



Tenison, E., Lithander, F. E., Smith, M., Brazier, D., Ben-Shlomo, Y., & Henderson, E. J. (2022). Needs of patients with parkinsonism and their caregivers: a protocol for the PRIME-UK cross-sectional study. *BMJ Open*, 12(5), e057947. [e057947].  
<https://doi.org/10.1136/bmjopen-2021-057947>

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# BMJ Open Needs of patients with parkinsonism and their caregivers: a protocol for the PRIME-UK cross-sectional study

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**To cite:** Tenison E, Lithander FE, Smith MD, *et al.* Needs of patients with parkinsonism and their caregivers: a protocol for the PRIME-UK cross-sectional study. *BMJ Open* 2022;**12**:e057947. doi:10.1136/bmjopen-2021-057947

► Prepublication history for this paper is available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2021-057947>).

Received 02 October 2021  
Accepted 10 April 2022



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## ABSTRACT

**Introduction** People with parkinsonism are a highly heterogeneous group and the disease encompasses a spectrum of motor and non-motor symptoms which variably emerge and manifest across the disease course, fluctuate over time and negatively impact quality of life. While parkinsonism is not directly the result of ageing, it is a condition that mostly affects older people, who may also be living with frailty and multimorbidity. This study aims to describe the broad range of health needs for people with parkinsonism and their carers in relation to their symptomatology, disability, disease stage, comorbidities and sociodemographic characteristics.

**Methods and analysis** In this single site cross-sectional study, people with parkinsonism will be sent a study information pack for themselves and their primary informal caregiver, if relevant. Data are collected via questionnaire, with additional support, if required, to maximise participation. A specific strategy has been developed to target and proactively recruit patients lacking capacity to consent, including those in residential care settings, with input from a personal consultee prior to completion of a bespoke questionnaire by a representative. Caregivers are also recruited to look at various health outcomes. Results will be displayed as descriptive statistics and regression models will be used to test simple associations and interactions.

**Ethics and dissemination** This protocol was approved by the London—Brighton & Sussex Research Ethics Committee (REC reference 20/L0/0890). The results of this protocol will be disseminated through publication in an international peer-reviewed journal; presentation at academic meetings and conferences; and a lay summary uploaded to the PRIME-Parkinson website.

**Trial registration number** ISRCTN11452969; Pre-results.

## INTRODUCTION

Parkinson's disease (PD), the most common cause of parkinsonism, is the second most frequent neurodegenerative disease after Alzheimer's disease and is estimated to affect around 0.3% of the population in industrialised countries, rising to 1% in those aged over 60 years.<sup>1</sup> A meta-analysis of worldwide data on prevalence of PD showed rising prevalence with age from 41 per 100 000 people in

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This study aims to recruit typically under-represented individuals with parkinsonism, specifically those who lack capacity, in order to describe a more representative sample and address an area of unmet need.
- ⇒ This study involves a detailed and holistic phenotyping of people with parkinsonism, rather than focusing on any one motor or non-motor domain in conjunction with data from the perspective of a caregiver.
- ⇒ Despite efforts to design a specific approach to promote inclusion of hard-to-reach individuals, we acknowledge that non-response bias may impact the findings.
- ⇒ Given the cross-sectional design, it will not be possible to establish causality of any associations observed.

those aged 40–49 years to 1903 per 100 000 in those aged over 80 years.<sup>2</sup>

People with parkinsonism are a highly heterogeneous group<sup>3</sup> and the disease encompasses a spectrum of motor and non-motor symptoms, including fatigue, sleep disturbance, neuropsychiatric complications and cognitive impairment, which manifest across the disease course and fluctuate over time.<sup>4</sup> While PD is not directly the result of ageing, it is a condition that more commonly affects older people,<sup>1</sup> who are more likely to also be living with frailty and multimorbidity. Frailty and multimorbidity act synergistically to drive clinical complexity<sup>5</sup> and heighten the risk of adverse outcomes for older people with PD. The impact of multimorbidity on an individual's risk profile may be greater than the sum of conditions.<sup>6</sup> In order to fully appreciate the level of clinical complexity of people with PD, it is necessary to integrate the multifaceted problems they may experience, together with their frailty status and additional comorbidities.



