilot Study of the First Comprehensive Self-Completed Nonmotor Symptoms Questionnaire for Parkinson's Disease: The NMSQuest Study

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Abstract: Nonmotor symptoms (NMS) of Parkinson's disease (PD) are not well recognized in clinical practice, either in primary or in secondary care, and are frequently missed during routine consultations. There is no single instrument (questionnaire or scale) that enables a comprehensive assessment of the range of NMS in PD both for the identification of problems and for the measurement of outcome. Against this background, a multidisciplinary group of experts, including patient group representatives, has developed an NMS screening questionnaire comprising 30 items. This instrument does not provide an overall score of disability and is not a graded or rating instrument. Instead, it is a screening tool designed to draw attention to the presence of NMS and initiate further investigation. In this article, we present the results from an international pilot study assessing feasibility, validity, and acceptability of a nonmotor questionnaire (NMSQuest). Data from 123 PD patients and 96 controls were analyzed. NMS were highly significantly more prevalent in PD compared to controls (PD NMS, median = 9.0, mean = 9.5 vs. control NMS, median = 5.5, mean = 4.0; Mann–Whitney, Kruskal–Wallis, and *t* test, $P < 0.0001$), with PD patients reporting at least 10 different NMS on average per patient. In PD, NMS were highly signifi-

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cantly more prevalent across all disease stages and the number of symptoms correlated significantly with advancing disease and duration of disease. Furthermore, frequently, problems such as diplopia, dribbling, apathy, blues, taste and smell problems were never previously disclosed to the health professionals.

Key words: Parkinson's disease; nonmotor; Unified Parkinson's Disease Rating Scale; questionnaire; quality of life

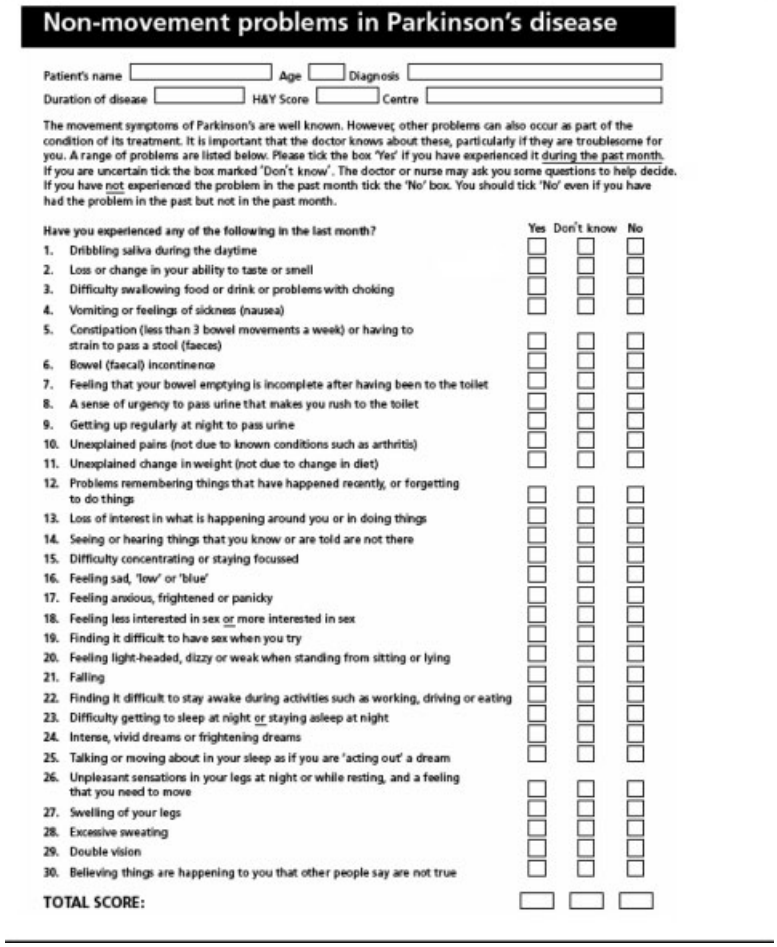
Even though more than 150 years have elapsed since James Parkinson described the key motor symptoms of Parkinson's disease (PD), the nonmotor symptoms (NMS) remain underrecognized, undertreated, and a major cause of disability for PD patients.[1–5] In terms of delivering modern and comprehensive healthcare for PD patients, recognition and treatment of NMS is an important and fundamental element.[6,7] NMS in PD are diverse (Table 1), and in a recent survey of people with Parkinson's disease in the United Kingdom conducted by the U.K. Parkinson's Disease Society (data not shown), patients listed depression, sleep problems, pain, apathy, memory problems, and balance problems as the key symptoms affecting their lives ahead of motor symptoms. NMS such as problems with balance, sleep disturbance, memory failure or confusional episodes, and dribbling of saliva were rated as the most disabling symptoms in 163 consecutive patients attending a PD clinic.[8] An observational study by Hely and colleagues[9] evaluated PD patients followed for a period of 15 to 18 years. One third of the original cohort was evaluated and most had significant NMS, which were more troublesome and disabling than the motor symptoms or levodopa-induced dyskinesias.

