

# Virtual research visits and direct-to-consumer genetic testing in Parkinson's disease

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## Abstract

**Objective:** The purpose of this study was to conduct a proof-of-concept study to evaluate remote recruitment and assessment of individuals (“virtual research visits”) with Parkinson's disease who have pursued direct-to-consumer genetic testing.

**Methods:** Participants in 23andMe's “Parkinson's Research Community” were contacted by 23andMe. Fifty willing participants living in 23 states underwent a remote, standardized assessment including cognitive and motor tests by a neurologist via video conferencing and then completed a survey. Primary outcomes assessed were (a) proportion of participants who completed the remote assessments; (b) level of agreement (using Cohen's kappa coefficient) of patient-reported data with that of a neurologist; and (c) interest in future virtual research visits.

**Results:** The self-reported diagnosis of Parkinson's disease was confirmed in all cases ( $k = 1.00$ ). The level of agreement for age of symptom onset ( $k = 0.97$ ) and family history ( $k = 0.85$ ) was very good but worse for falling ( $k = 0.59$ ), tremor ( $k = 0.56$ ), light-headedness ( $k = 0.31$ ), and urine control ( $k = 0.15$ ). Thirty-eight (76%) of the 50 participants completed a post-assessment survey, and 87% of respondents said they would be more or much more willing to participate in future clinical trials if they could do research visits remotely.

**Conclusion:** Remote clinical assessments of individuals with known genotypes were conducted nationally and rapidly from a single site, confirmed self-reported diagnosis, and were received favorably. Direct-to-consumer genetic testing and virtual research visits together may enable characterization of genotype and phenotype for geographically diverse populations.

## Keywords

Direct-to-consumer genetic testing, telemedicine, Parkinson's disease, genetics, technology

## Introduction

Technology is rapidly reshaping genetics and research studies, as new techniques identify the genetic underpinnings of many diseases.<sup>1</sup> Aided by the falling cost of DNA sequencing,<sup>2</sup> consumers can now assess their relative genetic risk for many disorders through direct-to-consumer genetic testing.<sup>3</sup> For example, in Parkinson's disease 16 genetic risk loci have been identified over the past 15 years.<sup>4,5</sup> Technology and rising drug development costs<sup>6</sup> are fueling novel approaches to conducting clinical research and clinical trials,<sup>7</sup> including enrichment for targeted genotypes, the use of social networks to conduct observational drug studies<sup>8</sup> and virtual clinical trials.<sup>9</sup>

New collaborations continue to arise from these trends in genetics and clinical research. For example, the partnership between the direct-to-consumer (DTC) genetics company 23andMe and the Michael J. Fox Foundation for Parkinson's disease research<sup>10,11</sup> has

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led to genotyping and collection of self-reported outcomes of over 10,000 individuals and currently represents the largest cohort of genotyped individuals with Parkinson's disease.<sup>12</sup> Preliminary analyses of this data have identified new phenotype-genotype associations, risk factors, and differences in disease progression and symptoms associated with factors such as gender and body mass index.<sup>13</sup> This research model has enabled broad and rapid research participation by individuals in 49 states and over 30 countries and allowed for the discovery of new genetic loci associated with Parkinson's disease and replicated previously known associations.<sup>14</sup> The ability to conduct more in-depth assessments and confirm self-reported data in this population could allow larger-scale participation in clinical trials and observational studies which could capture clinician-assessed phenotypic data at a single time point or longitudinally. Therapeutic trials targeted at specific genetic subpopulations could also use remote assessments to facilitate participation among geographically diverse cohorts of genotypically similar individuals. These genetic subpopulations may have different phenotypes,<sup>15</sup> responses to current treatments,<sup>16</sup> and almost certainly will be the preferred study population for future gene-targeted therapies, as has been the case for cancer,<sup>17</sup> and is increasingly the case for other central nervous system disorders.<sup>18</sup>

One means of connecting to remote populations is virtual visits. These video visits, conducted via secure video conferencing, are increasingly used for clinical care,<sup>19–22</sup> including for Parkinson's disease,<sup>23,24</sup> but their application to research has been limited to date.

We conducted a proof of concept study aimed at (a) evaluating remote recruitment and assessment of individuals who have undergone DTC genetic testing, (b) assessing the level of agreement of self-reported phenotypic data with that of a specialist, and (c) soliciting feedback on virtual research visits.

## Methods

### Study design and participants

Members of 23andMe's "Parkinson's Research Community"<sup>25</sup> were invited to participate. Eligible members had contributed a DNA sample to 23andMe, reported a diagnosis of Parkinson's disease, completed 23andMe's Parkinson's disease symptom survey developed in collaboration with expert Parkinson's disease clinicians (Appendix 1), and had been active in the 23andMe community in the previous three months. To obtain a convenience sample of 50 participants, a random sample of 166 of these individuals received an email from 23andMe inviting them to participate, and to review and electronically sign

the consent document and a data release authorization form. Participants had to have access to a non-public internet-enabled device. Researchers at Johns Hopkins (KCD, ERD) received contact information for interested participants and reviewed consent over the phone. Consenting participants received a web camera (Logitech C110 or C210 model) if needed, and an email link to download secure, Health Insurance Portability and Accountability Act-compliant videoconferencing software from Vidyo (Hackensack, New Jersey, USA), hosted by ID Solutions (Indianapolis, Indiana, USA). The study team (KCD, SD) also provided technical assistance by phone if necessary. Researchers performed a test connection between the remote research site and the participant's home prior to the one-time assessment. The Institutional Review Board at Johns Hopkins Medicine approved the research protocol and consent form.

