

Promoting Independence in Dementia (PRIDE): A Feasibility Randomised Controlled Trial

Statistical Analysis Plan

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Based on Protocol version 2.1 (dated 22 May 2019)

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The following people have reviewed the Statistical Analysis Plan and are in agreement with the contents

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Abbreviations

Abbreviation	Description
AUC	Area under the curve
CASP	Control, Autonomy, Self-realisation and Pleasure
CDR	Clinical Dementia Rating
CI	Confidence interval
DMC	Data monitoring committee
GDS	Geriatric Depression Scale
IADL	Instrumental Activities of Daily Living
IPAQ-O	Impact on Participation and Autonomy Questionnaire for older people
MIC	Minimal important change
PPOM	Positive Psychology Outcome Measure
ROC	Receiver Operating Characteristic
SAP	Statistical Analysis Plan
S-MMSE	Standardised Mini Mental State Exam
TMG	Trial Management Group
TSC	Trial Steering Committee
VAS	Visual analogue scale

Changes from protocol

The table below details changes to the planned analyses in the SAP compared to the protocol which after discussion with the TMG are not considered to require a protocol amendment.

Protocol version and section	Protocol text	SAP version and section	SAP text	Justification
<i>Not applicable – no changes to planned analysis</i>				

Amendments to versions

Version	Date	Change/comment	Statistician
1.0	21 Jan 2020	Final version 1.0	LB

Additional contributors to the SAP (non-signatory)

Name	Trial role	Job Title	Affiliation
<i>Not applicable</i>			

1. INTRODUCTION & PURPOSE

This document details the rules proposed and the presentation that will be followed, as closely as possible, when analysing and reporting the main results from the Promoting Independence in Dementia Feasibility Randomised Controlled Trial funded by Economic and Social Research Council & National Institute of Health Research (Ref. ES/L001802/1).

The purpose of the plan is to:

1. Ensure that the analysis is appropriate for the aims of the trial, reflects good statistical practice, and that interpretation of a priori and post hoc analyses respectively is appropriate.
2. Explain in detail how the data will be handled and analysed to enable others to perform or replicate these analyses

Additional exploratory or auxiliary analyses of data not specified in the protocol may be included in this analysis plan.

This analysis plan will be made available if required by journal editors or referees when the main papers are submitted for publication. Additional analyses suggested by reviewers or editors will be performed if considered appropriate. This should be documented in a file note.

Amendments to the statistical analysis plan will be described and justified in the final report of the trial and where appropriate in publications arising from the analysis.

Health economic and qualitative analysis plans are beyond the scope of this document.

2. SYNOPSIS OF STUDY DESIGN AND PROCEDURES

Title	Promoting Independence in Dementia (PRIDE): a feasibility randomised controlled trial.
Short title	PRIDE Feasibility RCT
Acronym	PRIDE
Chief Investigator	Professor Martin Orrell
Objectives	To investigate the feasibility and acceptability of conducting a randomised controlled trial (RCT) to compare the clinical and cost effectiveness of the PRIDE intervention delivered in addition to usual care with usual care only for people with mild dementia.
Trial configuration	Prospective, parallel group, two-arm, multicentre, feasibility, randomised controlled trial (RCT).
Setting	Services for people with dementia within NHS Secondary Care Trusts in England.
Sample size estimate	As this is a feasibility study, a formal sample size calculation for between group comparisons is not appropriate. However a sample size of 75-80 randomised participants will allow estimation of recruitment fraction with a margin of error (half-width of 95% confidence interval) of around 8 percentage points, and retention of 12 percentage points.
Number of participants	A target sample size of 75-80 participants and up to 80 supporters will be sought from up to 6 sites over the recruitment period.
Eligibility criteria	<i>Inclusion criteria for the person with dementia</i> - Resident within the catchment area of one of the participating NHS sites. - Aged 18 or over; there is no upper age limit. - Meet the Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition (DSM-IV) criteria for dementia of any type, including Alzheimer's, vascular, Lewy body type and mixed. - Able to engage with and participate in the intervention in the judgement of the investigator or designee. - Able to provide informed consent in the judgement of the investigator or designee. - Able to read and communicate verbally in English. - Mild dementia, defined as a score of 0.5 or 1 on the Clinical Dementia Rating (CDR) Scale. The CDR will be completed as a post-consent screening assessment to determine eligibility for randomisation. <i>Exclusion criteria for the person with dementia</i> - Living in institutional care. <i>Inclusion criteria for supportive others (participation is optional)</i> - Aged 18 or over; there is no upper age limit. - Able to engage with and participate in the intervention. - Able to provide informed consent.