Although the nonmotor features of PD are common, these symptoms are often not well recognized in clinical practice; indeed, even specialists often confine treatment and discussion to the management of motor symptoms and motor complications such as dyskinesias.[10,11] It has been reported that nonmotor symptoms of PD are not identified by neurologists in over 50% of consultations and sleep disturbance in particular is not recognized in over 40% of PD patients.[11,12] This is obviously detrimental to patient care and deprives many patients of appropriate therapy.[10]

Individual nonmotor symptoms such as falls, dementia, and hallucinations are now recognized as some of the major reasons for admission to institutional care.[4,13] To enhance identification of NMS in PD patients and to evaluate new and existing strategies, it would be desirable to have a quantitative and validated NMS instrument. Currently available symptom-specific instruments may not be relevant to people with PD and are likely to provide variable and conflicting results, for example, while assessing rates of the prevalence of depression in PD.[14] There are existing PD-specific rating scales but most of these largely concentrate on motor symptoms. To date, there is no single questionnaire or scale that provides a comprehensive assessment of the range of

TABLE 1. *Nonmotor symptom complex of Parkinson's disease*[21]

Neuropsychiatric symptoms
Depression, apathy, anxiety
Anhedonia
Attention deficit
Hallucinations
Delusions
Dementia
Obsessional behavior
Sleep disorders
Restless legs
Periodic limb movements
REM behavior disorder
Excessive daytime somnolence
Vivid dreaming
Non-REM sleep-related movement disorders
Insomnia
Autonomic symptoms
Bladder disturbances
Urgency
Nocturia
Frequency
Sweating
Orthostatic hypotension (OH)
Falls related to OH
Coat hanger pain
Sexual dysfunction
Hypersexuality
Erectile impotence
Hypotestosterone state
Gastrointestinal symptoms (also overlaps with autonomic)
Dribbling of saliva
Ageusia
Dysphagia/choking
Reflux
Vomiting
Nausea
Constipation
Unsatisfactory voiding of bowel
Fecal incontinence
Sensory symptoms
Pain
Paraesthesia
Olfactory disturbance
Other symptoms
Fatigue
Diplopia
Blurred vision
Seborrhea
Weight loss



Non-movement problems in Parkinson's disease

Patient's name ____ Age ____ Diagnosis ____
Duration of disease ____ H&Y Score ____ Centre ____

The movement symptoms of Parkinson's are well known. However, other problems can also occur as part of the condition or its treatment. It is important that the doctor knows about these, particularly if they are troublesome for you. A range of problems are listed below. Please tick the box 'Yes' if you have experienced it during the past month. If you are uncertain tick the box marked 'Don't know'. The doctor or nurse may ask you some questions to help decide. If you have not experienced the problem in the past month tick the 'No' box. You should tick 'No' even if you have had the problem in the past but not in the past month.