### Assessments

A neurologist (ERD) conducted the 30–60 min remote assessment, which was structured to elicit information confirming the participants' responses to the survey participants had completed upon enrollment in the 23andMe project (Appendix 1). Visits, which were modeled similar to a remote clinic visit,<sup>24</sup> included a review of participants' histories, including symptoms of atypical parkinsonian disorders, onset of specific symptoms (age-at-onset of parkinsonian symptoms, falling, urine control problems, light-headedness, and tremor), and family history (first or second degree relative with Parkinson's disease). The specialist completed part IA, non-motor aspects of experiences of daily living, part III, motor examination (excluding rigidity and postural stability tests which require in-person assessment), and part IV, motor complications, of the Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS).<sup>26</sup> For the motor portion of the examination, individuals were asked to perform the tasks (e.g. tapping thumb and index finger, walking) in front of the camera, in line with a previous remote study.<sup>23</sup> Visits also included the Montreal Cognitive Assessment, a cognitive assessment tool commonly used in Parkinson's disease.<sup>27,28</sup> Participants were emailed a copy of the visuospatial/executive and naming portions, and completed and demonstrated these tasks in the video call before the examiner completed the remainder of the test. The neurologist determined the most likely diagnosis based on the history and examination focused on the cardinal features of parkinsonism that can be assessed remotely (e.g. rest tremor, bradykinesia, and gait difficulties). Parkinson's disease was identified as the diagnosis if it was the most likely explanation for the

individual's condition as opposed to other causes of parkinsonism (e.g. multiple system atrophy).

Following completion of the clinical assessments, participants were emailed a survey developed for this study asking about their satisfaction with the virtual research visit, comfort in discussing their condition with the specialist, and willingness to participate in future trials remotely (Appendix 2). Completed surveys were returned via US mail, email, or fax and labeled with participant names. Responses were entered manually into an Excel database.

### Analysis

Most of the analyses performed were descriptive. Cohen's kappa coefficient<sup>29</sup> was calculated to determine the level of agreement between the participants' self-reported outcomes on the survey that they initially completed as part of the 23andMe project (Appendix 1) and those assessed by the specialists. The analyses were conducted by NE using Excel.

## Results

### Study participants and feasibility

A total of 166 individuals were invited to participate, and 103 opened the email invitation. Fifty-four (32%) agreed to participate and 50 (30%) completed the one-time assessment as scheduled between 25 March 2013–5 June 2013. The reasons for not completing the assessment were: unreachable by phone ( $n=2$ ); withdrawal of consent ( $n=1$ ); and a scheduling conflict ( $n=1$ ). The baseline characteristics of those invited to participate and those that did were generally similar (Table 1). The severity of Parkinson's disease among participants varied widely, including duration (mean 9.2 years, range from 2–28 years), motor signs (mean motor score 31, range from 18–52; higher scores indicate greater impairment), and cognitive impairment (mean score on the Montreal Cognitive Assessment was 27, range from 18–30; higher scores indicate less impairment). Overall, the characteristics of the participants in this study were similar to those in clinical trials aimed at individuals with moderate Parkinson's disease.<sup>30</sup> Six (12%) participants had genotypes associated with at least 50% increased relative risk of developing Parkinson's disease (Table 1). The participants came from 23 states and the District of Columbia (Figure 1).

### Level of agreement

Based on the history and examination, all individuals with self-reported Parkinson's disease were judged by the clinician to have Parkinson's disease ( $k=1.00$ ). The

level of agreement between the self-reported data and that assessed by the remote clinician was also very high for age of onset ( $k=0.97$ ) and presence of family history ( $k=0.85$ ) but much lower for the presence of falling ( $k=0.59$ ), tremor ( $k=0.56$ ), and non-motor symptoms of light-headedness ( $k=0.31$ ), and problems with urine control ( $k=0.15$ ).

### Post-assessment survey

Thirty-eight of the 50 participants (76% response rate) completed the post-assessment survey. Respondents were satisfied or highly satisfied with the virtual research visit and with the specialist's ability to assess their symptoms (95%), and comfortable or very comfortable discussing their condition with the specialist (100%). Nearly all respondents were comfortable or very comfortable (97%) with the software. Satisfaction with connection quality was lower (84% satisfied or very satisfied). Nearly all (95%) reported interest in future virtual research visits, and 87% reported that they would be willing or much more willing to participate in clinical trials if they could do visits remotely from their home.

## Discussion

Remote recruitment and conduct of research visits in individuals who have undergone DTC genetic testing is feasible, shows relatively good agreement with self-reported data, and is well received by participants. While the benefits of DTC genetic testing continue to be debated,<sup>1,2,11,31–39</sup> this proof of concept study demonstrates its potential to identify, follow, and engage geographically dispersed populations with a given disorder and an underlying genotype in research.<sup>40</sup> Our 32% response rate to a single recruitment email suggests that targeted electronic recruitment in populations unrestricted by geography may improve participation in research studies. Traditional approaches requiring genetic testing of large populations at multiple medical centers require substantial investment in time and resources to satisfy regulatory needs, execute contracts, and conduct in-person assessments at each institution. By contrast, this study took less than three months and utilized a single investigator to assess individuals throughout the country. This approach lays the foundation for larger scale, broader scope studies that can target genetic sub-populations of different disorders and foster partnerships between consumer genetics companies, pharmaceutical firms, academic institutions, and patient communities. We envision the possibility of conducting remote phenotypic assessments in very large cohorts, marrying data from clinical rating scales such as the MDS-UPDRS with genetic

**Table 1.** Baseline characteristics of study participants.

	Invited to participate ( <i>n</i> = 166)	Completed remote assessment ( <i>n</i> = 50)	Completed survey ( <i>n</i> = 38)
Demographics			
Age in years (SE)	63.6 (0.8)	62.4 (1.5)	63.3 (1.8)
Number (%) women	64 (38.6)	16 (32.0)	13 (34.2)
Number (%) Caucasian	153 (92.2)	48 (95.7)	34 (89.5)
Education (number (%) completing college)	101 (60.9) <sup>a</sup>	37 (73.5)	28 (73.7)
Parkinson's disease characteristics			
Number (%) with Parkinson's disease	166 (100.0)	50 (100.0)	38 (100.0)
Disease duration in years (SE)	9.6 (0.5)	9.2 (0.9)	9.2 (0.8)
Movement Disorder Society-Unified Parkinson's Disease Rating Scale, part Ia: Non-Motor Aspects of Experiences of Daily Living score (SE) <sup>b</sup>	NA	3.0 (0.4)	3.4 (0.6)
Movement Disorder Society - Unified Parkinson's Disease Rating Scale, Part III: Modified Motor Score (SE) <sup>c</sup>	NA	31.3 (1.1)	30.6 (1.5)
Movement Disorder Society - Unified Parkinson's Disease Rating Scale, Part IV: Motor Complications Score (SE) <sup>b</sup>	NA	3.5 (0.5)	3.8 (0.7)
Montreal Cognitive Assessment <sup>d</sup> (SE)	NA	26.9 (0.4)	26.5 (0.5)
Number (%) with a family history of Parkinson's disease	56 (33.7)	19 (38.0)	14 (36.8)
Number (%) with <i>GBA</i> or <i>LRRK2</i> mutations	6 (3.6)	3 (6.0)	1 (2.6)
Number (%) with substantially increased risk due to other common genetic variants <sup>e</sup>	12 (7.2)	3 (6.0)	3 (7.9)

*GBA*: glucocerebrosidase gene; *LRRK2*: leucine-rich repeat kinase 2; SE: standard error.