PD impacts negatively on the physical and psychosocial well-being of those who care for or support these individuals.<sup>7</sup> As PD progresses, many individuals will require care and a large proportion of this is provided informally. In one study of patients with moderate to advanced parkinsonism, over 80% were receiving input from an informal caregiver, while only a quarter of people received formal domestic or personal care.<sup>8</sup> Increasing age, functional disability, non-motor symptom burden, and declining cognitive and physical function are associated with greater care need and, in turn, with worsening caregiver quality of life.<sup>9</sup> Caregivers are often older adults,<sup>9</sup> so may themselves be living with frailty and multimorbidity, making them vulnerable to negative health outcomes which can limit their ability to provide informal support; thus studying the needs of, and supporting, caregivers is important to optimise the well-being of people with parkinsonism.

The extent to which findings from many large observational studies of people with parkinsonism can be extrapolated is limited as patients are frequently excluded on the bases of age, comorbidities, cognitive impairment or inability to consent. The COhort of Patients with PArkinson's DIsease in Spain study restricted inclusion to those aged 30–75 years and excluded patients with dementia (defined as a Mini-Mental State Examination score <26) or who were unable to provide informed consent.<sup>10</sup> The international, multicentre Non-motor International Longitudinal Study excluded patients with dementia or who were unable to consent.<sup>11</sup> Similarly, existing UK-based PD cohort studies have generally focused on patients with idiopathic PD, including the Discovery cohort which recruited from neurology clinics and excluded individuals if they were suspected to have non-idiopathic PD, Lewy Body dementia or had cognitive impairment which precluded consent.<sup>12</sup> The prospective, multicentre Tracking Parkinson's cohort excluded those with other forms of parkinsonism or severe comorbid illness.<sup>13</sup> It is, however, encouraging to note that some ongoing biomarker development cohorts are taking an inclusive approach towards recruitment, including the Cincinnati Biomarker Programme which is enrolling participants with any form of parkinsonism or dementia, at any disease stage, though participant burden may implicitly exclude some participants.<sup>14</sup> Even studies focusing on later stage PD are often not wholly inclusive: a Dutch cross-sectional study of nursing home residents with PD opted to exclude individuals with moderate to severe cognitive decline<sup>15</sup> and a cross-sectional study investigating the clinical burden of advanced PD required patients to be able to provide written informed consent.<sup>16</sup> This limits the generalisability of the findings and likely provides an overly optimistic clinical picture of PD.

In this study, we aim to quantitatively describe the overall symptomatology and phenomenology of people with parkinsonism, rather than focus on any one motor or non-motor symptom of the disease. Early studies focused almost exclusively on the motor manifestations of Parkinson's with more recent work better profiling

the non-motor aspects.<sup>17</sup> However, more global aspects such as patient activation, nutritional risk, well-being and exploration of wider impacts on caregivers have been undervalued. We will recruit people with parkinsonism who are additionally living with frailty, multimorbidity and cognitive impairment, in order to describe a representative population and address this area of unmet need. We will also gain vital information on the lived experience of caregivers by co-enrolling individuals who live with, care for or support someone with parkinsonism. Understanding the profile of people with parkinsonism in terms of their disease stage, symptom burden and multimorbidity, as well as characterising the population of caregivers associated with people with parkinsonism will inform the development of a person-centred and individualised multicomponent intervention and allow us to target patients and caregivers most at risk of adverse outcomes.<sup>18</sup> We will also use this cross-sectional study as a sampling frame whereby information on disease stage and health needs is utilised to stratify a subgroup of participants into a future randomised controlled trial of a new care model (PRIME) with an intervention that is targeted according to clinical complexity.<sup>19</sup>

