Live Well With Parkinson's

As part of the Personalised Care for People with Parkinson's: PD-Care programme grant

Co- Chief Investigator:
Professor Anette Schrag

Co-Chief Investigator:
Professor Kate Walters

Supported by:
RP-PG-1016-20001

Sponsored by:
Royal Free London NHS Foundation Trust

Protocol Version: V1.4

R&D / Sponsor Reference Number(s):
142053

PROTOCOL VERSIONS

Version Stage Draft	Versions No	Version Date	Protocol updated & finalised by;	Appendix No detail the reason(s) for the protocol update
Current	V1.0	25/06/2021	MA, JR, AS, KW	**Protocol for RCT**
Following REC review	V1.1	01 09 21	MA, AS, KW	**Amended following REC review**
Amendment	V1.2	23 02 22	MA, AS, KW	**Amended following additional funding to enhance process evaluation**
Amendment	V1.3	11 11 22	CF, TR, AS, KW	**Amended process evaluation timeline, saliva sample collection timepoints and additional sites.**
Amendment	V1.4	23 03 23	CF, AS, KW, AK	**Amended Outcomes Schedule to include reaching out by post to Participants we have been unable to contact, sending a reduced Assessment Pack and reply slip to complete and return before we mark 'lost to follow-up'**

SIGNATURES

The investigators and Priment have discussed this protocol. The investigators agree to perform the investigations and to abide by this protocol.

The investigators agree to conduct the trial in compliance with the approved protocol, GCP, the UK Data Protection Act (2018), any applicable EU/UK amended acts to the Data Protection regulation, the Trust Information Governance Policy (or other local equivalent), the UK Policy Framework for Health and Social Care Research, Priment's SOPs, and other regulatory requirements as amended.

Co-chief Investigator Professor Anette Schrag		25th June 2021
	Signature	Date
Co-chief investigator Professor Kate Walters		25th June 2021
	Signature	Date

STUDY SUMMARY

Identifiers	
IRAS Number	294372
REC Reference No	21/LO/0562
Sponsor Reference No	142053
Funder Reference No	NIHR PGfAR - RP-PG-1016-20001
ClinicalTrials.gov and/ or ISRCTN	Awaiting approval at clinicaltrials.gov. ISRCTN: 92831552
Full (Scientific) title	Live Well with Parkinson's (as part of the program Personalised care for people with Parkinson's Disease: PD-Care WP4)
Health condition(s) or problem(s) studied	Parkinson's
Study Type i.e., Cohort etc	Following completion of an evidence synthesis, qualitative study, co-design of intervention and feasibility study, this protocol focuses on a randomised-controlled trial of effectiveness and cost-effectiveness and process evaluation of the intervention This programme of research is based on the MRC framework for complex interventions.
Target sample size	338 patient participants, and their informal (unpaid) carers for the RCT. Process Evaluation will use participants (n=35) who received the treatment intervention.
STUDY TIMELINES	
Study Duration/length	36 months
Expected Start Date	01/08/2021
End of Study definition and anticipated date	(Total programme) 01/03/2024
Key Study milestones	Internal pilot commencing 01/08/2021 Main participant recruitment commencing 01/02/2022 Data analysis and process evaluation starting 01/08/2023
FUNDING & Other	
Funding	NIHR PGffAR: RP-PG-1016-20001
Other support	
STORAGE of SAMPLES (if applicable)	Saliva samples will be stored at the neurogenetic laboratory at the Institute of Neurology until used in future ethically approved study.
Data collected / Storage	Questionnaire and interview data will be de-identified and stored in accordance with 2018 General Data Protection Regulation (GDPR).
KEY STUDY CONTACTS	
Chief Investigators	Professor Anette Schrag Department of Clinical and Movement Neurosciences UCL Institute of Neurology Royal Free campus U3, Rowland Hill Street, London NW3 2PF Tel: 020 8016 8135 Professor Kate Walters Department of Primary Care and Population Health UCL Royal Free Campus Rowland Hill Street London NW3 2PF Tel: 0208 016 8039

KEY ROLES AND RESPONSIBILITIES

SPONSOR: The sponsor is responsible for ensuring before a study begins that arrangements are in place for the research team to access resources and support to deliver the research as proposed and allocate responsibilities for the management, monitoring and reporting of the research. The Sponsor also has to be satisfied there is agreement on appropriate arrangements to record, report and review significant developments as the research proceeds, and approve any modifications to the design.

FUNDER: The funder is the entity that will provide the funds (financial support) for the conduction of the study. Funders are expected to provide assistance to any enquiry, audit or investigation related to the funded work.

CHIEF INVESTIGATORS (CI): Professor Anette Schrag, UCL and Professor Kate Walters, UCL
The person(s) who takes overall responsibility for the design, conduct and reporting of a study. If the study involves researchers at more than once site, the CI takes on the primary responsibility whether or not he/she is an investigator at any particular site.

The CI role is to complete and to ensure that all relevant regulatory approvals are in place before the study begins. Ensure arrangements are in place for good study conduct, robust monitoring and reporting, including prompt reporting of incidents, this includes putting in place adequate training for study staff to conduct the study as per the protocol and relevant standards.

The Chief Investigators are responsible for submission of annual reports as required. The Chief Investigators will notify the RE of the end of the study, including the reasons for the premature termination. Within one year after the end of study, the Chief Investigators will submit a final report with the results, including any publications/abstracts to the REC.

PRINCIPLE INVESTIGATOR (PI):
Individually or as leader of the researchers at a site; ensuring that the study is conducted as per the approved study protocol, and report/notify the relevant parties – this includes the CI of any breaches or incidents related to the study.

OTHER collaborators:

Full Name	Professor Richard Brown
Organisation	King's College London
Full Name	Professor Jill Manthorpe
Organisation	King's College London
Full Name	Professor Kallol Ray Chaudhuri
Organisation	King's College Hospital NHS Foundation Trust
Full Name	Professor Elizabeth Murray
Organisation	University College London
Full Name	Dr Benjamin Gardner
Organisation	King's College London
Full Name	Miss Rachael Hunter
Organisation	University College London
Full Name	Dr Gareth Ambler
Organisation	University College London
Full Name	Dr Daniel Davis
Organisation	University College London
Full Name	Mrs Rachel Leuw
Organisation	Royal Free London NHS Foundation Trust
Full Name	Dr Nathan Davies
Organisation	University College London
Full Name	Mrs Beverley Maydon
Organisation	Royal Free London NHS Foundation Trust
Full Name	Catherine Atkinson
Organisation	Homerton University Hospital NHS Foundation Trust

KEY WORDS

Parkinson's, personal care plan, evidence-based supported self-management intervention, Live well with Parkinson's' toolkit, Long Term Conditions (LTCs).

LIST OF ABBREVIATIONS

AE	Adverse Event	PI	Principle Investigator
AR	Adverse Reaction	PD-QOL	Parkinson's disease quality of life
CACE	Complier Average Cause Effect	PDNS	Parkinson's disease nurse specialist
CI	Chief Investigator	PIS	Participant Information Sheet
CRF	Case Report Form	PPI	Patient & Public Involvement
CRO	Contract Research Organisation	PSC	Programme Steering Committee
CSRI	Client Service Receipt Inventory-shortened, adapted for Parkinson's	PSS	Personal Social Services
DMC	Data Monitoring Committee	PUK	Parkinson's UK Charity
EPDA	European Parkinson's Disease Association	PWP	Person with Parkinson's
EQ-5D-5L	Quality of life measure	QA	Quality Assurance
GCP	Good Clinical Practice	QALY	Incremental cost per quality adjusted life year
GDPR	General Data Protection Regulation	QC	Quality Control
GAfREC	Governance Arrangement for NHS Research Ethics	RCT	Randomised Controlled Trial
IB	Investigator Brochure	REC	Research Ethics committee
HCP	Healthcare professional	SAR	Serious Adverse Reaction
ICECAP-O	Capability measure	SAE	Serious Adverse Event
ICF	Informed Consent Form	SDV	Source Data Verification
ISRCTN	International Standard Randomised Controlled Studies Number	SOP	Standard Operating Procedure
GHQ12	General Health questionnaire: Short form	SSI	Site Specific Information
LCRN	Local Clinical Research Network	TAU	Treatment as usual
MDS-UPDRS	Movement Disorders Society-Unified Parkinson's Disease Rating Scale	UCL	University College London
MOCA	Montreal Cognitive Assessment test	VPN	Virtual Private Network
MRC	Medical Research Council		
NICE	The National Institute for Health and Care Excellence		
NMSS	Non-Motor Rating Scale		

Contents

1. BACKGROUND AND RATIONALE

Parkinson's is a progressive neurodegenerative disorder, causing motor disability, reduced mobility, and falls. It is associated with a complex range of disabling and distressing non-motor symptoms (NMS) including dementia and cognitive impairment, apathy, depression/anxiety, psychosis, bowel/bladder dysfunction, fatigue, sleep problems and pain. Parkinson's is the second most common neurodegenerative disorder affecting around 127,000 people with the condition in the UK, and one in 50 of people over 65 years [1]. The annual costs to the NHS of Parkinson's are conservatively estimated at ~£13,804 per person, not including cost borne by people themselves or their family, local authority care or loss of employment [2]. The numbers affected and associated costs are increasing with the ageing of the population and predicted to double by 2030 [3].

The complexity of motor and non-motor morbidity results in an increased need for specialist services as well as primary care services and hospitalization with disease progression [4]. However, due to this complexity of Parkinson's, the treatment of common symptoms is difficult for non-specialist health professionals, such as General Practitioners (GPs). Parkinson's specialist nurses can provide an important access point for people with Parkinson's between scheduled hospital appointments and primary care attendances, but with large caseloads (300+ patients) their time and capacity can be limited. The lack of time and resources coupled with people with Parkinson's failing to report their deterioration, leads to complications due to Parkinson's often going unidentified until severe [5, 6]. Parkinson's is associated with 45% increased risk of hospital admission and longer stays than others of the same age [7]. Admissions are also associated with hospital acquired infections and other complications, errors and delays in timely administration of medications and increased mortality [7, 8]. In-patient deterioration typically takes a considerable time to reverse after discharge, with an increased rate of subsequent care home moves with associated social care and personally borne costs [9].