<sup>a</sup>Responses on education are only available for the individuals who were invited to participate.

<sup>b</sup>Scale ranges from 0–24 with higher scores indicating greater impairment.

<sup>c</sup>Excludes assessments of rigidity and balance. Scale ranges from 0–116 with higher scores indicating greater impairment.

<sup>d</sup>Scale ranges from 0–30 with lower scores indicating greater cognitive impairment.

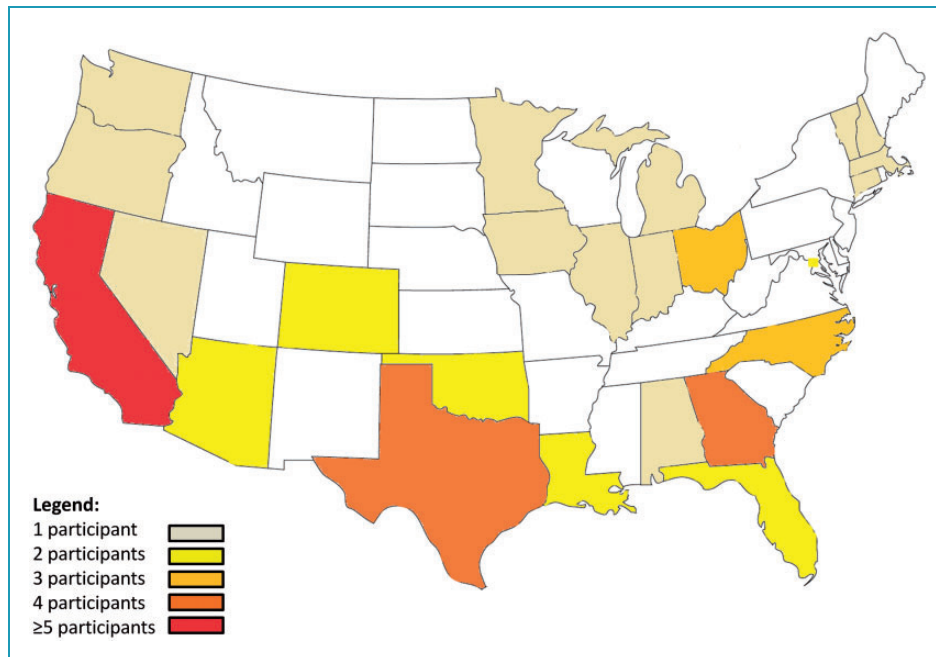
<sup>e</sup>Over 1.5 times average risk due to common genetic variants associated with Parkinson's disease in populations of European descent (single nucleotide polymorphisms near *SNCA*, *MAPT*, *PARK16*, *BST1*, *DGKQ*, and *STK39*).

information to better characterize and elucidate variability in Parkinson's disease symptoms in relation to genetic markers.

The Institute of Medicine has recently called for such collaborations. In its 2012 workshop on genome-based therapies, the Institute highlighted the need to mobilize patient communities to spur research.<sup>41</sup> In its *Rare diseases and orphan products* report, one of the key elements of its national strategy to promote rare diseases research and development is “[timely] application of advances in science and technology that can make rare diseases research and product development faster, easier, and less expensive.[3]”<sup>42</sup>

Remote assessments are likely to play an increasingly large role in clinical studies of Parkinson's disease<sup>43</sup> and other chronic conditions.<sup>44</sup> Several clinical trials have been conducted over the internet<sup>45–49</sup> with many forgoing in-person visits altogether.<sup>45,47–49</sup> Previous clinical studies have found self-reported data to be valid,<sup>50</sup> including for self-reported diagnosis.<sup>51</sup> This study extends these disruptive models for clinical research by laying the foundation for the inclusion of increasingly available genotypic data into remotely conducted studies.

This study has three key limitations. First, the study population was highly selected — only the most recent and active participants in the 10,000-member



**Figure 1.** Map of locations of research participants by state.

“Parkinson’s Community” were asked to participate. These individuals who are highly educated are also more likely to have the internet and technology savvy required to be able to install and operate videoconferencing software, as well as access to high-speed broadband connections, without which remote assessment would be much more difficult. However, many individuals show interest in Parkinson’s disease clinical trial participation, including more than 30,000 individuals registered (all remotely) in the Michael J. Fox Foundation’s “Fox Trial Finder” as of September 2014.<sup>52</sup> Because less than a third ( $n=50$ ) of the invited population ( $n=166$ ) participated in the study, the results should be interpreted with caution as the low response rate may have resulted in selection bias. Similarly, while the survey response was good (76%), the respondents may have been more satisfied than non-respondents.

Second, some questions used in the background survey on falls, tremor, lightheadedness, and urine control were subjective and non-specific and may have contributed to the low level of agreement with the remote assessment. In addition, while a previous study demonstrated good agreement between remote and in-person assessments of the original UPDRS,<sup>53</sup> remote administrations of the newer MDS-UPDRS and the Montreal Cognitive Assessment scales remain to be validated.

Third, this study only included a one-time assessment. Future studies could be used to evaluate remote research visits in assessing the natural history of different genetic subpopulations, or as a screening or interim assessment in interventional studies.

Notwithstanding these limitations, this study demonstrates the feasibility and potential value of combining phenotypic and genotypic data for research participants across half the country using remote videoconferencing assessments. These novel technology applications and partnerships can accelerate research at low cost and enhance our understanding of the natural history of genetically linked disorders.

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**Conflict of interest:** ERD is an advisor to, and has stock options in, Grand Rounds; is a compensated consultant to Clintrex, mc10, Shire, and National Institute of Neurological Disorders and Stroke; is an unpaid advisor to SBR Health and Vidyo; receives grant support from Auspex Pharmaceuticals, Prana Biotechnology, the Patient-Centered Outcomes Research Institute, Davis Phinney Foundation, Michael J. Fox Foundation, Huntington Study Group, and Great Lakes Neurotechnologies; and has filed a patent application related to neurology and telemedicine. KD, SD, AT and MA have no conflicting interests. EC is an employee of Biogen Idec. SM and EC are employees of 23andMe. NE was an employee of 23andMe. BR and SW were previously employees of Biogen Idec.