## METHODS AND ANALYSIS

### Study design and population

This is a single-centre, cross-sectional study. People with parkinsonism living in the catchment area of Royal United Hospital Bath NHS Foundation Trust (RUH Bath), a district general hospital in the UK, will be recruited to the study over approximately 12–24 months from September 2020. We will also enrol primary informal caregivers of a patient with parkinsonism. A person with parkinsonism may take part in the study regardless of whether they have an informal caregiver and, if they do, whether this person wishes to take part. Likewise, a caregiver may participate regardless of whether the person with parkinsonism, for whom they care, wishes to take part.

The catchment area for the RUH Bath includes North-East Somerset, parts of South Gloucestershire and West Wiltshire. People with parkinsonism are cared for by the separate Parkinson's specialist clinicians in the older person's unit (OPU) and neurology teams with outpatient clinics at the RUH site; St Martin's Hospital in Bath; and Chippenham and Devizes in Wiltshire. Home visits to patients in residential care are also undertaken by the OPU Parkinson's clinicians.

### Inclusion/exclusion criteria

#### Patient participants

##### Inclusion criteria

- ▶ Have a diagnosis of parkinsonism (including idiopathic PD, progressive supranuclear palsy, corticobasal degeneration, multiple system atrophy, dementia with Lewy bodies, vascular parkinsonism), made by a movement disorder specialist (a physician subspecialising in neurology or geriatric medicine).

- ▶ Be willing to participate.
- ▶ Have the ability to provide informed consent to participate or, where unable to do so due to cognitive impairment, availability of a close friend or relative to act as a personal consultee.
- ▶ Be aged 18 years or over.
- ▶ Live in the catchment area of RUH Bath.

#### Exclusion criteria

- ▶ Individuals with drug-induced parkinsonism.
- ▶ Individuals who lack capacity to consent to participate but do not have anyone who can be a consultee to provide advice regarding their wishes and views.
- ▶ Current medical, cognitive or psychosocial issue or co-enrolment in another study that, in the opinion of the site investigator, would interfere with adherence to study requirements (eg, individuals in the last days/weeks of life).

#### Caregiver participants

##### Inclusion criteria

- ▶ Provide informal care or support for a patient with parkinsonism and, where a patient has more than one informal caregiver, be considered by the patient to be their primary caregiver.
- ▶ Be willing to participate.
- ▶ Have the ability to provide informed consent to participate.
- ▶ Be aged 18 years or over.

##### Exclusion criteria

- ▶ Professional carers, who are paid to deliver care

#### Sampling and recruitment procedures

Potentially eligible participants will be identified from lists of patients coded with parkinsonism during an inpatient admission and from lists of patients followed up or seen as a new referral within the movement disorder services at the main regional hospital (RUH Bath) and ancillary clinics within the surrounding area.

Patients who meet the eligibility criteria will be sent an invitation letter, by the study team on behalf of their Parkinson's clinician, in the post, together with information about the study for them and for any informal caregiver. Willing patients/caregivers will be asked to complete the written consent form and return it by post to the study team at RUH Bath. Participants who do not respond to this invitation letter will receive one or more telephone calls from the study team, after they have had at least 1 week to consider the information. The purpose of these calls will be to answer any questions the patient may have about study participation; ascertain how the team can support the patient to participate should they wish to; identify if there are any requirements for translation and, where necessary, assess capacity to consent to taking part in the study. Research participants do not receive any remuneration or incentive for taking part, but all postal costs are covered. If the patient declines to participate, they will not receive further contact about this study.

#### Identification of caregivers

The envelope sent to potential patient participants will contain an information booklet and consent form for people who provide care or support to someone with parkinsonism. The invitation letter asks the person with parkinsonism to pass this information to the person who is their main source of help or support, where relevant. Potential caregiver participants may also be identified from the 'About Me' form, which willing patient participants are asked to return together with their completed consent form. If they tick that they live with someone or that they receive support from family or friends, the patient participant will receive a telephone call to clarify whether this individual is eligible and willing to take part as caregiver.