Have you experienced any of the following in the last month?	Yes	Don't know	No
1. Dribbling saliva during the daytime	☐	☐	☐
2. Loss or change in your ability to taste or smell	☐	☐	☐
3. Difficulty swallowing food or drink or problems with choking	☐	☐	☐
4. Vomiting or feelings of sickness (nausea)	☐	☐	☐
5. Constipation (less than 3 bowel movements a week) or having to strain to pass a stool (faeces)	☐	☐	☐
6. Bowel (faecal) incontinence	☐	☐	☐
7. Feeling that your bowel emptying is incomplete after having been to the toilet	☐	☐	☐
8. A sense of urgency to pass urine that makes you rush to the toilet	☐	☐	☐
9. Getting up regularly at night to pass urine	☐	☐	☐
10. Unexplained pains (not due to known conditions such as arthritis)	☐	☐	☐
11. Unexplained change in weight (not due to change in diet)	☐	☐	☐
12. Problems remembering things that have happened recently, or forgetting to do things	☐	☐	☐
13. Loss of interest in what is happening around you or in doing things	☐	☐	☐
14. Seeing or hearing things that you know or are told are not there	☐	☐	☐
15. Difficulty concentrating or staying focussed	☐	☐	☐
16. Feeling sad, 'low' or 'blue'	☐	☐	☐
17. Feeling anxious, frightened or panicky	☐	☐	☐
18. Feeling less interested in sex or more interested in sex	☐	☐	☐
19. Finding it difficult to have sex when you try	☐	☐	☐
20. Feeling light-headed, dizzy or weak when standing from sitting or lying	☐	☐	☐
21. Falling	☐	☐	☐
22. Finding it difficult to stay awake during activities such as working, driving or eating	☐	☐	☐
23. Difficulty getting to sleep at night or staying asleep at night	☐	☐	☐
24. Intense, vivid dreams or frightening dreams	☐	☐	☐
25. Talking or moving about in your sleep as if you are 'acting out' a dream	☐	☐	☐
26. Unpleasant sensations in your legs at night or while resting, and a feeling that you need to move	☐	☐	☐
27. Swelling of your legs	☐	☐	☐
28. Excessive sweating	☐	☐	☐
29. Double vision	☐	☐	☐
30. Believing things are happening to you that other people say are not true	☐	☐	☐
TOTAL SCORE:	☐	☐	☐

FIG. 1. Nonmotor symptoms: 30-item screening questionnaire for PD.

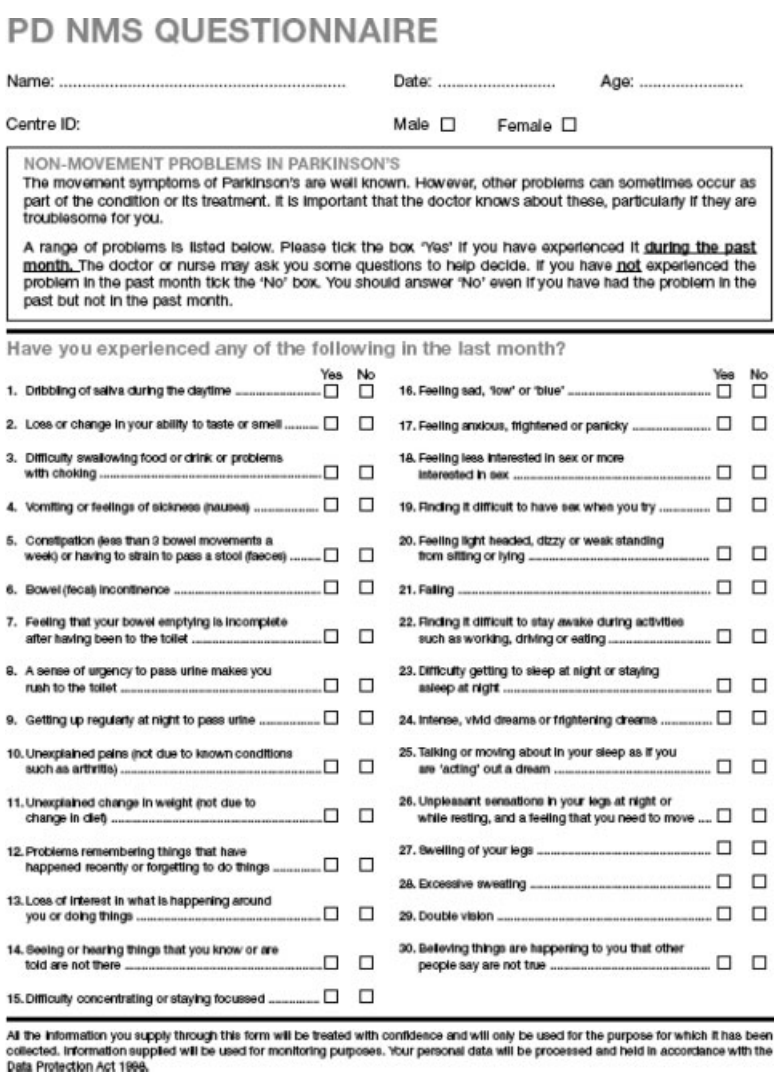
nonmotor symptoms that occur in PD. The development of such an instrument would help to improve individualized and integrated delivery of care.[15]