**Ethical approval:** The Institutional Review Board at Johns Hopkins Medicine approved the research protocol and consent form (IRB Application Number NA\_00081180).

**Guarantor:** ERD

**Contributorship:** Contributors to the study were as follows: ERD contributed to the design, organization, and execution of



the research, participated in designing and reviewing the statistical analysis, and wrote the first draft of the manuscript with KCD. KCD, SM, SD, AT contributed to the execution of the research. EDC contributed to the design, organization, and execution of the research. NE led the design and execution of the statistical analysis. BR contributed to the design of the research and participated in designing and reviewing the statistical analysis. All authors contributed to the analysis and interpretation of the data and review and edited the manuscript and approved the final version of the manuscript.

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## Appendix 1. 23andMe Parkinson's disease baseline survey

Has a doctor ever diagnosed you with Parkinson's disease?

- Yes
- No
- I'm not sure/I don't remember

[if yes, diagnosed with Parkinson's disease]

Which of the following best describes who diagnosed you with Parkinson's disease? Please check all that apply.

- Family physician
- Internist
- Neurologist
- Parkinson's specialist
- Another physician
- Someone other than a physician
- None of the above

[if another physician or someone other than a physician]

Please describe who diagnosed you with Parkinson's disease.

[free text]

[if no or not sure]

Has a doctor ever diagnosed you with any of the following? Please check all that apply.

- Another form of parkinsonism (other than Parkinson's disease)
- Dementia, cognitive impairment, or senility
- A tremor disorder
- None of the above

[if another form of parkinsonism]

Which of the following have you been diagnosed with? Please check all that apply.

- Progressive supranuclear palsy (PSP)
- Multiple system atrophy (MSA), Shy-Drager syndrome, or striatonigral degeneration
- Spinal cerebellar ataxia (SCA), cerebellar degeneration, olivopontocerebellar atrophy (OPCA)
- Cortical basal ganglionic degeneration
- Atypical parkinsonism or Parkinson's plus
- Genetic or familial parkinsonism
- Parkinsonism due to medications, drug-induced parkinsonism
- Alzheimer's disease with parkinsonism
- Frontotemporal dementia with parkinsonism
- Parkinson's disease dementia (PDD)
- Dementia with Lewy bodies (DLB), Lewy body dementia or cortical Lewy body disease
- Another form of dementia
- Vascular parkinsonism
- None of the above

[if dementia, cognitive impairment, senility]

Which of the following have you been diagnosed with? Please check all that apply.

- Alzheimer's disease
- Dementia with Lewy bodies (DLB), Lewy body dementia or cortical Lewy body disease
- Frontotemporal dementia (FTD)
- Parkinson's disease dementia (PDD)
- Vascular dementia
- Picks disease
- Mild cognitive impairment (MCI)
- Another form of dementia
- None of the above

[if a tremor disorder]

Which of the following have you been diagnosed with? Please check all that apply.

- Essential tremor (ET), benign tremor, or senile tremor
- Dystonic tremor

- Rubral tremor
- Primary writing tremor
- Tremor due to a stroke
- Cerebellar tremor
- Multiple sclerosis (MS)
- Another tremor disorder
- None of the above

How old were you when you were first diagnosed with Parkinson's disease?

- [free text]

How old were you when you first experienced symptoms of Parkinson's disease?

- [free text]

What were the first symptoms of Parkinson's disease you experienced? Please check all that apply.

- Tremor or shaking
- Changes in handwriting
- Soft voice or speech
- Changes in walking
- Slowness of movement
- Balance problems or falling
- Other symptoms

How did your symptoms start?

- Gradually
- Suddenly
- I'm not sure/I don't remember

When they first started, were your symptoms more noticeable on one side of your body than the other?

- Yes
- No
- I'm not sure/I don't remember

Are your symptoms currently more noticeable on one side of your body than the other?

- Yes
- No
- I'm not sure/I don't remember

Overall, how do your symptoms compare to when they first began?

- They are worse
- They are about the same
- They have improved



- I'm not sure/I don't remember

Did your symptoms improve because of medications you are taking?

- Yes
- No
- I'm not sure/I don't remember

Is your diagnosis still Parkinson's disease or has your diagnosis changed?

- My diagnosis is still Parkinson's disease
- My diagnosis changed
- I'm not sure/I don't remember

*[if diagnosis changed]*

Which of the following best describes how your diagnosis change?

- I no longer have the symptoms that led to the Parkinson's disease diagnosis
- I still have the symptoms, but the cause is unknown
- I was diagnosed with a different disease

*[if diagnosed with different disease]*

Did your diagnosis change to any of the following?

- Another form of parkinsonism
- Dementia, cognitive impairment, or senility
- A tremor disorder
- Something else

*[if another form of parkinsonism]*

Did your diagnosis change to any of the following? Please check all that apply.

- Progressive supranuclear palsy (PSP)
- Multiple system atrophy (MSA), Shy-Drager syndrome, or striatonigral degeneration
- Spinal cerebellar ataxia (SCA), cerebellar degeneration, olivopontocerebellar atrophy (OPCA)
- Cortical basal ganglionic degeneration
- Atypical parkinsonism or Parkinson's plus
- Genetic or familial parkinsonism
- Parkinsonism due to medications, drug-induced parkinsonism
- Alzheimer's disease with parkinsonism
- Frontotemporal dementia with parkinsonism
- Parkinson's disease dementia (PDD)
- Dementia with Lewy bodies (DLB), Lewy body dementia or cortical Lewy body disease
- Another form of dementia
- Vascular parkinsonism
- None of the above

*[if dementia]*

Did your diagnosis change to any of the following? Please check all that apply.

- Alzheimer's disease
- Dementia with Lewy bodies (DLB), Lewy body dementia or cortical Lewy body disease
- Frontotemporal dementia (FTD)
- Parkinson's disease dementia (PDD)
- Vascular dementia
- Picks disease
- Mild cognitive impairment (MCI)
- Another form of dementia
- None of the above

*[if a tremor disorder]*

Did your diagnosis change to any of the following? Please check all that apply.