#### Adults lacking capacity to consent to participation in research

Patients will be assumed to have capacity to consent to the study unless there is evidence to suggest otherwise. Situations which will prompt capacity assessment include return of incomplete or partially completed consent forms; an individual (such as care home staff or a family member), who answers the phone on behalf of a patient during a follow-up call, expressing concern that the patient may struggle to understand the study information. If a capacity assessment is triggered, this will be conducted by telephone by a trained member of the team in accordance with the Mental Capacity Act 2005 two-stage test.<sup>20</sup> This individual will take all possible steps to facilitate the potential participant to make a capacitous decision (e.g., by calling back on another occasion; by ensuring that a family member or friend is with the potential participant during the assessment, if possible).

#### Identification and involvement of a personal consultee

If the potential participant does not have capacity to give consent to participate in the study, a personal consultee, usually a close family member or friend who knows the potential participant in a personal capacity, will be sought to review the requirements for study participation and offer advice on the wishes and views of the patient, including the patient's view on taking part in research at the time they had capacity. Personal consultees will be identified from next of kin details held within clinical records, discussion with care home staff and, where relevant, asking to speak to anyone who lives with or is supporting the potential patient participant.

If the consultee advises that the person would have consented at a time they had capacity, they will be asked to sign the consultee declaration form. The personal consultee, or another close friend or relative of the person with parkinsonism, will be asked to complete questionnaires on behalf of the patient, acting as their 'representative'. We will not involve nominated consultees such as healthcare professionals or paid carers. Where no personal consultee is available, for example because the person lacking capacity has no family member or friend,

or they are not willing to act as a personal consultee, the patient shall be excluded from the study.

## Data collection

### Methods of assessment

Recruited participants will complete a single questionnaire booklet at home during the study period and will be asked to return this to the research team in the prepaid envelope provided. Where able, participants will self-complete the questionnaires and can do this over a number of days. Questionnaire completion can also be facilitated over the telephone or in person to support individuals with, for example, visual impairment or tremor/dyskinesia limiting ability to write, to participate. Where participants have capacity but have a physical inability to mark responses on the questionnaire (e.g., due to tremor or bradykinesia), assistance with making a physical response can be undertaken by another person, which could include their paid carer, with the answer communicated by the participant.

People with parkinsonism, who can consent to the study, will be asked to complete a full patient questionnaire booklet, which may take up to 2 hours to complete. Representatives of those unable to consent to the study will complete a specially designed and adapted patient questionnaire booklet on their behalf; this may take up to 1 hour to complete. Caregivers will be asked to complete the caregiver questionnaire booklet, about their own perspective, which is estimated to take up to 1 hour to complete. The contents of all three questionnaire booklets are detailed in [table 1](#).

If questionnaire booklets have not been received by the research team within 2 weeks of them being posted to participants, the research team will telephone the participant to answer any queries and to offer support. If the participant returns a questionnaire with one or more questions left blank or incorrectly completed (e.g., multiple options are selected for a question which requires only one answer), the participant will be contacted by telephone and asked if they are willing to clarify their answers.

### Rationale for selected questionnaires

#### *Measures for people with parkinsonism*

In order to capture the other comorbidities affecting people with parkinsonism, we are using a list designed as a research tool for the self-report of chronic conditions in primary care.<sup>21</sup>

The 39-item Parkinson's Disease Questionnaire (PDQ-39) is a Movement Disorder Society (MDS)-recommended, PD-specific measure of health-related quality of life and has been well-validated and utilised in this population.<sup>22</sup> A well-being measure, ICEpop CAPability measure for Older People (ICECAP-O) will be used to capture the broader impact of PD on participants. ICECAP-O is a relatively new measure of capability in older people which has been previously used in patients with PD.<sup>23</sup> A proxy version has been used to assess capability in older adults with cognitive impairment<sup>24 25</sup> so this

measure will be completed by a representative for patients lacking capacity and unable to complete questionnaires.

