


Plain Language Summary of Publication

Plain language summary: what symptoms should be measured in clinical studies for people living with early-stage Parkinson's?

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First draft submitted: 6 October 2022; Accepted for publication: 24 November 2022; Published online: 6 January 2023

Summary

What is this summary about?

Clinical studies test whether a new treatment is safe and if the treatment works in people who have a particular condition. Most current questionnaires used in clinical studies investigating Parkinson's measure symptoms in people who have been diagnosed for many years. This means that these existing questionnaires may not be useful for people living with early-stage Parkinson's, where the symptoms experienced can be quite different to later stages, or may not show if a new treatment is helpful for them.

The most common symptoms in Parkinson's are involuntary shaking of parts of the body ("tremor"), slow movement ("bradykinesia") and stiff, inflexible muscles ("rigidity"), which worsen with time. Symptoms specific to early-stage Parkinson's are not fully understood and research is ongoing in this area. New measures are therefore needed to assess the symptoms affecting people living with early-stage Parkinson's, especially the symptoms that they find most troublesome. This study investigated which symptoms are of most importance to people in the earlier stages of their condition and which would be appropriate to measure in future clinical studies.

Who was involved in the study?

The research team that led the study was made up of people living with Parkinson's, as well as technical experts and representatives from Parkinson's patient organizations (Parkinson's UK and the Parkinson's Foundation). The participants in the study were people living with early-stage Parkinson's and their care partners.

What were the results?





Slowness of movement (called "bradykinesia") was noted as a key symptom. "Functional slowness" was especially noted. This symptom caused people to feel slower during many daily tasks, such as brushing teeth, walking and cooking. The loss of ability to move easily and freely, termed "mobility", was also a key symptom. It was noticeable in walking abnormalities and difficulties performing "fine motor skills". These are tasks that require precision, dexterity and coordination. Other impactful symptoms were: tremor, rigidity/stiffness, feelings of exhaustion (fatigue), depression, sleeping problems and pain.

What do the results of the study mean?

The personal views gathered in this study show the wide-ranging effects of early-stage Parkinson's. The study also identifies functional slowness and loss of mobility as key symptoms that would be appropriate to measure in future early-stage Parkinson's clinical studies to test if treatments are working or not.

How to say

(double click sound icon to play sound)...

- **Bradykinesia:** bra-DEE-KY-NEE-ZEE-ah 
- **Multidisciplinary:** mul-TEE-di-si-pli-neh-REE 
- **Unilateral:** U-NEE-la-ter-all 
- **Bilateral:** BY-la-ter-all 

Where can I find the original article on which this summary is based?

You can read the original article published in *Neurology and Therapy* for free at:
<https://link.springer.com/article/10.1007/s40120-022-00375-3>

Who is this article for?

This article is for the Parkinson's community, people living with Parkinson's, care partners of people living with Parkinson's, healthcare professionals involved in the care of people living with Parkinson's, and researchers of Parkinson's who are involved with clinical studies.

Why was the study carried out?

This study was carried out to explore the patient experience in early-stage Parkinson's. The study aimed to identify:

- Which symptoms are of most importance to people living with early-stage Parkinson's?
- Which symptoms are most appropriate to measure in future clinical studies?

Parkinson's is an ongoing, worsening condition of the brain, which causes a wide range of motor (movement) symptoms and non-motor symptoms. These symptoms can vary greatly from person to person. They also change over time as the condition worsens.

Although these are not present in all people, the most common motor symptoms of Parkinson's are:

- Involuntary shaking of parts of the body ("tremor")
- Slow movement ("bradykinesia")
- Stiff, inflexible muscles ("rigidity")

Non-motor symptoms are particularly wide-ranging and can include:

- Pain
- Anxiety
- Depression
- Loss of sense of smell
- Problems with thinking, balance, sleeping and memory

There is currently no treatment that can slow, stop or reverse the progression of Parkinson's.

Following early-stage Parkinson's, the stages are well defined. They have been studied at length in clinical studies with existing questionnaires. In contrast, doctors, scientists and health authorities have not been able to agree on a single definition for early-stage Parkinson's. Also, there has been very little research on the impact of this condition in its early stages.