- Essential tremor (ET), benign tremor, or senile tremor
- Dystonic tremor
- Rubral tremor
- Primary writing tremor
- Tremor due to a stroke
- Cerebellar tremor
- Multiple sclerosis (MS)
- Another tremor disorder
- None of the above

*[if something else]*

Did your diagnosis change to any of the following? Please check all that apply.

- Motor neuron disease (MND), amyotrophic lateral sclerosis (ALS), Lou Gehrig's disease
- Spinal muscular atrophy (SMA), Progressive muscular atrophy (PMA), primary lateral sclerosis (PLS)
- Spinal cerebellar ataxia (SCA), cerebellar degeneration, olivopontocerebellar atrophy (OPCA)
- Multiple sclerosis (MS)
- Stroke or cerebrovascular accident (CVA)
- Epilepsy, seizure disorder
- Myoclonus
- Dystonia
- Tourette syndrome, tic disorder
- Another brain or neurological disorder
- Parkinsonism due to medications, drug-induced parkinsonism
- Depression
- Thyroid disease
- Arthritis
- Benign positional vertigo, vertigo, balance problems due to the inner ear, or vestibular disease
- Another medical problem

- None of the above

**We are now going to ask you a few questions about the characteristics of your movement.**

Do you have trembling or shaking of any part of your body?

- Yes
- No
- I'm not sure/I don't remember

*[if yes]*

What parts of your body tremble or shake?

- Head
- Jaw or chin
- Tongue
- Voice
- Hands or arms
- Feet or legs
- Entire body
- None of the above

Is the trembling or shaking more noticeable on one side of your body than the other?

- Yes
- No
- I'm not sure/I don't remember

Does this problem occur every day?

- Yes
- No
- I'm not sure/I don't remember

About how old were you when you first noticed the trembling or shaking?

- *[free text]*

How did the trembling or shaking begin?

- Gradually
- Suddenly
- I'm not sure/I don't remember

Since you first noticed it, has the trembling or shaking...

- Become worse
- Stayed about the same
- Improved
- I'm not sure/I don't remember

Have you noticed any of the following changes in your handwriting? Please check all that apply.

- Handwriting became slower
- Handwriting became smaller
- Handwriting became shakier
- None of the above

*[if changes in handwriting]*

Does this problem occur every time you write?

- Yes
- No
- I'm not sure/I don't remember

About how old were you when you first noticed the changes in your handwriting?

- *[free text]*

How did the changes in your handwriting begin?

- Gradually
- Suddenly
- I'm not sure/I don't remember

Since you first noticed a change, has your handwriting...

- Become worse
- Stayed about the same
- Improved
- I'm not sure/I don't remember

Have you noticed or have people told you that your speech or voice has become softer than before?

- Yes
- No
- I'm not sure/I don't remember

*[if speech is softer]*

Does this problem occur every day?

- Yes
- No
- I'm not sure/I don't remember

About how old were you when you first noticed changes in your speech or voice?

- *[free text]*

How did the changes in your speech or voice begin?

- Gradually
- Suddenly
- I'm not sure/I don't remember

Since you first noticed a change, has the problem with your speech/voice...

- Become worse
- Stayed about the same
- Improved
- I'm not sure/I don't remember

Have you noticed any of the following changes in the way you walk? Please check all that apply.

- Dragging one or both feet
- Feet shuffling
- Walking more slowly
- Taking smaller steps than before
- Steps becoming faster and faster
- Feet getting stuck as if glued to the floor
- None of the above

*[if changes in walk]*

Does this problem occur every day?

- Yes
- No
- I'm not sure/I don't remember

About how old were you when you first noticed changes in the way you walk?

- *[free text]*

How did the changes in the way you walk begin?

- Gradually
- Suddenly
- I'm not sure/I don't remember

Since you first noticed a change, has the way you walk...

- Become worse
- Stayed about the same
- Improved
- I'm not sure/I don't remember

When walking, do you swing your arms less than you used to?

- Yes
- No
- I'm not sure

*[if yes]*

Which arm do you swing less?

- Left
- Right
- Both
- I'm not sure/I don't remember

Does this problem occur every day?

- Yes
- No
- I'm not sure

About how old were you when you noticed that you swing your arms less?

- *[free text]*

How did the changes in the way you swing your arms begin?

- Gradually
- Suddenly
- I'm not sure/I don't remember

Since you first noticed that you swing your arms less, has this problem...

- Become worse
- Stayed about the same
- Improved
- I'm not sure/I don't remember

When standing or walking, do you stoop or bend forward more than you used to?

- Yes
- No
- I'm not sure/I don't remember

Does this problem occur every day?

- Yes
- No
- I'm not sure/I don't remember

About how old were you when you noticed changes in your posture?

- *[free text]*

How did the changes in your posture begin?

- Gradually

- Suddenly
- I'm not sure/I don't remember

Since you first noticed a change, has your posture...

- Become worse
- Stayed about the same
- Improved
- I'm not sure/I don't remember

Do you have trouble with your balance or fall sometimes?

- Yes
- No
- I'm not sure/I don't remember

Does this problem occur every day?

- Yes
- No
- I'm not sure/I don't remember

About how old were you when you noticed <symptom>?

- [free text]

How did the changes in your <symptom> begin?

- Gradually
- Suddenly
- I'm not sure/I don't remember

Since you first noticed a change, has your <symptom>...

- Become worse
- Stayed about the same
- Improved
- I'm not sure/I don't remember

[if diagnosis is not Parkinson's disease]

Are you currently taking any prescription medication for the following reasons? Please check all that apply.

- Shaking, tremor, balance problems, or problems walking
- Indigestion
- Depression, nervous breakdown, hallucinations, psychosis, or another psychiatric problem
- None of the above

[if shaking, tremor, balance problems or problems walking]

Are you currently taking any of the following medications? Please check all that apply.

- Azilect (rasagiline)
- Eldepryl, Carbex, Atapryl, or Emsam patch (selegiline or deprenyl)
- Mirapex (pramipexole)
- Parcopa (carbidopa/levodopa orally disintegrating tablet)
- Parlodel (bromocriptine)
- Permax (pergolide)
- Requip (ropinerole)
- Sinemet or Atamet (carbidopa/levodopa)
- Stalevo (carbidopa, levodopa and entacapone)
- Symmetrel (amantadine)
- None of the above

[if indigestion or depression]

Are you taking any of the following medications? Please check all that apply.