Non-motor symptoms can be particularly troubling for patients and can negatively influence quality of life<sup>26</sup> and so are important to capture as part of this holistic and in-depth assessment. While the PD Nonmotor Symptoms Questionnaire is a screening tool, rather than a rating instrument, it was selected for this study because it does not require rater administration and is relatively quick for participants to self-complete.<sup>27</sup> The Beck Depression Inventory has been validated for use in people with PD and is widely used to screen for depression and assess the severity of depression symptoms in the group.<sup>28</sup>

The Scales for Outcomes in Parkinson's disease-autonomic dysfunction questionnaire has been included to characterise the burden of autonomic symptoms that are responsible for many non-motor symptoms. These can be diffuse and wide-reaching and include important yet seldom considered issues such as sexual function, as well common phenomena including orthostatic hypotension. Bladder symptoms contribute significantly to quality of life and will be further explored in more depth using the International Consultation on Incontinence Questionnaire male and female short form Lower Urinary Tract Symptoms tools, which have been recommended for use in PD.<sup>29</sup> These broadly cover all urinary symptoms specific to each gender. Bowel symptoms will be similarly explored using the neurogenic bowel score.<sup>30</sup>

Test Your Memory is a self-administered cognitive screening test<sup>31</sup> which has been used among people with PD and compared with the Montreal Cognitive Assessment.<sup>32</sup>

Self-reported motor symptoms will be captured using questions adapted from a motor rating form based on motor tasks from the MDS-Unified Parkinson's Disease Rating Scale.<sup>33</sup>

Freezing of gait is a common symptom, particularly in the advanced phases of PD, which can cause disability, negatively impact quality of life<sup>34</sup> and increase falls risk.<sup>35</sup> The New-Freezing of Gait Questionnaire is a self-reported tool to assess the impact and severity of freezing symptoms.<sup>36</sup>

The Patient Activation Measure is a metric used to quantify the self-management capabilities of patients.<sup>37</sup> There is an increasing awareness that patients who have the knowledge, skills and confidence to look after their health and feel empowered to do so have better health outcomes<sup>37</sup> and so it is important to gain an understanding of activation levels among people with PD and their caregivers.

The Bristol Activities of Daily Living (Bristol ADL) has been shown to have good content and construct validity when used with people with dementia<sup>38</sup> and was one of only two scales rated as moderate quality in a systematic review of ADL scales in dementia and, of these, the only one suitable for self-completion by a caregiver.<sup>39</sup> This will allow the quantification of functional ability in participants who take part with a representative. Neuropsychiatric

**Table 1** Contents of questionnaire booklets

Metric	Data	Items	PPT +	PPT -	CG
Demographics	Gender	1	✓	✓	✓
	Date of birth	1	✓	✓	✓
	Ethnicity	1	✓	✓	✓
	Employment status	1	✓		✓
	Highest qualification	1	✓	✓	✓
	Marital status	1	✓	✓	✓
	Living situation	1	✓	✓	✓
Medication	Medication (name, dose, frequency, route)	1	✓		
Parkinson's history	Diagnosis	1	✓	✓	
	Year of diagnosis	1	✓	✓	
	Laterality of first symptoms	1	✓	✓	
	Advanced therapies	3	✓	✓	
General medical history	Past medical history	1	✓	✓	
	Healthcare contacts	2	✓	✓	
	Falls and near falls	2	✓	✓	
	Height, weight, weight 3–6 months ago	3	✓	✓	✓
	Health status question	1			✓
About the care	Relationship to recipient	1			✓
	Living with recipient	1			✓
	Intensity of caring and tasks of caring	2			✓
	Duration of caring	1			✓
Information about care recipient (if the patient is not participating)	Gender	1			✓
	Age	1			✓
	Living situation	1			✓
	Diagnosis	1			✓
	Year of diagnosis	1			✓
Nutritional risk	Seniors in the community: Risk Evaluation for Eating and Nutrition II–14 item version <sup>56–58</sup>	17	✓	✓	✓
Frailty	Survey of Health, Ageing and Retirement in Europe 75+ <sup>52</sup>	5	✓	✓	✓
Sarcopenia screen	SARC-F questionnaire <sup>54</sup>	5	✓	✓	✓
Covid-19 questions	Symptoms, self-isolation/shielding, access to care	13	✓	✓	✓
Lifestyle	Smoking	1	✓	✓	
	Alcohol intake	2	✓	✓	
	Physical activity	3	✓	✓	
Capability/well-being	ICEpop CAPability measure for Older People <sup>59</sup>	5	✓	✓ (proxy version)	
Quality of life	Parkinson's Disease Questionnaire-39 (PDQ-39) <sup>60</sup>	39	✓		