Although detailed quantitative assessment of NMS is critical, it is also necessary to find an economical way to screen for possible problems prior to routine clinical consultation. Such a screening exercise will serve the dual function of providing the patient with an opportunity and explicit permission to flag possible problems, and alerting the clinician that further detailed evaluation may be required. The above international group has therefore developed a 30-item screening questionnaire to be used by the patient/caregiver while waiting to be seen in the clinic. This is a screening tool and not meant for assessing severity of symptoms or effect of treatment. In this article, we report the results of the first pilot study of the feasibility, reliability, usefulness, and validation of this questionnaire based on patients and healthy subjects recruited from centers in the United Kingdom, the United States, Germany, Spain, and Italy.

PATIENTS AND METHODS

NMS Questionnaire

The NMS questionnaire (NMSQuest; Figs. 1 and 2) is a 30-item self-completed questionnaire featuring responses as "yes," "no," and "don't know" to each item. The 30 items were derived from consultations based on the experiences of the members of the PD nonmotor group as well as published literature, patient group responses, the experience of the nurse specialists, and results from the U.K. Parkinson's Disease Society survey of patients and caregivers (conducted among 1,000 members of the society) and a hospital-based survey conducted by Gulati and colleagues.[8] The steering group of the project met on three different occasions to finalize the 30 items, which were reduced from an overall question base of 50 items based on the above factors. The questions were then grouped to several relevant domains, which are shown in Table 2.



PD NMS QUESTIONNAIRE

Name: ..... Date: ..... Age: .....

Centre ID: Male ☐ Female ☐

NON-MOVEMENT PROBLEMS IN PARKINSON'S

The movement symptoms of Parkinson's are well known. However, other problems can sometimes occur as part of the condition or its treatment. It is important that the doctor knows about these, particularly if they are troublesome for you.

A range of problems is listed below. Please tick the box 'Yes' if you have experienced it during the past month. The doctor or nurse may ask you some questions to help decide. If you have not experienced the problem in the past month tick the 'No' box. You should answer 'No' even if you have had the problem in the past but not in the past month.

Have you experienced any of the following in the last month?

	Yes	No
1. Dribbling of saliva during the daytime	☐	☐
2. Loss or change in your ability to taste or smell	☐	☐
3. Difficulty swallowing food or drink or problems with choking	☐	☐
4. Vomiting or feelings of sickness (nausea)	☐	☐
5. Constipation (less than 3 bowel movements a week) or having to strain to pass a stool (faeces)	☐	☐
6. Bowel (fecal) incontinence	☐	☐
7. Feeling that your bowel emptying is incomplete after having been to the toilet	☐	☐
8. A sense of urgency to pass urine makes you rush to the toilet	☐	☐
9. Getting up regularly at night to pass urine	☐	☐
10. Unexplained pains (not due to known conditions such as arthritis)	☐	☐
11. Unexplained change in weight (not due to change in diet)	☐	☐
12. Problems remembering things that have happened recently or forgetting to do things	☐	☐
13. Loss of interest in what is happening around you or doing things	☐	☐
14. Seeing or hearing things that you know or are told are not there	☐	☐
15. Difficulty concentrating or staying focussed	☐	☐
16. Feeling sad, 'low' or 'blue'	☐	☐
17. Feeling anxious, frightened or panicky	☐	☐
18. Feeling less interested in sex or more interested in sex	☐	☐
19. Finding it difficult to have sex when you try	☐	☐
20. Feeling light headed, dizzy or weak standing from sitting or lying	☐	☐
21. Falling	☐	☐
22. Finding it difficult to stay awake during activities such as working, driving or eating	☐	☐
23. Difficulty getting to sleep at night or staying asleep at night	☐	☐
24. Intense, vivid dreams or frightening dreams	☐	☐
25. Talking or moving about in your sleep as if you are 'acting' out a dream	☐	☐
26. Unpleasant sensations in your legs at night or while resting, and a feeling that you need to move	☐	☐
27. Swelling of your legs	☐	☐
28. Excessive sweating	☐	☐
29. Double vision	☐	☐
30. Believing things are happening to you that other people say are not true	☐	☐

All the information you supply through this form will be treated with confidence and will only be used for the purpose for which it has been collected. Information supplied will be used for monitoring purposes. Your personal data will be processed and held in accordance with the Data Protection Act 1998.