- Abilify (aripiprazole)
- Eldepryl, Carbex, Atapryl, or Emsam patch (selegiline or deprenyl)
- Eskalith, Lithobid (lithium)
- Haldol (haloperidol)
- Prolixin (flupenthixal)
- Reglan (metoclopramide)
- Risperdal (risperidone)
- Seroquel (quetiapine)
- Zyprexa (olanzapine)
- None of the above

Have you experienced any of the following symptoms at any time since you developed Parkinson's disease? Please check all that apply.

- Falling
- Trouble with urine control
- Frequently feeling light-headed on standing
- Shaking or tremor
- None of the above

[if yes to any of above symptoms]

How old were you when you first experienced [symptom]?

- [free text]

**Now we would like to find out more about your average or usual function over the past week, including today. Some patients can do things better at one time of the day than at others. However, only one answer is allowed for each question, so please mark the answer that best describes what you can do most of the time.**



Over the past week, have you had trouble going to sleep at night or staying asleep through the night? Consider how rested you felt after waking up in the morning.

- Normal (No problems.)
- Slight (Sleep problems are present but usually do not cause trouble getting a full night of sleep.)
- Mild (Sleep problems usually cause some difficulties getting a full night of sleep.)
- Moderate (Sleep problems cause a lot of difficulties getting a full night of sleep, but I still usually sleep for more than half the night.)
- Severe (I usually do not sleep for most of the night.)

Over the past week, have you had trouble staying awake during the daytime?

- Normal (No daytime sleepiness.)
- Slight (Daytime sleepiness occurs but I can resist and I stay awake.)
- Mild (Sometimes I fall asleep when alone and relaxing. For example, while reading or watching TV.)
- Moderate (I sometimes fall asleep when I should not. For example, while eating or talking with other people.)
- Severe (I often fall asleep when I should not. For example, while eating or talking with other people.)

Over the past week, have you had uncomfortable feelings in your body like pain, aches tingling or cramps?

- Normal (No uncomfortable feelings.)
- Slight (I have these feelings. However, I can do things and be with other people without difficulty.)
- Mild (These feelings cause some problems when I do things or am with other people.)
- Moderate (These feelings cause a lot of problems, but they do not stop me from doing things or being with other people.)
- Severe (These feelings stop me from doing things or being with other people.)

Over the past week, have you had trouble with urine control? For example, an urgent need to urinate, a need to urinate too often, or urine accidents?

- Normal (No urine control problems.)
- Slight (I need to urinate often or urgently. However, these problems do not cause difficulties with my daily activities.)
- Mild (Urine problems cause some difficulties with my daily activities. However, I do not have urine accidents.)

- Moderate (Urine problems cause a lot of difficulties with my daily activities, including urine accidents.)
- Severe (I cannot control my urine and use a protective garment or have a bladder tube.)

Over the past week have you had constipation troubles that cause you difficulty moving your bowels?

- Normal (No constipation.)
- Slight (I have been constipated. I use extra effort to move my bowels. However, this problem does not disturb my activities or my being comfortable.)
- Mild (Constipation causes me to have some troubles doing things or being comfortable.)
- Moderate (Constipation causes me to have a lot of trouble doing things or being comfortable. However, it does not stop me from doing anything.)
- Severe (I usually need physical help from someone else to empty my bowels.)

Over the past week, have you felt faint, dizzy or foggy when you stand up after sitting or lying down?

- Normal (No dizzy or foggy feelings.)
- Slight (Dizzy or foggy feelings occur. However, they do not cause me troubles doing things.)
- Mild (Dizzy or foggy feelings cause me to hold on to something, but I do not need to sit or lie back down.)
- Moderate (Dizzy or foggy feelings cause me to sit or lie down to avoid fainting or falling.)
- Severe (Dizzy or foggy feelings cause me to fall or faint.)

Over the past week, have you usually felt fatigued? This feeling is not part of being sleepy or sad.

- Normal (No fatigue.)
- Slight (Fatigue occurs. However it does not cause me troubles doing things or being with people.)
- Mild (Fatigue causes me some troubles doing things or being with people.)
- Moderate (Fatigue causes me a lot of troubles doing things or being with people. However, it does not stop me from doing anything.)
- Severe (Fatigue stops me from doing things or being with people.)

Over the past week, have you had problems with your speech?

- Normal (Not at all.)
- Slight (My speech is soft, slurred or uneven, but it does not cause others to ask me to repeat myself.)

- Mild (My speech causes people to ask me to occasionally repeat myself, but not everyday.)
- Moderate (My speech is unclear enough that others ask me to repeat myself every day even though most of my speech is understood.)
- Severe (Most or all of my speech cannot be understood.)

Over the past week, have you usually had too much saliva while you are awake or while you sleep?

- Normal (Not at all.)
- Slight (I have too much saliva, but do not drool.)
- Mild (I have some drooling during sleep, but none when I am awake.)
- Moderate (I have some drooling when I am awake, but I usually do not need tissues or a handkerchief.)
- Severe (I have so much drooling that I regularly need to use tissues or a handkerchief to protect my clothes.)

Over the past week, have you usually had problems swallowing pills or eating meals? Do you need your pills cut or crushed or your meals to be made soft, chopped or blended to avoid choking?

- Normal (No problems.)
- Slight (I am aware of slowness in my chewing or increased effort at swallowing, but I do not choke or need to have my food specially prepared.)
- Mild (I need to have my pills cut or my food specially prepared because of chewing or swallowing problems, but I have not choked over the past week.)
- Moderate (I choked at least once in the past week.)
- Severe (Because of chewing and swallowing problems, I need a feeding tube.)

Over the past week, have you usually had troubles handling your food and using eating utensils? For example, do you have trouble handling finger foods or using forks, knives, spoons, chopsticks?

- Normal (Not at all.)
- Slight (I am slow, but I do not need any help handling my food and have not had food spills while eating.)
- Mild (I am slow with my eating and have occasional food spills. I may need help with a few tasks such as cutting meat.)
- Moderate (I need help with many eating tasks but can manage some alone.)
- Severe (I need help for most or all eating tasks.)

Over the past week, have you usually had problems dressing? For example, are you slow or do you need

help with buttoning, using zippers, putting on or taking off your clothes or jewelry?