Continued

**Table 1** Continued

Metric	Data	Items	PPT +	PPT -	CG
Non-motor symptom burden	Non-Motor Symptom Questionnaire (NMSQ) <sup>61</sup>	30	✓		
Autonomic symptoms	Scales for Outcomes in Parkinson's disease-autonomic dysfunction <sup>62</sup>	25	✓		
Depression	Beck depression inventory-II <sup>63</sup>	21	✓		
Bowel function	Neurogenic bowel dysfunction score <sup>30</sup>	11	✓		
Urinary tract symptoms	International Consultation on Incontinence Questionnaire: ICIQ-mLUTS (for men) and ICIQ-fLUTS (for women) <sup>29</sup>	12 (female) 13 (male)	✓		
Cognition	Test Your Memory <sup>32</sup>	16	✓		
Motor symptom burden	Motor rating scale- adapted from Parveen <sup>33</sup>	4	✓		
Freezing of gait	New Freezing of Gait <sup>36</sup>	9	✓		
Patient activation	Patient Activation Measure <sup>64</sup>	13	✓		
Symptoms and behaviour	Neuropsychiatric Inventory <sup>65</sup>	12		✓	
Activities of daily living	Bristol Activities of Daily Living Scale <sup>38</sup>	20		✓	
Quality of life	Parkinson's Disease Questionnaire (PDQ) carer <sup>44</sup>	29			✓
Caregiver burden	Zarit Burden Interview <sup>66</sup>	22			✓
Caregiver activation	Caregiver Patient Activation Measure (CG-PAM)	13			✓
Caregiver coping strategies	Brief Coping Orientation to Problems Experienced (BriefCOPE) <sup>67</sup>	28			✓
Perceived social support	Multidimensional scale of perceived social support <sup>46</sup>	12			✓

CG, Caregiver participant; fLUTS, female short form Lower Urinary Tract Symptoms; mLUTS, male short form Lower Urinary Tract Symptoms; PPT-, Participant with parkinsonism without capacity to consent to research (questionnaires completed by a representative); PPT+, Participant with parkinsonism with capacity to consent to research.

symptoms are a common feature of PD dementia and can negatively impact caregiver burden,<sup>40</sup> hence particularly important to measure for participants with cognitive impairment. The questionnaire form of the Neuropsychiatric Inventory is a brief proxy-completed assessment.<sup>41</sup>

Measures which have not been validated for proxy report, or for which it would not be feasible for someone to complete on behalf of the patient, have not been included in the shorter patient questionnaire booklet for completion by a representative.

### Measures for caregivers

Several tools will be used to measure caregiver burden and experience. The number of hours spent caregiving will be captured using a grid which allows the caregiver to document the hours spent on each of four categories of tasks, which are based on the categories included within the Caregiver Indirect and Informal Care Cost

Assessment Questionnaire, developed by Landfeldt *et al.*<sup>42</sup> Caregivers can report the hours spent on each day of the week to account for the fact that their input may differ throughout the week.