In Parkinson's research, greater focus is now being placed on treatments that can be given at earlier stages of the disease. These treatments aim to slow, stop or even reverse the progression of Parkinson's, and they are known as **disease-modifying treatments**. It is key to improve our knowledge of early-stage Parkinson's. This would allow us to understand which symptoms are most bothersome to people, which symptoms are appropriate to measure in future clinical studies, and whether disease-modifying treatments can improve these symptoms.

Patient-reported outcomes (also called PROs) are measures used in clinical studies. They determine whether a treatment has a meaningful benefit for participants. For example, although a treatment may improve a symptom that a doctor measures at a check-up, the person may not be troubled by it and they would not experience a benefit if it improves.



PROs allow people to report whether they feel a treatment is providing a useful benefit which matters to them, including:

- ✓ Being in less pain
- ✓ Being able to perform a task they couldn't perform before

However, PROs often used in Parkinson's research, like the 39-item Parkinson's Disease Questionnaire (PDQ-39) and Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS), were not developed for use with people living with early-stage Parkinson's. As such, these measures are not completely suited for people with early-stage Parkinson's as they:



- ✗ Do not capture the full range of symptoms experienced by people living with early-stage Parkinson's
- ✗ Cannot gauge how the condition progresses
- ✗ Are limited in assessing whether a new treatment can provide a meaningful benefit

All these things are vital to assess in future clinical studies.

The aim of this study was to identify which symptoms people find most troublesome in early-stage Parkinson's, resulting in the development of better and more meaningful measures to be used in clinical studies.

Multidisciplinary research team

The study was designed by a group of experts from different specialties who aimed to work together to try to gain a better understanding of early-stage Parkinson's and were called the '**multidisciplinary research team**'. This group comprised:



Multidisciplinary research team



- 3 patient experts
- 2 patient advocacy organization representatives

PARKINSON'S^{UK}

- 3 patient experts
- 1 patient advocacy organization representative

- 2 clinical experts
- 1 expert in patient-focused research
- 1 expert in science-related regulations
- 2 research experts
- 2 experts in movement disorders

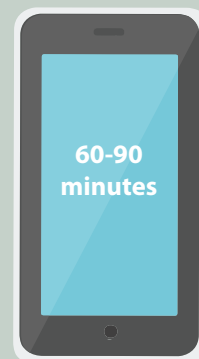
'Patient experts' are people living with Parkinson's as they are experts in their own condition.

Structure of the study

One-to-one telephone interviews were conducted with people living with early-stage Parkinson's and their care partners. The interviews lasted 60–90 minutes. During the interviews, they were asked to describe:

- 1. Their symptoms of early-stage Parkinson's
- 2. How early-stage Parkinson's affects them

Each participant was interviewed once. The interviews were analyzed to identify the most common symptoms and experiences that would be appropriate to measure in future clinical studies.



Analysis

Information and quotes from the interviews were grouped into common themes to build a picture of early-stage Parkinson's. Common symptoms and experiences were counted to see which were reported by study participants most often. The key symptoms and experiences considered appropriate to measure in future clinical studies were identified in 3 ways:

1. How often a symptom/experience was mentioned in interviews
2. Review by the 6 patient experts
3. Input from 9 healthcare professionals that specialize in movement disorders (these reviewers were separate to the people included in the multidisciplinary research team)

Who took part in the study?

A total of **50 people** living with early-stage Parkinson's were recruited. For this study, people with early-stage Parkinson's were those who had been diagnosed within the past 2 years. Also, **9 care partners**, who were either the spouse or partner of people living with early-stage Parkinson's, were recruited to the study.