- Normal (Not at all.)
- Slight (I am slow but I do not need help.)
- Mild (I am slow and need help for a few dressing tasks, such as with buttons, bracelets.)
- Moderate (I need help for many dressing tasks.)
- Severe (I need help for most or all dressing tasks.)

Over the past week, have you usually been slow or do you need help with washing, bathing, shaving, brushing teeth, combing your hair or with other personal hygiene?

- Normal (Not at all.)
- Slight (I am slow but I do not need any help.)
- Mild (I need someone else to help me with some hygiene tasks.)
- Moderate (I need help for many hygiene tasks.)
- Severe (I need help for most or all of my hygiene tasks.)

Over the past week, have people usually had trouble reading your handwriting?

- Normal (Not at all.)
- Slight (My writing is slow, clumsy or uneven, but all words are clear.)
- Mild (Some words are unclear and difficult to read.)
- Moderate (Many words are unclear and difficult to read.)
- Severe (Most or all words cannot be read.)

Over the past week, have you usually had trouble doing your hobbies or other things that you like to do?

- Normal (Not at all.)
- Slight (I am a bit slow but do these activities easily.)
- Mild (I have some difficulty doing these activities.)
- Moderate (I have major problems doing these activities, but still do most.)
- Severe (I am unable to do most or all of these activities.)

Over the past week, have you usually had trouble turning over in bed?

- Normal (Not at all.)
- Slight (I have a bit of trouble turning, but I do not need any help.)
- Mild (I have a lot of trouble turning and need occasional help from someone else.)
- Moderate (To turn over, I often need help from someone else.)

- Severe (I am unable to turn over without help from someone else.)

Over the past week, have you usually had shaking or tremor?

- Normal (Not at all.)
- Slight (Shaking or tremor occurs but does not cause problems with any activities.)
- Mild (Shaking or tremor causes problems with only a few activities.)
- Moderate (Shaking or tremor causes problems with many of my daily activities.)
- Severe (Shaking or tremor causes problems with most or all activities.)

Over the past week, have you usually had trouble getting out of bed, a car seat, or a deep chair?

- Normal (Not at all.)
- Slight (I am slow or awkward, but I usually can do it on my first try.)
- Mild (I need more than one try to get up or need occasional help.)
- Moderate (I sometimes need help to get up, but most times I can still do it on my own.)
- Severe (I need help most or all of the time.)

Over the past week, have you usually had problems with balance and walking?

- Normal (Not at all.)
- Slight (I am slightly slow or may drag a leg. I never use a walking aid.)
- Mild (I occasionally use a walking aid, but I do not need any help from another person.)
- Moderate (I usually use a walking aid to walk safely without falling. However, I do not usually need the support of another person.)
- Severe (I usually use the support of another persons to walk safely without falling.)

Over the past week, on your usual day when walking, do you suddenly stop or freeze as if your feet are stuck to the floor?

- Normal (Not at all.)
- Slight (I briefly freeze but I can easily start walking again. I do not need help from someone else or a walking aid because of freezing.)
- Mild (I freeze and have trouble starting to walk again, but I do not need someone's help or a walking aid because of freezing.)
- Moderate (When I freeze I have a lot of trouble starting to walk again and, because of freezing, I

sometimes need to use a walking aid or need someone else's help.)

- Severe (Because of freezing, most or all of the time, I need to use a walking aid or someone's help.)

**The questions in this section will ask about the medications you are taking and have taken in the past.**

Which of the following Parkinson's disease medications have you ever taken? Please check all that apply.

- Aricept (donepezil)
- Artane (trihexyphenidyl)
- Apokyn injection (apomorphine)
- Azilect (rasagiline)
- Cogentin (benztropine)
- Comtan (entacapone)
- Eldepryl, Carbex, Atapryl, or Emsam patch (selegiline or deprenyl)
- Exelon patch (rivastigmine transdermal system)
- Mirapex (pramipexole)
- Neupro patch (rotigotine patch)
- Parcopa (carbidopa/levodopa orally disintegrating tablet)
- Parlodel (bromocriptine)
- Permax (pergolide)
- Razadyne (galantamine)
- Requip (ropinerole)
- Sinemet or Atamet (carbidopa/levodopa)
- Sinemet CR (controlled release carbidopa/levodopa)
- Stalevo (carbidopa, levodopa and entacapone)
- Symmetrel (amantadine)
- Tasmar (tolcapone)
- Some other Parkinson's disease medication
- None of the above

Which of the following Parkinson's disease medications are you currently taking? Please check all that apply.

- Aricept (donepezil)
- Artane (trihexyphenidyl)
- Apokyn injection (apomorphine)
- Azilect (rasagiline)
- Cogentin (benztropine)
- Comtan (entacapone)
- Eldepryl, Carbex, Atapryl, or Emsam patch (selegiline or deprenyl)
- Exelon patch (rivastigmine transdermal system)
- Mirapex (pramipexole)
- Neupro patch (rotigotine patch)
- Parcopa (carbidopa/levodopa orally disintegrating tablet)
- Parlodel (bromocriptine)
- Permax (pergolide)

- Razadyne (galantamine)
- Requip (ropinerole)
- Sinemet or Atamet (carbidopa/levodopa)
- Sinemet CR (controlled release carbidopa/levodopa)
- Stalevo (carbidopa, levodopa and entacapone)
- Symmetrel (amantadine)
- Tasmar (tolcapone)
- Some other Parkinson's disease medication
- I'm not taking any Parkinson's disease medication

During a typical day, are you better after you take your first dose of Parkinson's disease medication in the morning?

- Yes
- No
- I'm not sure/I don't remember

During a typical day, is it very clear to you when your Parkinson's disease medication stops working?

- Yes, the effect of the medication wears off and doesn't come back until I take my next dose
- No, my function is the same all day long
- I'm not sure/I don't remember

On average, during a typical day, how much of the time are you having a good response to the medications you take for Parkinson's disease? In other words, how much of the time do you think the medications are working well?

- 1/4 of the day or less
- More than 1/4 of the day up to 1/2 the day
- More than 1/2 the day up to 3/4 of the day
- More than 3/4 of the day up to all day
- I'm not sure/I don't remember

**The questions in this final section will help us better understand your background and family characteristics.**

Has a doctor ever diagnosed any of your biological family members with Parkinson's disease? Please check all that apply.