Many aspects of Parkinson's can be treated or usefully managed before they become severe problems, if recognised and managed appropriately. Management guidelines exist but are primarily aimed at secondary care and not always accessible or applicable in non-specialised settings. Therefore, appropriate advice may not be given, or referrals made, and medication may remain unchanged. Many patients are not aware of information on locally available services, such as Parkinson's UK branch meetings, peer-mentoring groups, exercise classes, or self-referral to psychological therapies. Personalised care was therefore identified as a clear priority in a survey of the European Parkinson's Disease Association [10]. Dopamine replacement and other therapies are highly effective at reducing symptoms in people with Parkinson's, at least initially, but can lead to complications, both motor and non-motor. These increasing complications of fluctuations, reduced mobility, pain, autonomic function, sleep, and mental health problems including impaired cognition leads to increasing disability, reduced quality of life and higher carer burden [11, 12].

Increasingly, patient or carer participation in management (i.e., self-management) is incorporated into health care for long-term conditions (LTCs), as this can allow people to take control and improve outcomes in the face of restricted resources and fragmentation of health care. The current policy direction of the NHS (e.g., NHS Long-term Plan) emphasises self-management [13]. Interventions to support self-management include education, psychological support, strategies to support adherence to treatment and

tailored practical support, including liaison with health care professionals and other agencies [14]. There is evidence that supported self-management for LTCs can be clinically effective, decrease health care utilization and does not compromise patient outcomes [15]. To date, there has been relatively little done in this area for people with Parkinson's, although some community interventions, such as support groups and peer mentoring have shown potential benefit [16, 17].

Not all self-management programmes have been successful in reducing disease burden and health care utilisation with the reasons for effectiveness unclear [18]. Important factors for success of self-management solutions include costs, motivation, expectations, cultural and social factors such as family support [19, 20]. It is therefore important for new interventions to address these factors and apply a robust framework for intervention development such as the Medical Research Council (MRC) framework for complex interventions [21]. Whilst effect sizes may be modest in self-management programmes (8), small differences can be clinically meaningful in preventing important adverse outcomes and interventions tend to be low cost and can thus be overall cost-effective. This is particularly relevant as with an ageing population, access to specialist resources may be increasingly constrained.

Information and advice are available from charities such as Parkinson's UK [22], who also support local Self-Management Programme/Peer-support groups. In the US, there are ongoing evaluations of proactive individual management approaches and social self-management in Parkinson's [23]. However, there is currently no effective comprehensive personalised self-management tool designed for use in the NHS to support people with Parkinson's, their carers and health professionals (both specialist and non-specialist) in the overall management of both motor and non-motor aspects of the condition.

The Live well with Parkinson's toolkit developed through the PD-Care research study bridges existing gaps in the NHS (as shown by the national Parkinson's audit data [24]), by enabling patients and carers to access personalised information, advice and support on symptom management and 'living well' with Parkinson's. It includes information on available resources and coordination of their care, supported by evidence based guidelines. The process used in development and evaluation will help ensure that it is practical, acceptable, and clinically and cost-effective for the NHS and its partners. If successful, the tool could potentially be used as a model for other complex long-term disorders, including dementia.

2. SUMMARY OF WORK TO DATE

This application is linked to IRAS application 235545, REC 18/LON/1470 and is the fourth work package of a five-year Programme Grant.

In the first three work packages of our programme we have developed a comprehensive evidence and theory-based intervention ('Live Well with Parkinson's) to support self-management in people with Parkinson's, informed by three systematic reviews of effectiveness and patient perspectives, qualitative research and a rigorous co-design process partnering with key stakeholders.

The research team has been working closely with a group of people affected by Parkinson's to:

1. Systematically review the evidence for self-management in Parkinson's and similar conditions and other management guidelines for Parkinson's.
2. Conduct a qualitative study exploring with people with Parkinson's, carers, health and care professionals their experiences and goals for Parkinson's care and self-care.
3. Bring together the expertise of health and care practitioners, people with Parkinson's and carers to jointly design a self-management toolkit and a training programme for professionals to support the use of the toolkit.
4. Test whether this toolkit is practical and acceptable for people to use in our feasibility study and adjust where necessary.

The first systematic review explored patients' perspectives of self-management interventions in Parkinson's and identified key components for our intervention (e.g., self-monitoring tools and psychological strategies) [25]. Our second systematic review explored how effective these components appeared to be and found that overall evidence to date for the effectiveness of self-management in Parkinson's to date is mixed with very few large scale high quality studies. A further additional systematic review explored Advanced Care Planning in Parkinson's as this was highlighted as a challenging area and identified some principles of good practice [26]. In our qualitative research we conducted interviews with 22 people with Parkinson's, 15 family carers and interviews and focus groups with 42 HCPs from a broad range of backgrounds and professions. These identified a key set of important features to include within the intervention. These reviews combined with a review of the key components of relevant clinical guidelines for the management of Parkinson's, our own primary evidence from HCPs and people with Parkinson's and their carers led to the development of a comprehensive self-management toolkit (see details in intervention section below).

We are now nearing completion of a successful feasibility study which recruited (n=35) to target, with excellent retention. Early findings from our process evaluation of the feasibility study have shown the intervention to be well-received and has given suggestions for optimising aspects of the intervention content and delivery. In this current application we now want to proceed to our definitive clinical trial to test whether the self-management toolkit we have developed makes a positive difference to the health and lives of people with Parkinson's and how cost-effective the approach would be if adopted by the NHS and its partners. We will further identify the resources needed to enable this approach to be rolled out across the NHS if it proves effective.

3. OBJECTIVES

The study objectives are to evaluate the effectiveness and cost-effectiveness of the "Live Well with Parkinson's" facilitated self-management toolkit, which aims to enable personalised care for community-living people with Parkinson's, to reduce disability and preventable hospital admissions and to improve quality of life.

The specific objectives are to:

1. Determine the clinical effectiveness of the 'Live Well with Parkinson's' intervention (facilitated self-management toolkit) through a definitive Randomised Controlled Trial, with internal pilot.
2. Determine the cost-effectiveness of the intervention from the perspective of the NHS and personal social services.
3. Determine the factors promoting or inhibiting implementation of the toolkit in the NHS.

4. TRIAL DESIGN

- Single-blind two-arm randomised-controlled trial (RCT) of effectiveness and cost-effectiveness
- Mixed methods process evaluation.

The RCT will follow the MRC framework for development and evaluation of complex interventions. The study will test clinical and cost effectiveness in improving function and quality of life and reducing unplanned hospital admissions in people with Parkinson's. Alongside this a comprehensive process evaluation will be conducted.

5. INTERVENTION AND CONTROL

5.1 Intervention

Treatment as usual (TAU; see below) plus a manualised intervention (i.e., supporter sessions and access to 'Live Well with Parkinson's' toolkit).

Toolkit

The toolkit was co-designed with people with Parkinson's, carers, health and social care professionals and Parkinson's disease experts. It is based on evidence from effective health promotion interventions and incorporates theory-based behaviour change techniques. The research team conducted three systematic reviews synthesising evidence on self-management techniques for people with Parkinson's and explored the barriers and facilitators of using them. We interviewed with people with Parkinson's, carers, and health care professionals to explore the challenges people with Parkinson's and those that support them face. Combining this evidence with key components of clinical guidelines and a series of co-design workshops and user testing led to the development of the toolkit of potential strategies, drawing on theory and evidence-based techniques, to help overcome the challenges people with Parkinson's face and to support them to live independently.

The key theories the toolkit draws upon are:

1) **Person-centred care:** working in partnership with the participant to develop a plan to address their needs or priorities.
2) **Self-management:** teaching participants to actively identify challenges and solve problems associated with their illness themselves with support.
3) **Behaviour change model**: This suggests that all behaviours depend on the presence of three core determinants: capability, opportunity, and motivation. Therefore, any changes the participant would like to make to their behaviour must incorporate those three components.

UCL Royal Free London NHS Foundation Trust | NHS FUNDED BY NIHR | National Institute for Health Research | Priment Clinical Trials Unit

4) **Asset based approached**: By encouraging participants to focus on their assets (i.e., what they enjoy and can do) as opposed to their deficits (i.e., what they can't do) may encourage some to maintain the positive behaviours.

The toolkit consists of 64 information sections on what Parkinson's is, symptoms, therapies/treatments, optimising wellbeing, and practical advice which were identified as important in co-design with people affected by Parkinson's and experts in the area. Each content section has been through review by two members of the team, an expert in the specific area and by PPI team members, and subject to 'readability' review.
The toolkit also comprises personalised sections on the following:

- About Me – including information on their contacts, support and planning future care.
- My Health – including information on their health conditions, medication, treatments, and research involvement.
- Symptom Review – a list of symptoms they experience and the severity of them. This will allow the participants to identify and explore the symptoms they are experiencing.
- My Wellbeing – to identify health behaviours they would like to maintain or improve.
- My Tracker – to track medications, activities, and symptoms. This section allows participants to identify patterns and specialists to get a better idea of what participants are experiencing.
- Appointments/calendar - In our co-design process, participants asked for a calendar within the toolkit, so that all their healthcare appointments could be stored in one place.
- To do lists/Notes – a way to note or list anything that participants feel is useful.

Both the paper and online version can be shared with participants' carers and HCPs if they wish. Participants can share the whole toolkit or select sections.

Intervention supporter sessions

Participants, and, if the participants would like, the carer, will receive around four (up to six if needed) sessions over six months led by a 'supporter'. The supporter will be a trained professional with a background in healthcare (e.g., psychology, occupational therapy, nursing), social care or third sector (e.g., care navigation, social prescribing) with some experience of working/caring for people with Parkinson's and will receive training to deliver the intervention. The sessions will be around 60-90 minutes for the first two sessions and around 30 minutes for the remaining sessions. The aim of the sessions is to encourage the participants to self-manage their condition by using the 'Live well with Parkinson's' toolkit. The supporter will follow a manual and checklists covering support navigating the toolkit, understanding the benefits of using the different sections and assist in the creation of wellbeing priorities (goals) and use behaviour change techniques to help implement priorities long-term. These sessions will be conducted online via Zoom, by telephone or face-to-face when appropriate.

5.2 Control

The control will be TAU: as confirmed in our feasibility study, usual care from existing sources (GP, Parkinson's specialist service +/- NHS PDNS). Treatment as usual in the current NHS, is delivered by primary care together with secondary care (neurology and geriatrics) consultations every six to 12

months, with a PDNS where available who provides information, reviews, and a telephone service for queries between appointments. Referrals to other specialties, therapists (physiotherapy, occupational therapy, speech and language therapy, social care services etc.) are made as appropriate.