The 21-item Zarit Burden Inventory is the most commonly used measure of caregiver burden among family caregivers of people with PD.<sup>43</sup> The PDQ carer has been specifically designed to measure quality of life among caregivers of people with PD<sup>44</sup> and will be used in this study.

The Brief Coping Orientation to Problems Experienced (Brief-COPE) is a frequently used coping scale and its subscales have been shown to predict distress and well-being.<sup>45</sup> The Multidimensional Scale of Perceived Social Support is a subjective assessment of social support.<sup>46</sup> Coping style may alter the way an informal caregiver deals with the challenges and stresses of caring and a caregiver's

perception that they have good social support may have a protective effect.<sup>43</sup>

### Measures used in all three groups

There is evidence to suggest that people with PD are at risk of weight loss and malnutrition.<sup>47</sup> Moreover, malnutrition is prevalent in older adults and is responsible for many significant health-related negative outcomes.<sup>48–50</sup> We will quantify nutrition risk using the Seniors in the community: risk evaluation for eating and nutrition, Version II (SCREEN-II) scale which is a valid and reliable tool to measure nutritional status.

Frailty is a syndrome of loss of physiological reserve which confers greater vulnerability to negative health outcomes; it is considered to be a dynamic condition in which individuals may transition to an improved, as well as more advanced, frailty state.<sup>51</sup> The Frailty Instrument for Primary Care of the Survey of Health, Ageing and Retirement in Europe (SHARE) is a phenotypic frailty assessment tool; in this study, we have opted to use the SHARE tool which was developed and validated in those aged 75 years and over, in which assessment of handgrip strength was substituted with a question about walking.<sup>52</sup> In the SHARE cohort, walking was assessed by a clinician; in this study, we have adapted the SHARE-FI75 +for self-reported completion. Sarcopenia, a disease characterised by low muscle strength, together with low muscle quantity or quality, may contribute to the development of physical frailty.<sup>53</sup> The SARC-F questionnaire is a rapid screening tool for sarcopenia<sup>54</sup> which will be used.

Caregivers are often older adults<sup>9</sup> and may themselves be living with frailty, sarcopenia and risk of malnutrition, hence the SARC-F, SHARE-FI75 +and SCREEN-II questionnaires will also be included in the caregiver questionnaire booklet, as well as the patient and representative-completed booklets.

In order to contextualise the responses to other questionnaires collected in this study, we have compiled some questions to gather information about any symptoms of COVID-19 infection experienced by participants, whether they have had to self-isolate or shield, and their experience of accessing care during the pandemic.

### Sample size

The sample size is pragmatic based on the total available number of potentially eligible people with parkinsonism at this single centre. There are approximately 1200 people with parkinsonism who are within the geographical catchment of the RUH Bath. The likely response rate is unclear but we anticipate we will achieve a response rate of over 40% which would result in 480 completed patient questionnaires.

A previous cross-sectional postal survey, with a response rate of 58.2%, noted a mean PDQ-39 summary index score of 44.6 (SD 17.6).<sup>55</sup> With a sample size of 480 we can estimate a mean PDQ-39 score with the following precision of approximately  $\pm 3.3$  points. This 95% CI range is sufficiently precise for descriptive purposes. Further

subgroups, for example, by age group and gender will be less precise.

### Statistical analysis

Results will be displayed as descriptive statistics using mean plus SD for normally distributed variables and median plus IQR for skewed variables. Multivariable linear and logistic regression models will be used to test simple associations. Our a priori hypotheses are that we will show worse health needs and greater disability with increasing age, disease duration and male gender. Other variables of interest include socioeconomic status, geography (urban–rural), and ethnicity (though we have limited numbers of ethnic minorities in this catchment area so will be underpowered). We are specifically interested to test how these factors could potentially interact with each, using goodness of fit or likelihood ratio tests. We will also examine if other covariates such as multimorbidity could act as potential mediators. For example, men with similar disease duration may have greater disability partially due to a greater burden of cardiorespiratory disease. Since these are exploratory subgroup analyses, we are cognisant of the potential for type 1 error due to multiple testing.