- Mother
- Father
- Sister
- Brother
- Daughter
- Son
- Maternal grandparent
- Paternal grandparent
- Maternal aunt or uncle
- Paternal aunt or uncle
- Maternal first cousin

- Paternal first cousin
- None of the above

In your lifetime, have you ever smoked cigarettes regularly (at least one cigarette per day for six months or longer)?

- Yes
- No
- I'm not sure/I don't remember

Have you ever had a job where you were regularly exposed to pesticides? Please include herbicides (to kill weeds), fungicides (to kill fungus or mold), insecticides (to kill insects), rodenticides (to kill rodents), or fumigants (a gas used to kill fungus, mold, or insects).

- Yes
- No
- I'm not sure/I don't remember

Have you regularly used pesticides in your home, garden or on your pets?

- Yes
- No
- I'm not sure/I don't remember

Have you ever had a head injury or concussion? Please include injuries that may have occurred during sporting activities, from falls, violence, car accidents, or other accidents, both during your childhood and adulthood.

- Yes
- No
- I'm not sure/I don't remember

*[if yes, head injury]*

How old were you the first time you had a head injury or concussion?

- *[free text]*

Did you lose consciousness after this injury?

- Yes
- No
- I'm not sure/I don't remember

**Now think about anti-inflammatory medications you have ever taken. These medications are commonly used to treat mild to moderate pain, fever, inflammation or swelling, and sometimes to thin the blood or to protect the heart.**



Have you used any of the following types of medications regularly (two or more tablets a week for six months or longer)? Please check all that apply.

- Ibuprofen-based non-aspirin medications (These medications are sometimes called non-steroidal anti-inflammatory drugs, or NSAIDS, and include Ibuprofen, Advil, Genpril, Haltran, IBU, Ibu-Tab, Menadol, Midol, Motrin, and Nuprin.)
- Other non-steroidal anti-inflammatory medications (For pain, inflammation, or swelling, such as Naprosyn, Aleve, Naproxen, Indocin, Indomethacin, Voltaren, Feldene, Clinoril, Relafen, Lodine, Orudis, and Ansaid. DO NOT include aspirin, Tylenol or acetaminophen, or narcotic pain relievers such as Vicodin or Codeine here.)
- Aspirin
- None of the above

In what year were you born?

- [free text]

Which of the following best describes who completed this questionnaire?

- The person diagnosed with Parkinson's disease, without assistance from someone else.
- The person diagnosed with Parkinson's disease, with help from someone else.
- Someone else on behalf of the person diagnosed with Parkinson's disease

Which of the following best describes the relationship between the person diagnosed with Parkinson's disease and the person who completed or assisted with completing the questionnaire?

- Spouse
- Adult child
- Adult grandchild
- Sister or brother
- Friend
- Someone else

## Appendix 2: Telemedicine satisfaction survey

### Participant follow-up questionnaire

Parkinson's telemedicine study

*Instructions:* Please complete this remote assessment follow-up survey. Return to Johns Hopkins University via email, paper mail, or fax (contact information is listed on the last page).

Participant name: \_\_\_\_\_

Date completed by participant (mm/dd/yy): \_\_\_\_\_

#### • I. Remote assessment

##### • A. Experience

Were you able to connect with the Parkinson's disease specialist and complete your web-based (video) appointment as scheduled?

- ☐ Yes  
☐ No

How much time did it take you to connect with the specialist?

- ☐ <15 minutes  
☐ 15–30 minutes  
☐ 30–45 minutes  
☐ 45–60 minutes  
☐ ≥60 minutes

How comfortable were you using the web-based software?

- ☐ Very comfortable  
☐ Comfortable  
☐ Neither comfortable nor uncomfortable  
☐ Uncomfortable  
☐ Very uncomfortable

How comfortable were you discussing your Parkinson's disease with the specialist?

- ☐ Very comfortable  
☐ Comfortable  
☐ Neutral  
☐ Uncomfortable  
☐ Very uncomfortable

Do you believe that the specialist was able to learn important information about your Parkinson's disease during the web-based visit?

- ☐ Yes  
☐ No

##### • B. Satisfaction

How satisfied were you with the technical quality of the connection during the web-based visit?

- ☐ Very satisfied  
☐ Satisfied  
☐ Neutral  
☐ Unsatisfied  
☐ Very unsatisfied

How satisfied were you with the specialist's ability to acquire information about your Parkinson's disease and overall health?

- ☐ Very satisfied  
☐ Satisfied  
☐ Neutral  
☐ Unsatisfied  
☐ Very unsatisfied

How satisfied were you with the overall experience of using videoconferencing for this research visit?

- ☐ Very satisfied  
☐ Satisfied  
☐ Neutral  
☐ Unsatisfied  
☐ Very unsatisfied

● **II. Clinical trials**

● **A. Awareness**

Have you ever sought information on any Parkinson's disease clinical trial or observational study for yourself?

- ☐ Yes  
☐ No

Have you ever participated in a research study or clinical trial?

- ☐ Yes  
☐ No

Would you like more information about clinical trials?

- ☐ Yes  
☐ No

● **B. Willingness**

How important to you is participating in a drug trial or observational study for Parkinson's disease?

- ☐ Highly important  
☐ Important  
☐ Not important  
☐ Undecided

Would you be interested in conducting clinical trial visits with a specialist or nurse via web-based appointments in the future?

- ☐ Yes

- ☐ No

How would the option to participate in remote visits (from your home) as part of a clinical trial affect your willingness to participate in a clinical trial?

- ☐ Much more willing  
☐ More willing  
☐ Neutral  
☐ Less willing  
☐ Much less willing

Would you be comfortable being contacted by someone other than your physician (i.e. a pharmaceutical firm) about becoming involved in a clinical trial?

- ☐ Very comfortable  
☐ Comfortable  
☐ Neutral  
☐ Uncomfortable  
☐ Very uncomfortable

● **C. Ability**

How close is the nearest Parkinson's disease research center to your home?

- ☐ <30 minutes  
☐ 30 minutes–1 hour  
☐ 1–3 hours  
☐ ≥3 hours  
☐ I don't know

Would remote visits make you more able to participate in a clinical trial?

- ☐ Yes  
☐ No  
☐ I don't know

**Please provide suggestions for how we may improve this research study:**

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