6. TRAINING AND SUPERVISION

The Chief Investigators will review and provide assurances of the training and experience of all staff working on this study. Appropriate training records will be maintained in the study files. All staff will be GCP trained. Research assistants (RA) will be trained and experienced in assessing capacity and interviewing people with Parkinson's, including those with dementia, and will be offered appropriate support and supervision. The supporters used in the delivery of the toolkit will receive appropriate support and training including on Parkinson's, the toolkit, behaviour change, motivational interviewing, and goal development. Furthermore, the supporters will receive group fortnightly supervision of around 30 minutes. If a fortnightly session is not needed, the supporters will provide an email update.

7. STUDY SCHEDULE

The trial will be conducted over 36 months and include a six-month internal pilot.

1. RCT site initiation/training (m.1-2)
2. Internal Pilot RCT (m.3-8)
3. Main RCT participant recruitment to the two-arm individually randomised RCT comparing Live Well with Parkinson's with treatment as usual (TAU) (m.8-20)
4. Follow-up complete (m.32)
5. Process evaluation (m.12-34)
6. Main RCT analysis (m.32-34)
7. Health Economic Analysis (m.32-34)
8. Study closure, reporting, dissemination (m.34-36)

8. OUTCOME ASSESSMENTS

Assessments will take place at a venue agreed with the participant and researcher, which may be clinic (hospital), GP practice, their home or virtually using a video conference platform (e.g., Microsoft Teams, zoom or similar technology) and by telephone if face to face is not possible due to the Covid pandemic. Virtual assessments by a combination of telephone, self-completion questionnaires and using a video-conference platform were acceptable and feasible for participants in our feasibility study, conducted during the pandemic. People with Parkinson's will be assessed face-to-face at baseline and 6 and 12 months, where this is possible. For baseline and follow-up visits questionnaire data will be collected over the telephone or by self-completion and returned by post for those unable to meet with researchers face-to-face, for example to reduce exposure risk to Covid-19. Assessors will be blind to treatment group. Measurements are detailed below (Table 1).

Outcome measurements have been chosen to capture important domains that might change with the intervention, including potential mechanisms (e.g., self-efficacy), using the best valid and reliable

measures available, with shorter instruments chosen where possible to reduce participant burden. The outcome assessments will take approximately 90 minutes to complete. This length has been acceptable to participants in our previous studies with similar populations [27], and for participants in our feasibility study (n=35 participants).

8.1 Primary Outcome

Parkinson's Disease Questionnaire (PDQ-39) [28] score change at 12 months between the two groups. PDQ-39 is a valid and reliable measure of quality of life, widely used in Parkinson's trials. A change in -4.72 and +4.22 is considered the minimal clinically important difference on the PDQ39 [29].

8.2 Secondary outcomes

From people with Parkinson's:

- Movement Disorders Society - Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part I and II [30]
- Quality of life (EQ-5D-5L, 5 items and visual analogue scale) [31]
- Off-time, MDS-UPDRS part 3 (motor), part 4 (motor-complications) and total score [30]
    - Videorecording of the administration of motor components of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) to validate ratings, to evaluate inter-rater reliability, improve accuracy and facilitate remote delivery. We will use 'KELVIN - PD' (https://machinemedicine.com/kelvin-pd/) a platform that assesses the videos as it records. KELVIN-PD is fully GDPR compliant and has been used in UCL and Royal Free NHS studies.
- Non-Motor Rating Scale (MDS-NMS) [32]
- Psychological well-being (GHQ12, 12 items) [33]
- Self-efficacy (Self-Efficacy for Managing Chronic Disease 6- Item Scale) [34]
- Capability (ICECAP-O, 5 items) [35]
- Patient Activation Measure (PAM) [36]
- Medication, deaths, health/social care resources, out of pocket costs, financial impact on carers, welfare payments and living arrangements (Client Service Receipt Inventory-shortened, adapted for Parkinson's from iMTA Valuation of Informal Care Questionnaire (iVICQ)[37, 38]

Health economic evaluation will include incremental cost per quality-adjusted and capability-adjusted life year gained from i) health/social care perspective and ii) societal perspective and a decision-analytic model extrapolating costs/consequences beyond the trial.

8.3 Outcomes for carers

- Zarit carer burden inventory (22 items) [39]
- Carer Quality of Life questionnaire for Parkinsonism (26 items) [40]

8.4 Ancillary Studies

Participants will be given the opportunity to donate a saliva sample for genetic analysis for use in future Parkinson's research unrelated to the aims of the current study. This is completely voluntary, and it will be emphasised that their participation in the main trial is not dependent on donating a saliva sample. They will also be given the opportunity for the data or samples to be destroyed if consent is withdrawn. Participants will be asked to give consent for future contact by the trial investigators for further information or consent for use of their saliva sample, or for further studies on long-term follow-up of trial outcomes.

Saliva samples will be collected using a compact self-collection kit, including an instruction sheet following manufacturer's instructions for use. Samples will be labelled with unique study code and stored at room temperature until secure delivery to the central laboratory. Due to sample stability there are no critical time frames for delivery to the laboratory for analysis.

In addition, to assess changes in motor function better, electronic measurements, which have been proposed as more accurate than clinical judgment on rating scales, are included as optional assessments. A wearable movement sensor, 'GENEActiv' (https://www.activinsights.com/actigraphy/geneactiv-original/), will be provided to the participant after their assessment and worn on the participant's wrist for 7-days. It will then be returned in the post in a provided stamped addressed envelope. All data collected will be anonymous and linked to the participants unique study code.

8.5 Outcome assessment schedule

Outcomes will be collected at baseline, 6-month follow up and 12-month follow up, ideally within +/- two weeks of this date. Participants will be contacted by the researcher to arrange a date and time suitable to them to collect the outcome assessments. We will attempt to contact the participants two times via phone or email to arrange this. If we cannot get hold of them, we will make a final contact through the post, attaching an Assessment Questionnaire Pack to complete and a reply slip to confirm if they want to continue or withdraw from the study. If no reply to this action, they will be marked 'lost to follow-up'. Please see table 1 for a detailed schedule.

Table 1: Outcome assessment schedule

	Baseline	6 months	12 months
People with Parkinson's			
Informed Consent	X		
Socio-demographic characteristics	X		
Montreal Cognitive Assessment test (MoCA) Version validated for phone administration	X		
Patient Activation measure (13 items)	X	X	X
Unified Parkinson's Disease Rating Scale (MDS-UPDRS)	X	X	X
Non-Motor Rating Scale (MDS-NMS)	X	X	X
EQ-5D-5L (5 item VAS)	X	X	X
General Health Questionnaire (GHQ12 - 12 items)	X	X	X
PDQ-39 (39 items)	X	X	X
Client Service Receipt Inventory-shortened, adapted for Parkinson's (CSRI)	X	X	X
Self-Efficacy for Managing Chronic Disease (6- Items)	X	X	X
ICECAP-O, (5 items)	X	X	X
Saliva sample	X	X	X
Motion sensor	X	X	X
Carers			
Informed Consent	X		
Socio-demographic characteristics	X		
Zarit carer burden inventory (22 items)	X	X	X
Carer Quality of Life questionnaire for Parkinsonism (26 items)	X	X	X

*note: saliva samples will only be collected once from each consenting participant, but this can be done at any 3 of the timepoints.

9. PROCESS EVALUATION

The work package will explore the factors promoting or inhibiting implementation, uptake, use, effectiveness and cost-effectiveness of the toolkit and sessions.

Acceptability and implementation

Questionnaires with all intervention participants n=169 and their carers to assess acceptability of service, utilisation, barriers/facilitators to implementation and recommendations.

Semi-structured qualitative interviews with a purposive sample of those receiving the intervention (including up to 35 people with Parkinson's and their carers), and service providers (all supporters providing the intervention across the sites). Fifteen of the participants taking part in the qualitative interviews will be from underserved groups (e.g., ethnic minorities, low socioeconomic status groups, etc.) These will explore in greater depth the context, mechanisms and implementation of the intervention following the MRC process evaluation guidelines (88). Participants will be purposively selected by an unblinded researcher for maximum diversity across disease severity, involvement of a carer, attitudes to the Live well with Parkinson's toolkit, receipt of paper or electronic version of the toolkit, use of the intervention/number of follow-up appointments, and socio-demographic characteristics (age, gender, education level and ethnic group). All supporters will be approached for interview. Interviews will explore important contextual factors that impacted on how the intervention was used, perceived impact and potential mechanisms of impact, and factors that affected the implementation of the intervention in routine care. Interviews will take place at a venue agreed with the participant and researcher. This may be clinic (hospital) GP practice, their home or using remote (videoconference or telephone) methods.

Fidelity

Audio-recording of intervention appointments, with a random sample of 10% of participants selected and assessed for fidelity to the intervention (what they received compared to that intended), assessed against a checklist of intervention content. Participants do not have to agree to their sessions being audio recorded to take part in the study and will be verbally consented each time.

Checklists completed after the session by the supporters will inform fidelity to the intervention manual and implementation.

Reach

Quantitative data on participation collected from study sites on the uptake of the intervention from those eligible (numbers agreeing to participate from those approached, reasons for non-participation), the characteristics of participants in comparison to that known in the eligible population (socio-demographic and disease severity, extent of carer involvement) via other published studies on this population. This data is to answer the questions: i) Did the intervention reach the intended population? ii) Were there any groups that participated less? (e.g., those without a carer).

Dose

Quantitative data on the 'dose' of the intervention: number/length of intervention appointments received by those in the intervention arm; online activity/use of the electronic version of the toolkit, data

from the questionnaire in item 1) on use of the toolkit, including creating and working towards well-being priorities.

10.ELIGIBILITY CRITERIA

10.1 Inclusion Criteria

- Community-dwelling adults (i.e., 18 and above) with a confirmed diagnosis of Parkinson's Disease, (defined using UK Brain Bank Criteria [41]), including those with dementia diagnosed at least one year after their Parkinson's diagnosis.
- Able to engage in the intervention and study assessments, if participant does not have a carer or family member.

10.2 Exclusion Criteria

- A clinical diagnosis of Atypical Parkinsonism
- Currently an inpatient or living in a care home
- Lack of capacity to take part (MoCA <11) [42]
- Unable to engage in the intervention due to visual impairment or language barriers (and no carer or family member to support them to engage)
- Life expectancy <6-months
- Participation in another clinical trial/study that is likely to impact or interfere with the PD Care intervention.

11.RECRUITMENT

11.1Recruitment calculations for RCT

To detect a 4.7 point difference in PDQ-39 with 90% power and 5% significance, 135 participants per arm are required, assuming a SD of 19.8 and a correlation between baseline and follow-up measurements of 0.8. Allowing for 20% attrition at 12 months increases the total to 338 people with Parkinsons. Participants (n=338) (PwP and their carers as one unit) will be recruited through secondary and primary care; based on previous successful recruitment of people with Parkinson's through neurology and care of the elderly clinics, PDNSs, and older, frailer people from primary care [27]. The study will collaborate with Parkinson's UK for recruitment, (www.parkinsons.org.uk), as in other large trials and recruitment will also be carried out through carers networks, social media, and snowballing approaches.