FIG. 2. The revised final version of 30-item screening questionnaire for PD (NMSQuest).

Patients (with the aid of caregivers where necessary) completed the questionnaire while waiting to be seen by the nurse practitioners or physicians. Average time taken to complete the questionnaire was 5 to 7 minutes. Patients were also asked about whether they had discussed these nonmotor features with their respective physicians. A subset of patients and caregivers also completed an additional questionnaire addressing the usefulness of the NMSQuest as shown in Table 3.

TABLE 2. *Domains included in the NMSQuest*

Number	Domain	Number of items
1	Gastrointestinal tract	8
2	Urinary tract	2
3	Sexual function	2
4	Cardiovascular	2
5	Apathy/attention/memory	3
6	Hallucinations/delusions	2
7	Depression/anxiety/anhedonia	2
8	Sleep/fatigue	5
9	Pain (unrelated to other causes)	1
10	Miscellaneous (e.g., diplopia, weight loss)	3

Patients

PD patients of all ages and in all stages of the disease participated in this study. Patients were recruited from both teaching hospital and movement disorders clinics that care for the elderly. Only patients diagnosed as having PD according to the U.K. PD Brain Bank criteria were included. During consultation, routine demographic details and drug history were noted. In predominantly non–English-speaking centers (Italy, Germany), the participating neurologist explained the questions to English-speaking patients before completion of the NMSQuest. A control population was selected from friends and medical

TABLE 3. *Caregiver and patient feedback on the NMS questionnaire*

Questions	% answering yes/ appropriate	
	Patients	Caregivers
Overall opinion		
Help doctors understand treatment better?	78.5	92.3
Help doctors understand and help caregiver better?	78.5	84.6
About the questions		
Are they clearly expressed?	92.8	92.3
Relevant in day-to-day life?	100	92.3
Phrased/asked in the right manner?	92.8	100
Comfortable while answering questions?	92.8	76.9
About the length of scale		
Too long		
Appropriate	92.8	84.6
Too short		
Don't know	7.1	15.3

workers within the participating institutions. Spousal controls were avoided. There were no significant differences in age and sex between PD patients and controls.

Statistical Analysis

Anonymized data, conforming with data protection legislation in the participating countries, were transferred to the Neuroepidemiology Department at the Carlos III Institute in Madrid (under the supervision of P.M.-M.) for detailed statistical analysis. These included descriptive statistics of the sample and computation of responses, both of patients and controls. For each item, a comparison of the proportion of "yes" and "no" responses between patients and controls was carried out applying the χ^2 test.

Although not designed as a quantitative scale, a total score for the questionnaire was calculated by summing all the positive ("yes") responses for every subject included in the study. This figure represents the number of NMS declared by each patient (total P) or control subject (total C). After checking for distribution of these summary indexes, which revealed a "not normal" pattern, comparison between both groups was performed by means of the nonparametric Mann–Whitney test.

Ethical Approval

The questionnaire was devised from structured questions already in use in several centers by nurse specialists (A.F., A.B.) and the assessment presents an example of good clinical practice and as such specific approval for use of the questionnaire was not required. However, ethical approval for studies related to the nonmotor project has now been obtained.

RESULTS

Completed NMSQuest data were compared to healthy age-matched control population. Data from 123 PD patients (mean ± SD; age, 68.1 ± 10.3 years; range, 41–87; male, 59.3%; mean disease duration, 6.4 ± 4.3 years; range, 0.5–22) and 96 controls (age, 65.3 ± 10.5 years; range, 44–84; male, 48%) collected from centers in the United Kingdom, the United States, Germany, and Italy were analyzed (Table 4). Of the PD population, 84% were on levodopa preparations (12% were on monotherapy), while 61% were taking dopamine agonists (36% on monotherapy). Patients ranged from Hoehn and Yahr (HY) stages 1 to 5, with most (70.5%) being in stages 2 and 3. Twenty percent had tremor dominant PD, 29% had the akinetic-rigid form of PD, and 51% had a mixed-pattern (akinesia and tremor) PD.