25 people with early-stage Parkinson's from the **USA** recruited by the



5 care partners from the **USA**



25 people with early-stage Parkinson's from the **UK** recruited by



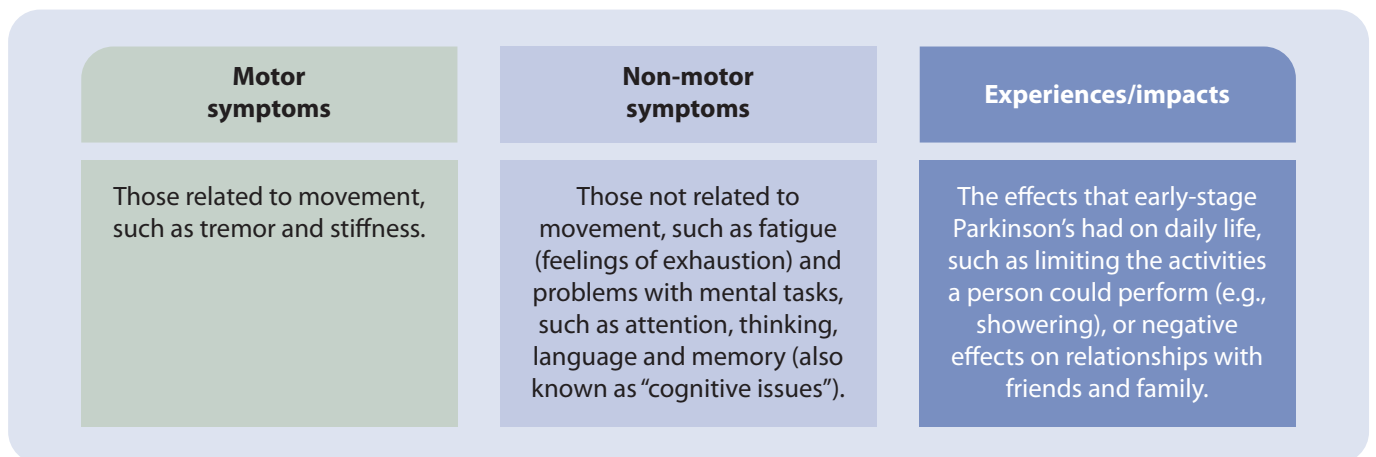
4 care partners from the **UK**

Different recruitment strategies were used by Parkinson's UK and the Parkinson's Foundation. On average, people from the UK were recruited 4 years after diagnosis, while those in the USA were recruited 1 year after diagnosis.

People with unilateral or bilateral (meaning 1 or both sides of the body were affected) Parkinson's symptoms were recruited in the study, which also allowed for a comparison between these groups of people. Most of the study participants (80% UK and 76% USA) reported symptoms on 1 side, which is common in early stages of the condition.

1 What symptoms or experiences of early-stage Parkinson's are most important to people living with the condition and their care partners?

The interviews with people living with early-stage Parkinson's and their care partners identified a range of symptoms and experiences that are important to people living with the condition. These were reviewed by the research team and grouped into 3 main categories:



Specifically, the symptoms most important to people living with early-stage Parkinson's included:

- Slowness of movement (also called "bradykinesia")
- Tremor
- Rigidity (stiffness in the arms or legs beyond what would result from normal aging)
- Loss of mobility, particularly fine motor skills/dexterity, for example, tasks that use small muscles in the hands, wrists and fingers, and difficulty walking
- Feelings of exhaustion (fatigue)
- Depression
- Trouble with sleep or having vivid/negative dreams
- Pain

2 The table below shows the symptoms/experiences important to people living with early-stage Parkinson's[†]

<p>Reported as important by the 9 healthcare professionals</p> 	<p>Reported as important by the 6 patient experts</p> 	<p>Reported as important by over 40% of people living with early-stage Parkinson's</p> 
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Motor symptoms			
Arm swing	✓	✓	
Balance/stability			✓
Complex/whole-body mobility	✓		✓
Cramps		✓	✓
Facial expressions	✓		
Fine motor/dexterity mobility	✓	✓	
Freezing of movement			✓
Functional slowness		✓	✓
Internal tremor		✓	
Mobility	✓	✓	
Posture	✓		
Resting tremor	✓	✓	
Rigidity/stiffness	✓	✓	✓
Saliva control			✓
Slowness			✓
Slowness of movement	✓	✓	
Slowness performing activities		✓	
Speech/voice	✓	✓	
Speech/voice quality			✓
Strength/weakness		✓	
Stumble/unstable		✓	
Tremor	✓	✓	
Uncontrolled movements	✓		✓
Upper limb mobility	✓		✓
Walking	✓	✓	✓