The following assumptions have been used to estimate the recruitment rate: Annual attendance at Parkinson's clinic (per Hospital site) = 400-600 people. Average number of people with Parkinson's in GP practices=20 people [43]. Each PDNS typically supports>300 patients, so there is a large pool of potentially eligible participants. Recruitment period six months for pilot wave, then 12 months for subsequent waves (18 months total). To achieve target N=338, the study will aim to recruit 19 people

per month over 18 months across all sites. Assuming 8 hospital sites and 34 GP practices, and recruitment of 60% of our sample from hospital and 40% from primary care, the RCT will need recruitment of 25 people with Parkinson's per hospital site and 4 people per GP practice over 18 months. Assuming an uptake of 30% of people approached, the study will need to approach 113 people per hospital site, and 13-14 people per GP site. Response rates/accruals from earlier work packages including the feasibility study has confirmed this is achievable.

11.2 Recruitment sites

The *Live well with Parkinson's* toolkit developed by the PD-Care study is intended to be widely applicable to people with Parkinson's and their carers, and therefore recruitment methods will ensure that a representative population is reached. Community-dwelling people with Parkinson's and their carers (where applicable) will therefore be recruited from sites in London, East of England, the Southeast, South West, the Midlands and Yorkshire. Study sites include Royal Free Hospital, Barnet Hospital, Chase Farm, Homerton Hospital, Luton and Dunstable Hospital, Kings College Hospital, Lewisham Hospital, Hertford County Hospital, Hertford, Lister Hospital, Stevenage and the New QEII hospital, Welwyn Garden City, North East London Foundation Trust, Cornwall Partnership NHS Foundation Trust, Central London Community Healthcare NHS Trust, and Bradford Teaching Hospitals NHS Foundation Trust; research registry of National Hospital Neurology & Neurosurgery (NHNN), and community settings via North Central London Research consortium (General Practice Research Clusters via NoCLoR), (GP research practices in Camden, Islington, Barnet, Enfield, Haringey and Redbridge), and General Practices recruited through the Eastern CRN, North West London CRN, North Thames CRN, West Midlands CRN, Yorkshire and Humber CRN, South West Peninsula CRN, and South London CRN. Further potential sites have been identified (Edgware Hospital, Bedford Hospital, The London, Southend Hospitals) and there is the capacity to extend recruitment to other sites (both hospital and primary care) if needed. Sites have been selected to represent teaching hospitals, district general hospitals and primary care across inner city, suburban and semi-rural locations. Specialist services will include those led by neurologists and geriatricians, and both hospital and community-based PDNSs. Royal Free hospitals, Homerton Hospital, Lister Hospital, and Luton and Dunstable Hospital, NHNN Registry, and NoCLoR successfully recruited for the feasibility study (WP3).

1.1 11.3 Recruitment methods

A combination of recruitment methods will be used, including initial approaches by clinic staff for people with Parkinson's and carers attending appointments, through the hospital research registry, through introduction by PDNSs including outreach work at home to those unable to attend hospital, and through electronic searches of GP lists for patients with Parkinson's who will be approached by letter from their practice to participate. Telephone reminders by practice/clinic staff will be used to follow-up non-responders to initial invitations, or a single postal reminder 3 weeks after the initially invitation where this is not possible. The aim of the primary care group is to include participants not currently engaged with PD-specialist services, who arguably may have the most to gain from the intervention.

Recruitment will also take place through Parkinson's UK. This will include approaches through local support groups; and the study will be listed on the PUK web pages so that participants can approach the study team through the online Research Support Network and 'take part hub'. The voluntary sector, including carers groups, social media, and snowballing approaches will also be used.

To be inclusive in the areas with a wide diversity study documents can be translated accordingly, and interpreters made available to assist in gaining informed consent for the RCT from those with limited or no English. The toolkit cannot be translated however and so the participant must be able to engage with the intervention even if this is with support of a carer or a family member.
We will develop additional tailored approaches to encourage people from underserved groups to take part in the study. These include short videos explaining the study in multiple languages played in outreach clinic waiting rooms, podcasts, local champions, adapted written materials, and additional incentives. These resources could be used across all sites.

11.3 Recruitment incentive

Participants will be offered £20 shopping voucher for taking part in the baseline assessments for the RCT and the qualitative interviews, and £10 per participant for shorter follow-up assessments in the RCT.

11.4 Internal pilot

The first six months of recruitment (n=80) will form an internal pilot with stop/go criteria.

Internal pilot:
The first wave of recruitment for the initial 6 months will form an internal pilot, to further test trial recruitment procedures and participant willingness to be randomised. The stop/go progression criteria at 6 months are the following:

1. Minimum recruitment and randomisation rate of 70% of the target of 80 people within 6 months (10 people per month for first 2 months during set-up phase, followed by 15 per month for 4 months).
2. Minimum uptake of the intervention of 70% of participants (evidence of use of the toolkit/attendance at follow-up appointments).
3. Minimum retention rate of 70% at 6 months (completion of main outcome measures).
4. No serious intervention-related adverse events.

If the trial is successful in meeting these criteria the full RCT will proceed, and data from the pilot phase contribute to the outcomes. Recruitment rate and attrition will be monitored very closely and if levels are less than expected contingency measures will be put in place (e.g., expand to further study sites, introduce incentives).

12.CONSENT

Eligibility of interested participants will be confirmed by the GCP trained research team delegated by the Investigator on the delegation log. Written informed consent will be obtained prior to participation in the

study. This will be following adequate explanation that participation is voluntary and that they can withdraw at any time during the trial without having to give a reason. The aims, methods, anticipated benefits and potential hazards of the study will be explained and adequate time will be given to consider taking part. Throughout the consent process we will adhere to the Mental Capacity Act (2005).

Where in-person written consent is not possible, due to risk of exposure to COVID-19 for example, consent will be collected by phone, videoconference or online systems depending on their preference. Consent forms or a link to our e-consent will be sent to participants via email if they have an email address/internet access. Participants will be required to email digital copies or post a hard copy of the consent form back to the researchers. Participants will also be given the option to fill this consent with the researcher over the telephone or virtually (using Microsoft Teams, Zoom or similar technology) to be able to resolve any questions. If participants do not have an email address/internet access, the researcher will go through the consent form in full with them over the telephone and ask them to verbally consent. Verbal consent will be recorded using an audio recorder. Once recording, each item in the consent form will be read out in full and the participant can verbally consent by saying 'I agree'. The researcher will sign the consent form and write a note that consent was obtained verbally. The audio-recordings of the consent will be stored separate to any other study activity.
A copy of the signed Informed Consent form will be given, posted, emailed to the participant. The original signed form will be retained securely and in adherence to General Data Protection Regulation (GDPR) at the study site and a copy placed in the medical notes.

13.RANDOMISATION

Randomisation of study participants will be performed by using a web-based service Sealed Envelope (https://www.sealedenvelope.com/) in a 1:1 ratio to the intervention or TAU. Minimisation will be used to perform individual randomisation based on site. Participants will be informed of their group allocation by phone call. Participants in the TAU arm will also receive a letter confirming their group allocation and reminding them of their follow-up time points. If they have been allocated to the treatment group their first session will be booked and login details for the website sent, if appropriate.

14.DATABASE

The CRFs will be entered into a web-based clinical data management system, Red Pill, provided by Sealed Envelope through Priment. Sealed Envelope has been assessed by Priment to ensure that adequate processes are in place and are being followed for quality management, software development and security. There will be an agreement in place between the Sponsor and Sealed Envelope to ensure compliance and agreement with clinical trial regulations and data protection laws. Priment SOPs 18 Validating Sealed Envelope Systems and 20 Change Control for Sealed Envelope Systems will be followed to set up and manage changes to the trial database. At the end of the trial, prior to analysis, Priment SOP Database Lock, Unlock and Closure will be followed.

15. DISCONTINUATION/WITHDRAWAL OF PARTICIPANTS AND 'STOPPING RULES'

For those who select to withdraw from the study for any reason a record will be made in the participants study and medical notes, including reasons and timing of withdrawal. Participants will be given the choice whether the data and samples already gathered can be used, or not, by the study.

In the event of a participant going into a care home during the study, they will be able to continue in the study if they still have capacity. If, however, the participant loses capacity, they will be withdrawn. In the unlikely event of a participant being withdrawn from the study (e.g., due to a lack of capacity), we will retain their data up to that point unless otherwise requested.

16. STATISTICAL METHODS

16.1 Main Statistical analysis

A comprehensive statistical analysis plan will be developed and agreed with the trial's oversight committees. Descriptive analysis (e.g., summary statistics, plots) will be performed to investigate the distribution of the primary outcome, PDQ-39, across participants. The primary analysis will be a comparison of PDQ-39 scores adjusting for site, baseline PDQ-39, age and socio-economic status using regression methods. All analyses will be performed on an intention-to-treat basis and all modelling assumptions will be checked (e.g., residuals). There will be adjustment for site in the main analysis using random intercepts within linear mixed models. A CACE analysis will be performed as a sensitivity analysis to investigate the potential impact of non-compliance. Missing data will be investigated, and multiple imputation used if appropriate. Secondary outcomes will be compared using similar methods to the primary outcome. We will undertake a pre-specified sub-group analysis exploring the effectiveness in early (diagnostic/maintenance) vs. advanced (complications/palliative) Parkinson's. Participant and carer data will be linked to explore possible associations between carer burden and QoL with participant factors such as disease severity.

16.2 Economic evaluation

The incremental cost per quality adjusted life year (QALY) gained of the intervention compared to TAU from i) health/social care perspective; ii) societal perspective using trial data will be calculated. Additional analyses will calculate the cost per capability adjusted life year gained from both cost perspectives. QALYs will be calculated from the EQ-5D-5L and as the area under the curve adjusting for baseline (91) Means and 95% confidence intervals will be based on bootstrapped results. Resource use will be costed using nationally published sources (PSSRU, NHS Reference costs and BNF). The cost of the intervention including staff training, administration and delivery will be included in the costs of the intervention group. Mean costs and 95% confidence intervals generated from bootstrapping for all key costs and resources will be reported. The difference in total cost at 12 months will be adjusted using baseline values and regression analysis (92). Cost-effectiveness acceptability curves and cost-effectiveness planes will be reported from i) health and social care cost and ii) societal cost perspectives to represent the probability

that the intervention is cost-effective compared to TAU for a range of values of willingness to pay for a QALY/capability adjusted life year gained. Analysis will conduct and report a range of sensitivity analyses for any assumptions made. Missing data and adjustment for covariates will be handled in the same way as the main statistical analysis plan. Multiple imputation will be used if there is a large percentage of missing data (>15% of patients missing complete cases).