Where possible, we will follow the recommendation of the questionnaires' authors for how to deal with missing questionnaire responses, for example pro rating the score, where appropriate. We will explore which factors predict the missing variables and then use multiple imputation methods, assuming these are 'missing at random' to combine the effects over 10 simulated datasets and incorporating uncertainty using Rubin's rules. This will allow us to conduct a sensitivity analysis to compare the complete case with the imputed results.

### Limitations

Despite our efforts to reduce barriers to participation, in order to recruit a representative sample of people with parkinsonism, there will inevitably be some non-response bias. We also acknowledge that the region around RUH Bath is not ethnically diverse. Additionally, some recruited participants may not complete and return all questionnaires, although we aim to minimise missing data by following up any queries by telephone. Finally, this study only assesses symptomatology using questionnaire-based measures; there would be benefit to triangulating these self-reported measures with digital measures in the future.

### Patient and public involvement statement

This study has been designed and performed in conjunction with the study public involvement advisory group (PIAG), all of whom have PD. The PIAG been critical to the design and content of participant information leaflets and consent forms. Changes made as a result of their valuable contribution include:

- ▶ Improved sensitivity around terminology for those who care for someone with PD, acknowledging that they may live with someone who has PD but not see



themselves as a carer/caregiver, but may 'provide support'. The term 'caregiver' was preferred over 'carer' and therefore used throughout the study documentation.

- ▶ Inclusion of an approximate time to complete the questionnaires in the participant information leaflet and we further emphasised that the questionnaires are intended to be completed at home
- ▶ Inclusion of information for plans regarding dissemination of results to participants.

### Ethics and dissemination

This protocol was approved by the London—Brighton & Sussex Research Ethics Committee on 27 July 2020 (REC reference 20/LO/0890). It is registered with the ISRCTN (11452969).

All participants will either provide written informed consent or, in the case of patient participants who lack capacity to consent to participation in the study, a consultee will provide advice on their prior wishes and will sign a consultee declaration if they believe the patient would be willing to participate.

If the person with parkinsonism has opted not to participate themselves, it is necessary, so far as possible, for us to collect some basic information about who the caregiver supports. In this case, the person with PD (or their personal consultee if they lack capacity to make decisions about the study) is asked to sign a section on the back of the caregiver consent form if they are happy for their caregiver to provide basic information about them.

Participants can choose to withdraw for any reason at any time during their involvement in the study and will not be followed up after withdrawal from the study. They will be asked their reason for withdrawal but do not have to provide this. Data collected up to the time of withdrawal will be used.

We plan to publish the results of this protocol in an international peer-reviewed journal and at academic national and international meetings and conferences. When we share the results of key findings, we will upload a lay summary to the PRIME-Parkinson website.

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**Contributors** ET, FEL, YB-S and EJH were responsible for the concept of the study and contributed to study development and design. ET, DP-B and MDS contributed to patient recruitment. ET drafted the manuscript and all authors provided critical revision and approved the final protocol.

**Funding** This work was supported by the Gatsby Charitable Foundation, grant number 3676.

**Competing interests** EJH received funding from the National Institute of Health Technology (NIHR), the Gatsby Foundation and Parkinson's UK; received fees for speaking and consultancy from Profile pharma Medicycs and Luye; and received travel support from Bial Abbvie and Ever pharma. YB-S is a recipient of a Radboud Excellence award. He has received research support from the UK Medical Research Council, Wellcome Trust, NIHR, Parkinson's UK, vs Arthritis, Gatsby Foundation, Dunhill Trust, and received a Radboud Excellence Award.

**Patient and public involvement** Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

**Patient consent for publication** Not applicable.

**Provenance and peer review** Not commissioned; externally peer reviewed.

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