NMS were significantly commoner in PD patients compared with controls (Table 5). Total NMS scores in PD patients ranged from 0 (3 patients; 2.4%) to 27 (1 patient; 0.8%), while in controls scores ranged from 0 (10 patients) to 19 (1 patient). Median total NMS score was 9 (interquartile rank, 5–13) in PD patients and 4 (interquartile rank, 2–8) in controls (Mann–Whitney test, $P < 0.0001$). On an average, most patients reported at least 10 different NMS. Three patients reported 20 NMS, while two had reports of 24 and 27. Specifically, PD patients had significantly higher scores than controls for complaints of dribbling, impaired taste/smell, impaired swallowing, constipation, urinary urgency, weight loss, forgetfulness, sadness, impaired concentration, hallucinations, anxiety, sexual dysfunction, falling, daytime sleepiness, vivid dreams, and sweating.

There was a significant association of total NMS score in PD patients with HY stage ($r_S = 0.31$; $P = 0.0006$), but not with age, sex distribution, or subtype of PD. A lower correlation was found with disease duration ($r_S = 0.22$; $P = 0.01$). Total score significantly increased with increasing severity of disease (Table 6), showing that the number of individual NMS suffered by PD patients is higher as the disease progresses. For this analysis, pa-

TABLE 4. *Demographics of patients and controls examined during the NMSQuest study*

Demographics	PD patients	Controls
Total number	123	96
% of male	59.3%	48%
Age (yr)	68.1 ± 10.3	65.3 ± 10.5
Duration of disease (yr)	6.4 ± 4.3	
Mean HY score	2.5 (1–5)	
Patients on levodopa	84% (12% monotherapy)	
Patients on dopamine agonists	61% (36% monotherapy)	

TABLE 5. *Distribution of responses between PD patients and controls in percentages*

	PD patients			Control group			χ^2 for yes–no, *P*
	Yes	No	Unknown	Yes	No	Unknown	
Dribbling	35.0	60.1	4.9	7.3	88.5	4.2	0.0000
Taste/smelling	26.00	69.1	4.9	7.3	86.5	6.2	0.0004
Swallowing	23.6	71.5	4.9	10.4	87.5	2.1	0.007
Vomiting	8.1	87.8	4.1	15.6	81.3	3.1	0.09
Constipation	46.7	48.4	4.9	26.0	69.8	4.2	0.001
Bowel incontinence	4.9	91.0	4.1	9.5	89.5	1.0	0.2
Bowel emptying incomplete	27.6	67.5	4.9	20.8	71.9	7.3	0.2
Urgency	61.0	31.0	8.0	45.8	49.0	5.2	0.01
Nocturia	66.7	24.4	8.9	60.4	38.5	1.1	0.06
Pains	27.6	62.6	9.8	30.2	58.3	11.5	0.6
Weight	22.0	70.7	7.3	6.3	86.3	7.4	0.001
Remembering	43.9	48.0	8.1	33.3	63.6	3.1	0.05
Loss of interest	29.3	64.2	6.5	12.5	82.3	5.2	0.002
Hallucinations	19.5	75.6	4.9	2.1	97.9	0	0.0000
Concentrating	37.4	51.2	11.4	18.8	76.0	5.2	0.0007
Sad, blues	44.7	52.0	3.3	26.0	69.8	7.2	0.005
Anxiety	39.9	52.0	8.1	15.6	77.1	7.3	0.0001
Sex drive	29.3	51.2	19.5	23.9	66.7	9.4	0.1
Sex difficulty	24.4	49.6	26.0	16.7	68.7	14.6	0.05
Dizzy	39.8	54.5	5.7	20.8	71.9	7.3	0.003
Falling	30.9	65.0	4.1	7.3	89.6	3.1	0.0000
Daytime sleepiness	28.4	67.5	4.1	9.4	84.4	6.2	0.0005
Insomnia	40.6	54.5	4.9	31.2	62.5	6.2	0.2
Intense vivid dreams	30.9	63.4	5.7	8.3	85.4	6.2	0.0001
Acting out during dreams	32.5	62.6	4.9	10.4	80.2	9.4	0.0002
Restless legs	37.4	55.3	7.3	28.1	69.8	2.1	0.08
Swelling	30.9	61.0	8.1	27.1	71.9	1.0	0.3
Sweating	25.2	67.5	7.3	13.5	84.4	2.1	0.02
Diplopia	21.9	73.2	4.9	4.2	94.8	1.0	0.0001
Delusions	12.3	82.8	4.9	2.1	97.9	0	0.003