A life-time decision model will be developed to project the lifetime costs and QALYs because of the intervention compared to TAU from a health and social care cost perspective. The model will be based on a previously developed model of Parkinson's progression and associated costs and QALYS [44]. The model will be updated using values from the trial in addition to evidence from literature where suitable based on assessment of the strength of evidence using the GRADE approach. A full probabilistic sensitivity analysis will be conducted which will be used to generate a cost-effectiveness plane and cost-effectiveness acceptability curves. Deterministic sensitivity analysis will be used to test for the impact of any assumptions made on the results of the analysis.

16.3 Process evaluation analysis

Qualitative data: Interviews will be transcribed by approved transcription services and entered into qualitative software. We will undertake a thematic analysis including searches for disconfirming evidence. All transcripts will be read by at least two team members, with a thematic framework developed independently and refined in team discussions (which will include PPI members). Analysis will continue alongside data collection to inform future interviews. Themes will be derived inductively to explore intervention fidelity and mechanisms of impact in relation to contextual factors. We will explore how and why participants choose certain goals, their experiences of remote delivery in the context of a pandemic and how these might impact upon outcomes. Data from providers will be mapped against constructs from Normalisation Process Theory (NPT) [45] to identify facilitators and barriers to implementation within newly evolving integrated care systems.

We will conduct a separate qualitative thematic analysis of interviews with underserved populations to explore components of the intervention that were most useful, how the intervention could be tailored for underserved populations, whether SES, education or ethnicity influences goals chosen, or which behaviour change techniques may work better and how well our extended recruitment methods worked.

Interpretations will be agreed in multi-disciplinary team discussions (qualitative sub-group, including PPI members) with a particular focus on how contextual factors such as Covid-19, rurality, age, gender, ethnicity, socio-economic status, health literacy, degree of impairment, co-morbidities and provider differences might influence delivery, fidelity, impact and implementation.

Quantitative data: Trial process and outcome data will be used to assess intervention reach, fidelity and dose and explore mechanisms of impact. The statistical analyses will be conducted once the main trial outcomes have been completed and the statistician has been unblinded.

1) *Reach:* Demographic data will be compared descriptively to that obtained from the published literature on Parkinson's population demographics in the UK, supplemented by general

population data for the regions of our recruitment sites (e.g. Office of National Statistics area level census data [46], and CCG/LA (Joint Strategic Needs Assessment, JSNA) and practice-level data where available). This will explore whether any populations are under-represented in those recruited to the trial and receiving the intervention. We will compare percentage recruited from typically underserved populations (e.g., ethnic minorities, those with low socioeconomic status, oldest age groups, those living alone) to data in each area. We will also explore differences in engagement with the intervention (goal progress, receiving a minimum dose and use of remote intervention delivery) according to these populations.

2) *Fidelity:* Two independent researchers will apply fidelity checklists to transcribed audio-recordings of intervention appointments for 10% of intervention participants. Inter-rater agreement will be calculated using kappa statistics and disagreements will be resolved through discussion. Researcher ratings will be compared to service provider ratings using appointment fidelity checklists.

3) *Dose:* Descriptive statistics will be calculated for: Number and percentage of appointments attended, average duration, number and percentage attending the minimum dose of appointments (>=3) to the intervention overall and per area/supporter.

We will carry out four statistical analyses to explore hypothesised mechanisms:

1. To determine whether those who get a 'therapeutic dose' of the intervention (defined as attending ≥3 appointments) have better outcome scores than those who do not, number of sessions attended will be dichotomised into those attending ≥3 sessions or not. Those in the TAU group will be coded <3 sessions. This will be analysed using linear regression with an interaction between sessions attended and randomised group, and baseline PDQ-39 score.
2. We will assess whether choice of goal is associated with differential effects on our primary outcome. Similar analyses will be conducted as above. Modelling will be undertaken separately for each category of goal. Additionally, if there are sufficient numbers for each goal type, we will explore if there are effects on the most related secondary outcome.
3. We will explore whether overall progress towards meeting goals is associated with greater impact on PDQ-39 score. We will model the PDQ-39 with an interaction between randomised group and mean progress towards goals. In the TAU group, this will be set at 0 as there were no goals set, so no progress will be made.
4. We will undertake an exploratory analysis of whether the effectiveness of the intervention on the PDQ-39 varies by ethnic minority, education, or SES status.

17.PATIENT AND PUBLIC INVOLVEMENT (PPI)

This study aims to address one of the top 10 priorities set by the charity Parkinson's UK, that of Personalised Treatments, and was developed following a collaboration with the European Parkinson's Disease Association (EPDA) in their "My Parkinson's Journey" project, which surveyed the experiences

and unmet needs of people with Parkinson's in Europe. The first recommendation from this project was the requirement for more personalised care for people with Parkinson's tailored to their individual needs. The project is based on the difficulties people with Parkinson's and carers report in clinical practice and were a central discussion point in meetings of the "UK Parkinson's Excellence Network" initiated by the charity Parkinson's UK. The study has the support of Parkinson's UK and CRISP (King's College Hospital NHS Foundation Trust), a nationally recognised expert patient group in Parkinson's.

This study involves people with Parkinson's and carers at all stages. This includes active involvement in study planning, sitting on the Programme Management Committee (BM, PPI Lead) and Independent Programme Steering Committee (two PPI members). The study has established a study-specific PPI Advisory Panel of people with experience of Parkinson's and carers of people with Parkinson's, acting as a consultative and advisory forum for all stages of the study, meeting regularly throughout the study and feeding back to the Steering Committee and study team. The PPI panel have taken an active role through our co-design process in developing the intervention itself, specifically in the selection and review of content topics, design and aspects of supporter role. The group will provide mutual support, co-facilitated by the research team (programme manager) and the PPI Lead (BM). The views of the PPI advisory panel will be integrated throughout.

This project is based on the experiences and priorities of people with Parkinson's/their carers and aims to improve their experience in the NHS. It is crucial to review the progress, challenges, and ways to overcome these with people with Parkinson's and their carers/supporters. Dissemination will similarly importantly involve guidance to ensure that the findings are communicated in a meaningful way, reaching the right audiences. Social and print media will be used and results disseminated through partnership with Parkinson's UK and presentations at patient/carer fora. PPI members will have an active role, leading on some aspects, co-author papers and be acknowledged, as appropriate.

18.FUNDING AND SUPPLY OF EQUIPMENT

The research costs for the study have been supported by and NIHR programme grant (RP-PG-1016-20001). The Royal Free NHS Foundation Trust is the lead site of the study and sub-contracts with all listed collaborating sites. No study specific equipment is required, apart from laptop computers to facilitate remote data collection, and encrypted digital audio-recorders for qualitative data collection, both funded from the research grant. NHS Excess Treatment and Service Support costs will be supported through the Local Clinical Research Networks.

19.DATA HANDLING AND MANAGEMENT

Participant confidentiality will be paramount throughout all aspects of the study and data management will be guided by Research Governance Framework and General Data Protection Regulation (GDPR)

The CIs are the 'Custodians' of the research data. Their details are as follows:
Professor Anette Schrag
Tel: 020 8016 8135

email: a.schrag@ucl.ac.uk

Professor Kate Walters
Tel: 0208 016 8039
email: k.walters@ucl.ac.uk

Data Collection
The following person-identifiable data points will be collected from the participants at the beginning of the study:

- Full name
- Date of birth
- Contact number
- NHS number
- Full post-code

Baseline data will be collected by proficient researchers and will include socio-demographic, clinical (including motor and cognitive ability) psychological well-being and economic information.

Data handling and record keeping
The data will be handled and records kept by the research team. All research staff clearly identified on the trial delegation log will be GCP trained and proficient in Information Governance. They will also receive training in the use of study specific documentation and data capture systems. All person-identifiable information and study related documentation will be stored on encrypted memory sticks, and password protected computers; and paper sources will stored in locked cabinets. All personally identifying paper information will be stored securely in locked cabinets, separately from the clinical trial/ study data. Study data will be labelled with a unique identifier; a pseudo-anonymization process will take place where the hospital number will be linked to the participant study number, which will be kept in one place; in a securely locked cabinet in the research office.

All resulting data will be entered, preferably on site, into a bespoke electronic case report form (e-CRF; developed by PRIMENT Clinical Trials Unit). Following UCL IT SLMS guidance and General Data Protection Regulation, logging and mapping systems will be in place to ensure timely and secure delivery of source data to the co-ordinating site for data entry, where applicable. Identifiable information will not leave Trusts. Qualitative/semi-structured interviews will be audio-recorded, transcribed, de-identified and organised using NVivo software. Audio data will be treated as personal data and will be labelled with a unique study identifier and stored in GCP, GDPR compliant systems.

The administration of motor components of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) will be video-recorded to validate ratings, to evaluate inter-rater reliability, improve accuracy and facilitate remote delivery. The data collected will be treated with confidentiality. When meeting face-to-face, the mobile video-recorder will be transported securely in a locked container, and recordings will be deleted from the mobile recorder as soon as saved on secure UCL data safe haven systems. If the recording has been taken remotely as part of a remote video assessment, the recording

will be immediately uploaded via secure VPN to our secure data storage system and deleted from the recording device.

The computer programme GENEActive is used to set up and import the data collected by the GENEActiv Movement Sensor. This data is in an anonymous format and only linked to the participants unique study code.

Access to Data, Source Data and Documents

Direct access will be granted to authorised representatives from the sponsor, host institution and the regulatory authorities to permit study-related monitoring, audits and inspections. Otherwise, only people who have a 'legitimate relationship' with the participant (if patient) (e.g., are members of the health care giving team) will have to have access to medical records of study participants. With participants consent, site research teams may make copies and remove identifiable details to make available for third parties. Those copies would have a unique identifier and research team would keep the key.

The process of recording and storing data will be explained in the Patient Information Sheet and Consent form.

Sample handling and management:

DNA samples extracted from saliva samples will be stored at the Institute of Neurology for long term storage. Database records of samples collected will be maintained on the NHS computer system.

Saliva samples will be collected using a compact self-collection kit, including an instruction sheet following manufacturer's instructions for use. Samples will be labelled with an anonymous unique study code and stored at room temperature until secure delivery to the central laboratory. Due to sample stability, there are no critical time frames for delivery to the laboratory for analysis.