Non-motor symptoms			
Anxiety/worry			✓
Depression	✓	✓	✓
Eyes/vision	✓		✓
Fatigue	✓	✓	✓
Frequent awakening			✓
Light headedness/dizziness	✓	✓	
Memory			✓
No energy/sleepiness			✓
Pain	✓	✓	✓
Sense of smell	✓		
Sleep/dreams	✓	✓	
Experiences			
Confidence/nervousness/avoidance			✓
Experience in daily activities			✓
Experience in instrumental daily activities			✓
Mental experience		✓	
Professional experience		✓	✓
Psychological		✓	
Social experiences			✓

Note: The bold font shows important groups within the motor/non-motor symptoms or experiences categories. These groups are made up of important sub-group symptoms/experiences, which are shown by the non-bold font.

Symptoms mentioned by the care partners, and not by the people living with early-stage Parkinson's, included:

- Drooping head and leaning
- Shaking whilst asleep
- Decision making
- Mental freezing/brain no longer communicating with the rest of the body
- Behavioral changes

[†]For clarity, this figure only shows symptoms/experiences that were identified as important in early-stage Parkinson's. Those symptoms/experiences not identified as important by any group have not been included in this figure, but were included in the original manuscript published by *Neurology and Therapy*.

Other experiences of early-stage Parkinson's that impact daily life were identified, including psychological effects and difficulties with work, finances, relationships and the ability to perform various activities. Although the research team recognized the importance of these experiences, the decision was made to develop a PRO measure specific only to the symptoms of early-stage Parkinson's for use in future Parkinson's clinical studies, because:

- 1 It can be difficult to know whether the identified experiences are a direct result of the condition itself, other progressive conditions a person may have, or other life circumstances
- 2 The current need is for a new measure that can better assess the *symptoms* of early-stage Parkinson's
- 3 The research team is mindful of the burden that including too many measures in a clinical study might place on the study participants
- 4 Ultimately, if Parkinson's symptoms are measured more accurately, then better assessments of the aspects of daily living that are directly impacted can be made

The impact of having 1 or both sides of the body affected by Parkinson's

Some people in the study were at earlier stages of the condition than others. This made it possible to consider results between the 2 groups of people to see how the symptoms of early-stage Parkinson's get worse over time.

People living with early-stage Parkinson's were those with symptoms on 1 side of their body (unilateral) and/or a diagnosis within the last 2 years. People living with early-stage Parkinson's that had progressed a bit further were those with symptoms on both sides of the body (bilateral) with no stability or balance issues, and who were diagnosed more than 2 years ago.

Our results suggest that overall symptoms and experiences were largely relevant across the 2 groups. In both groups, tremor, upper limb (arm) issues, gait/walking abnormalities and fatigue were the 4 most frequently reported issues.

However, some symptoms and experiences were reported more often in one group than the other.

Symptoms reported more in the group with symptoms on 1 side of the body (less than 2 years since diagnosis):

- Fine motor issues
- Arm swing issues

Symptoms reported more in the group with symptoms on both sides of the body (more than 2 years since diagnosis):

- Rigidity/stiffness
- Speech/voice quality
- Saliva control
- Difficulties in performing daily activities, carrying things, stumbling or being unstable

What do the results of this study mean?

It is important to include people living with Parkinson's as partners throughout the research process. This properly captures the impact of their condition and what is meaningful to them.

This study confirms a growing recognition that existing measures used in clinical studies may not fully assess the symptoms that are most important to people living with early-stage Parkinson's.

A broad range of symptoms and experiences were identified during the interviews. This demonstrated that the impact of symptoms highlighted by people living with Parkinson's did not always align with the views of clinical experts.

The research team analyzed the symptoms and experiences identified in interviews. Bradykinesia/slowness of movement, particularly functional slowness (slowness involving upper limbs, complex movement and general activities) and mobility (particularly upper limb and gait/walking) were identified as the most appropriate for measurement in future clinical studies involving Parkinson's.

There were some limitations to the study. Only participants from the UK and USA were interviewed. Their experiences may not reflect the experiences of people living with early-stage Parkinson's from the rest of the world. This study included only White and non-Hispanic/non-Latino participants, so their experiences may not reflect the experience of other races/ethnicities. To address this limitation, the team is working on a strategy focused on diversity and inclusivity.