tients were grouped together as mild disease (HY 1–2), moderate disease (HY 2.5–3), and severe disease (HY 4–5). No difference in total P was found between patients on treatment with levodopa or dopamine agonist.

To assess the impact and practical use of the NMSQuest, we conducted a separate survey of caregiver and patient response to various aspects of the NMSQuest via the U.K. Parkinson's Disease Society using a structured questionnaire. The responses of the patients and caregivers in relation to the scale are summarized in Table 6. Fourteen patients and 13 caregivers completed the response survey about the questionnaire. Over 75% of caregivers and patients felt that the NMSQuest helped doctors treat PD better, while over 90% reported that the items contained in the NMSQuest was appropriate and relevant to day-to-day life.

TABLE 6. *Relationship between number of NMS present (total P) and severity of disease*

PD severity	Total P*		
	Mean	SD	n
Mild	8.0	5.3	64
Moderate	10.4	5.0	40
Severe	12.7	5.7	18

Mild, HY stages 1, 1.5, and 2; moderate, HY stages 2.5 and 3; severe, HY stages 4 and 5.

*Kruskal–Wallis test, $P = 0.003$.

DISCUSSION

This is the first report of a comprehensive assessment of NMS in PD using a self-completed questionnaire in real-life patients across several countries. The key results suggest that a range of nonmotor symptoms occur across all stages of PD. These are more common as the disease advances in severity and duration. Nonmotor symptoms ranging from gastrointestinal problems to cognitive difficulties may be experienced by the same patients and this underlines the need for a comprehensive assessment tool. An independent analysis of the usefulness of the questionnaire by patients and caregivers overwhelmingly supported the need for such an instrument. Many of these symptoms are often not declared to physicians and nurses unless specifically sought.

The importance of NMS in relation to treatment and management of PD is being increasingly recog-

nized.[9–11,16,17] Several nonmotor symptoms of PD such as olfactory problems, rapid eye movement (REM) behavior disorder, constipation, and excessive daytime sleepiness have been proposed as symptoms that may predate the diagnosis of PD.[18–21] Assessment of NMS in a structured, unified, and integrated manner, therefore, may be a key issue to consider for future neuroprotection and clinical trials.

Scales available for individual assessment of NMS in PD are often disparate and focus on the individual symptom such as sleep, depression, or fatigue rather than addressing the whole picture.[21] Our data show that in clinical practice, a range of NMS may occur in the same patient and it is likely that the burden of NMS complex on health-related quality of life is considerable. Currently, there is no comprehensive screening instrument that flags, identifies, and leads the clinician to address the range of NMS-related issues in PD. We feel that the NMSQuest goes some way toward providing the clinician and nurse specialists with such a tool to screen for NMS in a simple manner.

While the NMSQuest is a screening questionnaire and cannot be directly compared to the UPDRS as the latter is a grade-rating scale, yet the closest instrument to the NMSQuest is the proposed revised version of the UPDRS, which will contain 11 nonmotor items (with 5 new items: anxious mood, sleep quality at night, ability to stay awake, urinary function, and constipation).[22] However, the amended UPDRS is unlikely to be fully comprehensive in terms of the range of NMS that occurs in PD. The UPDRS recommends tools for inclusion as an appendix item and it is hoped that the NMSQuest will become such an appendix item and be complementary to the amended UPDRS. Our study revealed that items such as diplopia, taste/smell difficulties, sadness and blues were much more common in PD than in controls, and these symptoms had not been disclosed to the physicians before the NMSQuest was administered. This is important as there is emerging evidence that many NMS such as pain, REM behavior disorder, constipation, and depression are treatable if they are identified. This issue will be partially addressed by the use of the newly described wearing-off questionnaire by Stacy and colleagues,[23] which will aim to capture some NMS in the context of motor fluctuations in treated PD. The SCOPA project addresses various domains of NMS in PD, but there are four scales for four domains and it does not provide a comprehensive assessment using a single unified and integrated assessment tool.[24]