20.PEER AND REGULATORY REVIEW

This protocol has been reviewed before it is authorised for use in accordance with the Sponsor's SOP on Peer Review (SOP 055).

The Sponsor considers the procedure for obtaining funding from NIHR to be of sufficient rigour and independence to be considered an adequate peer review.

The study was deemed to require regulatory approval from the following bodies: NHS Research Ethics Committee and Health Research Authority. Approvals will be obtained before the study commences.

21.ASSESMENT AND MANAGEMENT OF RISK

We do not consider this trial to be high risk. The study personnel and co-investigators will ensure that the study is conducted in line with NHS and professional ethical and research governance guidelines. Training and regular supervision will be provided to researchers on study procedures by the CI, PIs and trial manager. Training and central supervision will also be provided to support workers delivering the intervention.

Lone working: Researchers will follow the UCL lone working policy which can be found on the UCL website: http://www.ucl.ac.uk/estates/safetynet/guidance/lone_working/lone_working.pdf Researchers will offer participants the option of remote follow up assessments. Researchers will carry mobile phones and they will be able to contact the CI or trial manager during work hours and out of hours. Researchers will contact a member of the study team if they are not returning to the office after an assessment. The study team will have addresses, phone numbers and next of kin details of all researchers. Support workers will follow lone working guidelines at their employing institution.

Confidentiality: All members of the research team will have undertaken and will provide certification for Good Clinical Practice, information governance and data protection training.
For baseline and outcome assessments, electronic and/or paper CRFs will be collected. Self-report questionnaires will be posted back to the research team if completed remotely. For the process evaluation, paper and electronic data will be collected. CRFs, intervention process data (e.g. fidelity checklist) and audio transcripts will be pseudonymised, labelled by participant ID and initials. Paper and audio recorded intervention and assessment data will be stored securely during transfer and will be transferred to the appropriate site secure storage as soon as feasible. Any videoconferencing for remote assessments or intervention delivery will be conducted over a secure platform. Intervention process and interview data will be stored separately to CRFs. Audio data will be uploaded as quickly as feasible to a secure folder and the recording deleted from the recorder. Sensitive personal data will be stored in the UCL Data Safe Haven or locked filing cabinets with limited access; pseudonymised data will be stored in separate locked filing cabinets or password protected folders with limited access to only authorised personnel.

If participants disclose information to a RA leading them to believe that the participant or others are at significant risk, the researcher will discuss it with the site PI and/or the trial's Clinical Safety lead and if appropriate, will seek consent from the participant to contact the participant's GP or a local safeguarding service as appropriate. If participants disclose information to a support worker leading us to believe that they or others are at significant risk, they will contact their clinical supervisor in the first instance and will seek consent to contact the participant's GP or a local safeguarding service as appropriate, and will also inform the study team (CI, Clinical Safety Lead and site PI).

Intervention fidelity: The intervention is manualised. Supporters will receive initial interactive case-based and skills focused training. Supporters delivering the toolkit will receive training on the content and its use and delivery, and made aware that their role is to support self-management. Core training will be supplemented by other UCL mandatory training (e.g., adult safeguarding, information

governance). We will document fidelity within the process evaluation through checklists completed by the supporter following each session and checking 10% of participants' audio recorded appointments against a checklist from our feasibility trial.

Trial conduct: The trial will be overseen by an independent Trial Steering Committee (see section 23) and supported by Priment CTU. Priment CTU will support and provide expertise in trial methodology, conduct, management, safety reporting, quality assurance monitoring Priment will also support the trial database development and will develop and implement the statistical and economic analysis plans and will lead on the health economic and statistical analysis. There will be regular team meetings in place and email, or phone communication as needed. The research team will keep in regular contact with the sites. As this is a single-blind study, there is a small risk that assessors may become unmasked. We will minimise this risk by asking the assessors to remind participants at each stage that they must not reveal their treatment arm allocation to their assessor. Assessors will be blinded to the arm allocation within the Sealed Envelope database via their access role. If an assessor does become unmasked, the study team will record this and ask an alternative assessor to complete future outcome measures for that participant. At the end of assessment for each participant the assessor will record which study group they believe the participant has been allocated to in order to verify blinding.

Taking part in the study will take a commitment of participants time and will involve discussing the symptoms and daily impact of Parkinson's. This may be tiring and upsetting for some participants. Any psychological distress will be discussed at the time and severe incidents will be reported to study leads and appropriate referrals made. Any such incidence will be recorded in the participants study and medical notes.

Participant becoming unwell or distressed

We do not anticipate this trial causing the participant to become distressed or unwell. If the participant was to become unwell or if any safe-guarding issues arise clear pathways will be in place to seek help from the participants own medical team, and researchers will be closely supervised by the two CIs who are both experienced clinicians (Neurologist and GP) and can provide guidance on appropriate course of action.

For any participant who becomes distressed during a remote interaction, management will be the same as for face-to-face visits. In cases of significant concern, the researchers will 1) discuss with the Co-leads as to how to best support them and 2) seek their consent to liaise with their GP to ensure that there is ongoing support. The research team will then contact the participant again later to ensure that they have received support and/or their distress has resolved. The method of remote interaction will be of the participants choosing. If a person is distressed during a video/zoom call, then we are also able to change to a telephone call. Researchers and the PD-Care facilitator are trained in supportive listening skills, which can be used to help manage any distress remotely on the phone or in video consultations.

22.RECORDING AND REPORTING OF EVENTS AND INCIDENTS

22.1Definitions of Adverse Events

Term	Definition
Adverse Event (AE)	Any untoward medical occurrence in a patient or study participant, which does not necessarily have a causal relationship with the procedure involved.
Serious Adverse Event (SAE).	Any adverse event that: • results in death, • is life-threatening*, • requires hospitalisation or prolongation of existing hospitalisation** • results in persistent or significant disability or incapacity, or • consists of a congenital anomaly or birth defect
*A life- threatening event, this refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe. ** Hospitalisation is defined as an in-patient admission, regardless of length of stay. Hospitalisation for pre-existing conditions, including elective procedures do not constitute an SAE.	

22.2 Assessments of Adverse Events

Each adverse event will be assessed for severity, causality, seriousness, and expectedness as described below.

Severity

Category	Definition
Mild	The adverse event does not interfere with the participant's daily routine, and does not require further procedure; it causes slight discomfort
Moderate	The adverse event interferes with some aspects of the participant's routine, or requires further procedure, but is not damaging to health; it causes moderate discomfort
Severe	The adverse event results in alteration, discomfort or disability which is clearly damaging to health

Causality

The assessment of relationship of adverse events to the procedure is a clinical decision based on all available information at the time of the completion of the case report form.

It is of particular importance in this study to capture events related to the product application procedure. The assessment of relationship of an adverse event to this/these additional safety issue(s) will also be carried out as part of the study.

The differentiated causality assessments will be captured in the study specific CRF/AE Log and SAE form.

The following categories will be used to define the causality of the adverse event:

Category	Definition
Definitely:	There is clear evidence to suggest a causal relationship, and other possible contributing factors can be ruled out.
Probably:	There is evidence to suggest a causal relationship, and the influence of other factors is unlikely
Possibly	There is some evidence to suggest a causal relationship (e.g., the event occurred within a reasonable time after administration of the study procedure). However, the influence of other factors may have contributed to the event (e.g., the participant's clinical condition, other concomitant events).
Unlikely	There is little evidence to suggest there is a causal relationship (e.g., the event did not occur within a reasonable time after administration of the study procedure). There is another reasonable explanation for the event (e.g., the participant's clinical condition).
Not related	There is no evidence of any causal relationship.
Not Assessable	Unable to assess on information available.

Expectedness

Category	Definition
Expected	An adverse event which is consistent with the information about the procedure listed in the Investigator Brochure, SPC, manual of Operation or clearly defined in this protocol.
Unexpected	An adverse event which is not consistent with the information about the procedure listed in the manual of operation or clearly defined in this protocol.

* this includes listed events that are more frequently reported or more severe than previously reported

22.3 Recording adverse events

Adverse events, with the date, clinical symptoms, and a simple, brief description of the event, will be recorded in the medical records, CRF and the PRIMENT AE log, until the participant completes the RCT study.

22.4 Procedures for recording and reporting Serious Adverse Events

All serious adverse events will be recorded in the medical records and the CRF, and the sponsor's AE log.

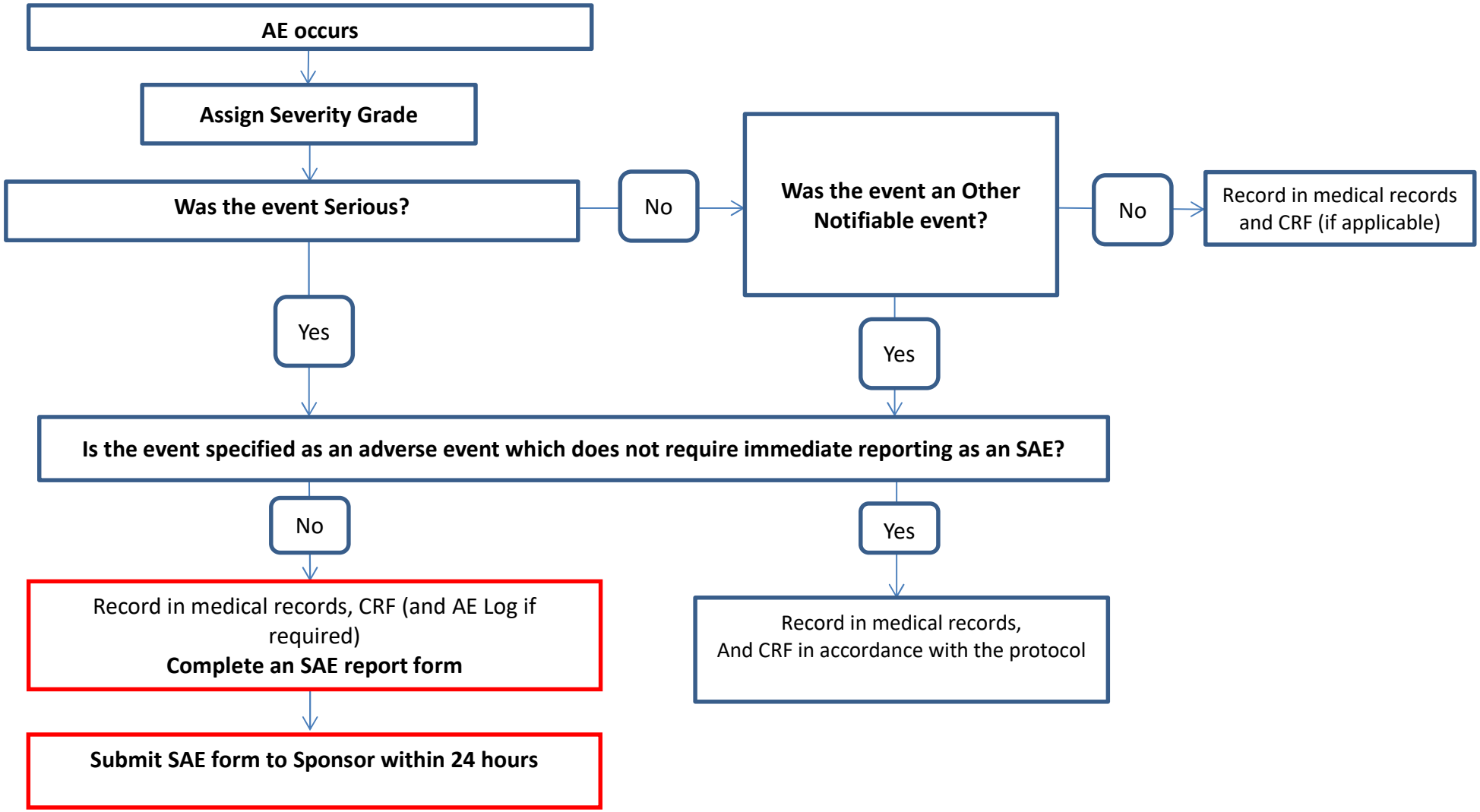
SAEs will be recorded and reviewed by one of the CIs (both practicing clinicians) and only those identified as being possibly, probably or definitely related to the study processes/intervention will be reported to the Sponsor. In the case of a SAE the Chief or Principal Investigator will complete the sponsor's serious adverse event form and the form will be emailed to primentsafetyreport@ucl.ac.uk within 24 hours of becoming aware of the event.