Although this is only 1 study, the results show that many important experiences of living with early-stage Parkinson's are not well covered by existing PRO measures. Therefore, there is a need to develop new PRO measures that better assess this stage of the condition. These new measures could then be used in clinical studies, which will help to evaluate the impact of new treatments more accurately in early-stage Parkinson's.

Who sponsored this study?

This study was funded by UCB Pharma.

Where can readers find more information on this study?

The original article on which this summary is based is called 'Patient Experience in Early-Stage Parkinson's Disease: Using a Mixed Methods Analysis to Identify Which Concepts Are Cardinal for Clinical Trial Outcome Assessment'.

The article was published in *Neurology and Therapy* and can be read for free at:

<https://link.springer.com/article/10.1007/s40120-022-00375-3>

Educational resources

Learn more about Parkinson's at these two websites:

- Parkinson's UK: <https://www.parkinsons.org.uk/>
- Parkinson's Foundation: <https://www.parkinson.org/>

Acknowledgments

The authors would like to thank the Parkinson's community for participating in this study, making this research possible. The authors would like to thank Gina Walter, of Parkinson's UK, and Mary Tidwell and Sarah Diaz, of the Parkinson's Foundation, for reviewing the PLSP. The authors thank Claire Nolan, formerly the Research Involvement Manager at Parkinson's UK, for her contribution to the early stages of this research. During research for the corresponding manuscript, the authors acknowledge reference to the Fox Insight Study, which is funded by The Michael J. Fox Foundation for Parkinson's Research. The authors would also like to acknowledge and thank Dr. Milton Biagioni, of UCB Pharma, for his input into the later stages of this research and the thorough advice and review of the corresponding manuscript to ensure clinical meaningfulness; Irene de la Torre Arenas, of UCB Pharma, for her contribution to the development of the figures, and Jessica Mills, of Modus Outcomes, who facilitated the qualitative analysis. The authors would also like to thank Jessica Mills, Nadine McGale, of Modus Outcomes, and Debi Rennie and Rakhee Ghelani, formerly of Modus Outcomes, for conducting the interviews alongside Sophie Cleanthous. The authors would also like to acknowledge Paul Burns, patient expert, for his contributions to this study. Prof. Roger A. Barker is supported through the NIHR-funded Cambridge Biomedical Research Center.

Financial & competing interests disclosure

Stefan Cano and Sophie Cleanthous are employees of Modus Outcomes that provided research and analysis services to UCB Pharma. Kate Trenam and Thomas Morel are employees and shareholders of UCB Pharma. Casey Gallagher and Karlin Schroeder (Parkinson's Foundation) and Natasha Ratcliffe (Parkinson's UK) are staff experts in patient engagement/involvement in research; since the completion of the study, Natasha Ratcliffe has changed her affiliation from Parkinson's UK, London, UK to COUCH Health, Manchester, UK. Geraldine Blavat, John Andrejack, and William Brooks (Parkinson's Foundation), and Carroll Siu and Lesley Gosden (Parkinson's UK) are patient experts. Ashley Slagle is an employee of Aspen Consulting, LLC that provides consulting services to UCB Pharma. Ashley Slagle reports personal fees from UCB Pharma outside of the submitted work. Casey Gallagher, Carroll Siu, Geraldine Blavat, John Andrejack, Karlin Schroeder, Lesley Gosden, Natasha Ratcliffe, Roger Barker, and William Brooks have no potential conflicts of interest to report.

The study received ethics approval from the Copernicus Group Independent Review Board (protocol number 420180240) in the USA. As this was a non-interventional interview study with recruitment facilitated by patient associations and not the National Health Service (NHS), the UK Health Research Authority ethics committee indicated no NHS ethics approval was required. All participants were required to complete consent forms before proceeding to the interview. The study was performed in accordance with the Helsinki declaration of 1964, and its later amendments.

The authors acknowledge Janet Davies, PhD, of UCB Pharma, for publication and editorial support and Saira Mal, BSc and Luke Edmonds, MSc of Ashfield MedComms, an Inizio Company, for editorial support that was funded by UCB Pharma in accordance with Good Publication Practice (GPP3) guidelines (<http://www.ismpp.org/gpp3>).