Most items of the NMSQuest were satisfactorily answered. Items 19 and 20 of the NMSQuest inquiring about sex drive and difficulty with sex, respectively, received the maximum number of "don't know" responses and 20% to 26% of the samples did not complete these questions. The reason for this is complex and may be because the questionnaire addressed an older population and many are widowed and not sexually active. Furthermore, some may have felt uncomfortable answering these questions. In terms of acceptability of the questionnaire, the parameters were good and included a low ceiling (0.8%) and floor (2.4%) effect, closeness of mean to median (9.5 vs. 9), and an almost complete range of scores (0–27).

To avoid bias in patient selection for our study, we adopted a real-life patient recruitment policy, with the questionnaire being administered in different settings ranging from teaching hospital tertiary regional clinics to district general hospitals and movement disorders clinics run by experts in the care of the elderly. However, in non–English-speaking centers, a standardized translated questionnaire was not used and we acknowledge that this remains a limitation of this study, as explanation of questions to patients in foreign language is likely to introduce bias by reducing standardization..

The patient sample included HY stages ranging from 1 to 5 and disease duration extending from 0.5 to 22 years. As anticipated, NMS scores correlated significantly with HY stage, with more NMS being declared as the condition advanced. A weaker but significant correlation was also observed with disease duration, but the study highlighted the fact that some NMS occur in early PD (stages 1–2), contrary to commonly held perceptions.

In this study, we did not address identification of NMS in the *on* and *off* state, although most patients were studied in the *on* state while attending clinics. There are logistic difficulties of assessing NMS in the *off* state as the study by Stacy and colleagues[23] reports that symptoms such as tiredness, slowness of thinking, cloudy/dull mind were identified during wearing-off, which could make completion of NMSQuest difficult. However, future studies using NMSQuest to identify NMS in individual patients in both the *on* and the *off* state are planned.

The NMSQuest was devised as a screening tool for physicians and nurses. The NMSQuest was not developed for measuring severity of symptoms or detect changes following treatment. As such, this is an evaluation and not a discriminant tool. Even so, our study shows that most items on the NMSQuest were significantly more common in PD than in controls. Seven items did not show significant difference in "yes" answers from controls. A revised form of the NMSQuest (containing 24 items) improved the discriminant power of the questionnaire. However, as the excluded items are still relevant to PD, we opted to include them in the final version of the questionnaire (Fig. 2). Indeed, many of our patients required targeted treatment directed toward NMS such as pain after this was flagged up in the NMSQuest, although pain was one of the nondis-

criminant item when compare to controls. Furthermore, it is not surprising that items such as pain, memory problems, and sexual difficulty were not significantly different between PD patients and controls given the age groups studied. Analysis of data suggested that the "don't know" option was a confounder and led to poor correlation with total P in some items such as sexual difficulties. As a result, we are recommending use of the NMSQuest in a revised version, which contains only the "yes" and "no" options (Fig. 2).

In conclusion, therefore, in this multicenter international study, we have shown that the NMSQuest provides a comprehensive symptom assessment strategy of NMS in PD. The present study has shown that: (1) NMS in PD are common, significant, and frequent across all disease stages; (2) NMS of PD correlates with the disease progression and duration and more NMS are seen in advanced disease; (3) on average, most patients with PD have at least 10 different NMS; (4) most of these have never been previously disclosed to healthcare professionals; (5) over 75% of patients and 80% of caregivers felt that the NMSQuest will improve the doctor's ability to treat PD better and over 90% of patients and caregivers felt that issues raised in the NMSQuest were relevant to day-to-day life; and (6) NMS are significantly more common in PD than in controls, and the range of symptoms can vary from the more commonly recognized problems such as constipation, sleep difficulties, and depression to the less-recognized problems such as diplopia, weight loss, sadness, and blues.

We would recommend routine use of the NMSQuest in clinics while the patient is waiting to be seen as a screening tool. Items flagged then can be addressed and treated as necessary, and more specific tools can be applied.[21] Based on the encouraging results of the NMSQuest study, it is envisaged that the NMSQuest would be complementary to the revised UPDRS.

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