Where the serious adverse event is unexpected and thought to be related to the procedure this must be reported to the REC by Priment within 15 days of becoming aware of the event.

Completed forms for **all** SAEs must be sent within 24 hours of becoming aware of the event to Priment

Email forms to: primentsaferyreporting@ucl.ac.uk

Flow Chart for SAE reporting



Serious Adverse Events that do not require reporting

It is expected with this population for SAEs (eg. hospitalisations) to occur as this is an older frailer population with high hospital admissions and mortality rate.

All SAEs will be recorded, anonymised and reviewed by one of the CIs (both practicing clinicians) and only those identified as being possibly, probably or definitely related to the study processes/intervention will be reported to the Sponsor. Only deaths occurring earlier than expected will be reported to the sponsor.

Managing serious adverse events at local sites

The investigator (PI) will send reports of suspected SAE to the CIs for review to decide if sponsor notification is appropriate.

Reporting Urgent Safety Measures

If any urgent safety measures are taken the CI/ PI shall immediately and in any event no later than 3 days from the date the measures are taken, give written notice to the relevant REC and Sponsor of the measures taken and the circumstances giving rise to those measures.

Protocol deviations and notification of protocol violations

A deviation is usually an unintended departure from the expected conduct of the study protocol/SOPs, which does not need to be reported to the sponsor. The CI will monitor protocol deviations.

A protocol violation is a breach which is likely to effect to a significant degree –

(a) the safety or physical or mental integrity of the participants of the study; or

(b) the scientific value of the study.

The CI and sponsor will be notified immediately of any case where the above definition applies during the study conduct phase.

Trust incidents and near misses

An incident or near miss is any unintended or unexpected event that could have or did lead to harm, loss or damage that contains one or more of the following components:

a. It is an accident or other incident which results in injury or ill health.
b. It is contrary to specified or expected standard of patient care or service.
c. It places patients, staff members, visitors, contractors or members of the public at unnecessary risk.
d. It puts the Trust in an adverse position with potential loss of reputation.
e. It puts Trust property or assets in an adverse position or at risk.

Incidents and near misses must be reported to the Trust as soon as the individual becomes aware of them.

A reportable incident is any unintended or unexpected event that could have or did lead to harm, loss or damage that contains one or more of the following components:

a) It is an accident or other incident which results in injury or ill health.
b) It is contrary to specified or expected standard of patient care or service.
c) It places patients, staff members, visitors, contractors or members of the public at unnecessary risk.
d) It puts the Trust in an adverse position with potential loss of reputation.
e) It puts Trust property or assets in an adverse position or at risk of loss or damage.

22.5 Notification of serious breaches to GCP and/or the protocol

A "serious breach" is a breach which is likely to effect to a significant degree –

1. the safety or physical or mental integrity of the participants of the trial; or
2. the scientific value of the trial.

The Sponsor of a clinical trial shall notify the licensing authority in writing of any serious breach of:

1. the conditions and principles of GCP in connection with that trial; or
2. the protocol relating to that trial, as amended from time to time, within 7 days of becoming aware of the breach.

PRM-SOP-006 Non-Compliance To Study Protocol. Regulatory Requirements and Serious breaches of GCP or trial protocol will be followed.

23. MONITORING AND AUDITING

The trial will be monitored according to the risk-based monitoring plan created by Priment Operations team. Priment initial risk assessment will determine the initial monitoring plan and change as the study progresses to adapt to any possible amendments.

It is the CI/TM's responsibility to ensure that any findings identified in any monitoring report are actioned appropriately and in a timely manner and that any violations of GCP or the protocol will be reported to the CTU & CI. Any serious breach will be handled according to PRM- SOP- 006 No compliance to Study Protocol, regulatory requirements, and serious breaches.

Any urgent safety measures at either the CI or a PI site must be reported by that site Investigator within 3 days, as per UK Regulations.

The CI will be provided with a copy of the study monitoring plan during the Trial Initiation monitoring visit.

The study activities for WP4 will be supported by PRIMENT CTU, as well as, database/data management, provision of Standard Operating Procedures (SOPs), safety reporting and quality assurance.

A Trial Management Group will be formed to oversee the trial progress which will include both CIs (AS and KW, who is also a PRIMENT Trialist), PRIMENT Senior Trials Operation Manager, Senior Statistician (GA), Senior Health Economist (RH), the Programme (Trial) Manager (MA), member of RF R&D. An

Independent Programme Steering Committee (PSC) will provide oversight and scrutiny, with an Independent Chair, PPI representatives, academic experts and key stakeholders from the voluntary sector, NHS and social care policy, professional development, and practice. This PSC will meet six-monthly throughout the programme and will report to the NIHR. For the period of WP4 the PSC will perform the role of the Trial Steering Committee and Data Monitoring Committee (as this is a low risk trial). The Chief Investigators and Trial Management Group will report to the PSC six-monthly.

24.INTELLECTUAL PROPERTY

All Intellectual Property Rights and Know How (IP) related to the Protocol and the Trial are and shall remain the property of the Sponsor excluding
1) Pre-existing IP related to clinical procedures of any Hospital.
2) Pre-existing IP related to analytical procedures of any external laboratory.

All contributors shall assign their its rights in relation to all Intellectual Property Rights and in all Know How not excluded above to the Sponsor and at the request and expense of the Sponsor shall execute all such documents and do all such other acts as the Sponsor may reasonably require in order to vest fully and effectively all such Intellectual Property Rights and Know How in the Sponsor or its nominee. The CI shall promptly disclose to the Sponsor any Know How generated pursuant to this Protocol and not excluded above and undertake treat such Know How as confidential information jointly owned between it and the Sponsor.
Nothing in this section shall be construed so as to prevent or hinder a medical professional from using Know How gained during the performance of the Trial in the furtherance of its normal business activities, to the extent such use does not result in the disclosure or misuse of Confidential Information or the infringement of any Intellectual Property Right of the Sponsor.

25.INDEMNITY ARRANGEMENTS

NHS bodies are liable for clinical negligence and other negligent harm to individuals covered by their duty of care. NHS Institutions employing researchers are liable for negligent harm caused by the design of studies they initiate.

26.ARCHIVING

During the study, all records are the responsibility of the Chief Investigators and will be kept in secure conditions. On completion of the study, as required by the UK Policy Framework for Health and Social Care Research and the Royal Free London Trust Policy, the records will be archived for 5 years after completion of the trial.
Archiving will be authorised by the Sponsor following submission of the end of study report. All data collected during the course of the study (essential documents and study database) will be stored for a 5-year period in the Iron Mountain, a repository approved by the Royal Free London NHS Foundation Trust for long-term storage of local records. Destruction of essential documents will require authorisation from the Sponsor.

The Principal Investigator at each participating site agrees to archive his/her respective site's study documents for end of study plus 5 years and in line with all relevant legal and statutory requirements.

27. PUBLICATION AND DISSEMINATION POLICY

The data arising from the study will be owned by the study Sponsor. On completion of the study, the data will be analysed and tabulated and a Final Study Report prepared. The full study report will be accessible on the UK Clinical Trial Network. We will acknowledge the National Institute of Health Research (NIHR) for their funding within the publications and they will be able to review it, but they will not have publication rights of the data from the study.

The findings from each work package will be disseminated, and the implementation strategies for commissioning PD-Care will be developed on completion of the main RCT, if the results demonstrate clinical and cost-effectiveness.

The planned outputs will consist of:

1. The Live well with Parkinson's Toolkit.
2. Training programme for facilitators to support self-management of Parkinson's.
3. Training and user guides written for service providers to support implementation.
4. The Programme website, hosted at UCL, bringing together all key resources to support implementation and dissemination, including programme newsletters, user guides, publications, blogs and a mechanism for user feedback. This will be maintained beyond the programme completion.
5. Costing models and policy briefing documents, to promote and facilitate commissioning the Live well with Parkinson's toolkit and HCP training to support use.
6. A model for long term sustainability and updating of the interventions.

The dissemination strategy will target policy makers, health care planners and commissioners, the public, participants, service providers/ practitioners via respective professional bodies, academic peer review publications. This strategy will include the following:

- *Engagement with stakeholders:* This includes a symposium to present findings on completion; policy briefing documents/individual engagement with key policy makers from Department of Health, NHS England, interest groups (e.g., Parkinson's UK); regional engagement with NHS Local Area Teams, Clinical Commissioning Groups (CCGs) and Local Authorities targeting Integrated Care leads.

- *Commissioning PD-care:* A costing model will be developed to commission PD-Care training and access longer term. Throughout the duration of the programme grant work will take place with the third sector, NIHR Head of Impact and NHS England to develop appropriate commissioning models and long-term sustainability of the intervention.

- *Supporting implementation:* Comprehensive user and training guides will be developed, including an online CPD module. Work will take place with relevant CPD providers (e.g.,

FUNDED BY NIHR | National Institute for Health Research

RCGP, RCN) to gain accreditation for this and work with local providers (e.g. CCGs) to promote access to the module.

- *Academic dissemination:* Traditional methods of academic dissemination and social media will be used for peer reviewed academic publications for each WP (8 in total). There will be two systematic reviews (i. RCTs; ii. Qualitative and observational studies), reports of the qualitative studies, intervention development, feasibility study, trial protocol, clinical effectiveness (RCT) and cost-effectiveness (Health Economic paper). Findings will be presented at key relevant national and international conferences (neuro-degenerative diseases/neurology, geriatrics, nursing, primary care, self-management/personalised care) and disseminate our findings/publicise our papers via social media (e.g., via ResearchGate project, Twitter).

- *Public dissemination:* Close work with the study PPI advisors and Parkinson's UK will take place to implement a comprehensive public dissemination strategy. Social and print media will be used, and dissemination of results through partnership with Parkinson's UK and presentations at patient/carer fora. PPI members will have an active role, leading on some aspects, co-author papers and be acknowledged, as appropriate.

- *Participants:* We plan to notify the participants of the outcome of the study, with access to the publication, and we will present the study locally for staff and the public, which participants will be invited to. Participants will be able to specifically request results from the PI and this information will be provided at the next consultation or in letter depending on the participant's preference.

- Participants will be offered the chance of being kept informed and updated about the study throughout their participation, through a study newsletter, emailed or by post (according to their preference), and the study website. At the end of the study, participants will be provided with a summary of the findings from the programme, written in plain English with input from our public advisory panel. More detailed information will be made available via our study website, with hard copies sent to those participants requesting them.

28. REFERENCES

1. De Rijk, M.d., et al., *Prevalence of Parkinson's disease in Europe: A collaborative study of population-based cohorts. Neurologic Diseases in the Elderly Research Group.* Neurology, 2000. **54**(11 Suppl 5): p. S21-3.
2. McCrone, P., L.M. Allcock, and D.J. Burn, *Predicting the cost of Parkinson's disease.* Movement Disorders, 2007. **22**(6): p. 804-812.
3. Dorsey, E.R., et al., *Projected number of people with Parkinson disease in the most populous nations, 2005 through 2030.* Neurology, 2007. **68**(5): p. 384-386.
4. Hassan, A., et al., *High rates and the risk factors for emergency room visits and hospitalization in Parkinson's disease.* Parkinsonism & related disorders, 2013. **19**(11): p. 949-954.
5. Chaudhuri, K.R., et al., *The nondeclaration of nonmotor symptoms of Parkinson's disease to health care professionals: an international study using the nonmotor symptoms questionnaire.* Movement Disorders, 2010. **25**(6): p. 704-709.
6. Gallagher, D.A., A.J. Lees, and A. Schrag, *What are the most important nonmotor symptoms in patients with Parkinson's disease and are we missing them?* Movement Disorders, 2010. **25**(15): p. 2493-2500.
7. Gerlach, O.H., A. Winogrodzka, and W.E. Weber, *Clinical problems in the hospitalized Parkinson's disease patient: systematic review.* Movement Disorders, 2011. **26**(2): p. 197-208.
8. Low, V., et al., *Measuring the burden and mortality of hospitalisation in Parkinson's disease: a cross-sectional analysis of the English Hospital Episodes Statistics database 2009–2013.* Parkinsonism & related disorders, 2015. **21**(5): p. 449-454.
9. Bliemel, C., et al., *Impact of Parkinson's disease on the acute care treatment and medium-term functional outcome in geriatric hip fracture patients.* Archives of orthopaedic and trauma surgery, 2015. **135**(11): p. 1519-1526.
10. Findley, L., et al., *Direct economic impact of Parkinson's disease: a research survey in the United Kingdom.* Movement disorders, 2003. **18**(10): p. 1139-1145.
11. Seppi, K., et al., *The Movement Disorder Society evidence-based medicine review update: treatments for the non-motor symptoms of Parkinson's disease.* Movement disorders, 2011. **26**(S3): p. S42-S80.
12. Schrag, A., *Quality of life and depression in Parkinson's disease.* Journal of the neurological sciences, 2006. **248**(1-2): p. 151-157.
13. Alderwick, H. and J. Dixon, *The NHS long term plan*. 2019, British Medical Journal Publishing Group.
14. Newman, S., L. Steed, and K. Mulligan, *Self-management interventions for chronic illness.* The Lancet, 2004. **364**(9444): p. 1523-1537.
15. Richardson, J., et al., *Self-management interventions for chronic disease: a systematic scoping review.* Clinical rehabilitation, 2014. **28**(11): p. 1067-1077.
16. Kessler, D. and C. Liddy, *Self-management support programs for persons with Parkinson's disease: An integrative review.* Patient education and counseling, 2017. **100**(10): p. 1787-1795.
17. Chandler, S.K., J.L. Robins, and P.A. Kinser, *Nonpharmacologic interventions for the self-management of anxiety in Parkinson's disease: A comprehensive review.* Behavioural neurology, 2019. **2019**.
18. Panagioti, M., et al., *Self-management support interventions to reduce health care utilisation without compromising outcomes: a systematic review and meta-analysis.* BMC health services research, 2014. **14**(1): p. 1-14.
19. Harvey, J., et al., *Factors influencing the adoption of self-management solutions: an interpretive synthesis of the literature on stakeholder experiences.* Implementation Science, 2015. **10**(1): p. 1-15.

20. Whitehead, L., et al., *The role of the family in supporting the self-management of chronic conditions: A qualitative systematic review.* Journal of clinical nursing, 2018. **27**(1-2): p. 22-30.
21. Craig, P., et al., *Developing and evaluating complex interventions: the new Medical Research Council guidance.* 2013.
22. UK, P.s.; Available from: https://www.parkinsons.org.uk/information-and-support.
23. Fereshtehnejad, S.-M., *Strategies to maintain quality of life among people with Parkinson's disease: what works?* Neurodegenerative disease management, 2016. **6**(5): p. 399-415.
24. Cockram, L., *Using the updated Parkinson's NICE guidelines.* British Journal of Neuroscience Nursing, 2017. **13**(5): p. 228-231.
25. Tuijt, R., et al., *Self-Management Components as Experienced by People with Parkinson's Disease and Their Carers: A Systematic Review and Synthesis of the Qualitative Literature.* Parkinson's Disease, 2020. **2020**.
26. Nimmons, D., et al., *Experiences of advance care planning in Parkinson's disease and atypical parkinsonian disorders: a mixed methods systematic review.* European Journal of Neurology, 2020. **27**(10): p. 1971-1987.
27. Walters, K., et al., *Home-based health promotion for older people with mild frailty: the HomeHealth intervention development and feasibility RCT.* Health Technology Assessment (Winchester, England), 2017. **21**(73): p. 1.
28. Peto, V., C. Jenkinson, and R. Fitzpatrick, *PDQ-39: a review of the development, validation and application of a Parkinson's disease quality of life questionnaire and its associated measures.* Journal of neurology, 1998. **245**(1): p. S10-S14.
29. Peto, V., C. Jenkinson, and R. Fitzpatrick, *Determining minimally important differences for the PDQ-39 Parkinson's disease questionnaire.* Age and ageing, 2001. **30**(4): p. 299-302.
30. Goetz, C.G., et al., *Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): scale presentation and clinimetric testing results.* Movement disorders: official journal of the Movement Disorder Society, 2008. **23**(15): p. 2129-2170.
31. Herdman, M., et al., *Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L).* Quality of life research, 2011. **20**(10): p. 1727-1736.
32. Martinez-Martin, P., et al., *Pilot study of the international Parkinson and movement disorder society-sponsored non-motor rating scale (MDS-NMS).* Movement disorders clinical practice, 2019. **6**(3): p. 227-234.
33. Gureje, O. and B. Obikoya, *The GHQ-12 as a screening tool in a primary care setting.* Social psychiatry and psychiatric epidemiology, 1990. **25**(5): p. 276-280.
34. Lorig, K.R., et al., *Effect of a self-management program on patients with chronic disease.* Effective clinical practice: ECP, 2001. **4**(6): p. 256-262.
35. Flynn, T.N., et al., *Assessing quality of life among British older people using the ICEPOP CAPability (ICECAP-O) measure.* Applied health economics and health policy, 2011. **9**(5): p. 317-329.
36. Hibbard, J.H., et al., *Development of the Patient Activation Measure (PAM): conceptualizing and measuring activation in patients and consumers.* Health services research, 2004. **39**(4p1): p. 1005-1026.
37. Hoefman, R., N. Van Exel, and W. Brouwer, *iMTA valuation of informal care questionnaire*. 2015.
38. McCrone, P., *Capturing the costs of end-of-life care: Comparisons of multiple sclerosis, Parkinson's disease, and dementia.* Journal of pain and symptom management, 2009. **38**(1): p. 62-67.
39. Yap, P., *Validity and reliability of the Zarit Burden Interview in assessing caregiving burden.* Ann Acad Med Singapore, 2010. **39**: p. 758-63.
40. Pillas, M., et al., *Development and validation of a carers quality-of-life questionnaire for parkinsonism (PQoL Carers).* Quality of Life Research, 2016. **25**(1): p. 81-88.

41. Reichmann, H., *Clinical criteria for the diagnosis of Parkinson's disease.* Neurodegenerative diseases, 2010. **7**(5): p. 284-290.
42. Nasreddine, Z.S., et al., *The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment.* Journal of the American Geriatrics Society, 2005. **53**(4): p. 695-699.
43. Schrag, A., et al., *Prediagnostic presentations of Parkinson's disease in primary care: a case-control study.* The Lancet Neurology, 2015. **14**(1): p. 57-64.
44. Hunter, R., et al., *Research into biomarkers to facilitate the early identification of Parkinson's disease: a decision analytic model to determine the feasibility and value.* Trials, 2013. **14**(1): p. 1-1.
45. May, C.R., et al., *Process evaluation for complex interventions in primary care: understanding trials using the normalization process model.* BMC Family Practice, 2007. **8**(1): p. 42.
46. Office of National Statistics, *2011 Census data*. 2011.

29.APPENDICES: Gantt chart

Project Month	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36
RCT with internal pilot study																																				
Site initiation/training																																				
Internal pilot recruitment																																				
Main RCT recruitment																																				
Deliver intervention																																				
Follow-up																																				
Process evaluation																																				
Main RCT analysis																																				
Health Economic Analysis																																				
Write up and diseminatin																																				