	- Able to read and communicate verbally in English.
Description of interventions	<i>PRIDE intervention</i> The PRIDE intervention is a social intervention encompassing social, physical, and cognitive dimensions for people in the early stages of dementia. It comprises a manual which is worked through with the support of a trained facilitator during three sessions of between 60-90 minutes, over two months. The objectives of the intervention are to promote independence and facilitate the person's access to opportunities to live well with dementia by supporting meaningful social, cognitive, and physical activities and healthy lifestyle choices and helping the person maintain their social roles. The PRIDE intervention will be delivered in addition to usual care. <i>Usual care</i> All participants will have access to the services and interventions usually available to people with dementia and their family at the participating sites. This will likely vary between and within centres and may change over time.
Duration of study	The expected recruitment period will be up to 10 months from enrolment of the first participant. Each participant will be in the trial for a maximum of 6 months, from randomisation to final follow-up. The duration of the trial is expected to be up to 24 months from recruitment of the first participant to reporting.
Randomisation and blinding	Participants will be individually allocated on a 1:1 ratio using minimisation with a probabilistic element. The minimisation variables will be study site, sex, age (< 80 or ≥ 80) and medication for dementia (any versus none). Clinicians delivering the intervention and participants and their supporters will be aware of treatment allocation. Outcomes will be collected by staff blinded to treatment allocation.
Outcome measures	Outcomes will be measures of the feasibility of conducting a full RCT related to participant recruitment and follow-up, intervention delivery including the recruitment, training and retention of PRIDE trained facilitators, clinical outcomes, intervention and resource use costs and the acceptability of the intervention and study related procedures.

2.1. Sample size and justification

As this is a feasibility study, a formal sample size calculation for between group comparisons of a primary outcome is not appropriate. A target sample size of 75-80 participants will be sought from up to 6 sites over the 7 month recruitment period. A sample size of 75 randomised participants will allow estimation of recruitment fraction with a margin of error (half-width of 95% confidence interval) of around 8 percentage points, and retention rate with a margin of error of 12 percentage points.

2.2. Blinding and breaking of blind

Due to the nature of the intervention, blinding of treatment allocation is impossible for participants and the staff delivering the intervention. The outcome assessment visits will be conducted by members of the local research team who will be blind to group allocation. Instances of unblinding at the outcome assessment visits will be recorded. The trial statisticians will remain blinded to treatment allocation until after database lock.

2.3. Trial committees

A trial management group (TMG) and trial steering committee (TSC) will be assembled to oversee the trial. The general purpose, responsibilities and structure of the committees are described in the protocol. Further details of the roles and responsibilities of the TSC can be found in the TSC Membership Agreement.

As the trial interventions and procedures have been assessed as low risk, safety oversight will be performed by the TSC without the need for a separate independent Data Monitoring Committee.

2.4. Outcome measures

Feasibility outcomes

The primary outcome of this study is the feasibility of conducting a full RCT of the PRIDE intervention, determined by a range of measures related to the study objectives. The feasibility outcomes, which will be measured to meet the objectives of this study, are shown in **Error!**
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Table 1: Feasibility objectives and outcomes

Feasibility Objectives	Feasibility Outcomes	Included in quantitative analysis to be conducted by NCTU
1. Determine the feasibility of recruitment to a large-scale RCT	a. Aggregate data on potential participants within NHS services b. Number of patients assessed for eligibility / consented / randomised c. Number and proportion of potential participants identified through NHS services, Join Dementia Research and by self-referral who are eligible d. Reasons for non-inclusion / non-eligibility e. Monthly recruitment rate per site f. Barriers and facilitators to recruitment (focus groups)	a. to e. – yes f. - no, will be analysed as part of the qualitative study

Feasibility Objectives	Feasibility Outcomes	Included in quantitative analysis to be conducted by NCTU
2. Refine the eligibility criteria for a future definitive RCT	a. Number of screening failures for eligibility, post-consent b. Participant and facilitator report (focus groups)	a. yes b. no, will be analysed as part of the qualitative study
3. Determine the acceptability to patients / clinicians of randomisation	a. Proportion of eligible patients that consent to randomisation b. Reasons for non-consent c. Participant and facilitator report (focus groups)	a. and b. yes c. no, will be analysed as part of the qualitative study
4. Determine the relevance and acceptability to patients / clinicians of the trial intervention	a. Premature discontinuation or non-attendance of treatment and reasons b. Feedback from participants and site staff delivering the intervention c. Participant and facilitator report (focus groups)	a. yes b. and c. no, will be analysed as part of the qualitative study
5. Determine the acceptability to patients / clinicians of the trial procedures	a. Proportion of approached NHS sites that agree to participate in the trial and reasons for non-participation b. Proportion of eligible patients that consent to randomisation c. Reasons for non-consent d. Withdrawals and losses to follow-up and reasons e. Feedback from participants and staff (focus groups)	a. to d. yes e. no, will be analysed as part of the qualitative study
6. Assess the ability of NHS sites to deliver the intervention	a. Measures of the feasibility of delivering the PRIDE intervention within NHS settings: i. Number / grade / experience of staff within the service ii. Staff turnover iii. Time to treatment initiation b. Measures of the recruitment and retention of PRIDE facilitators during the study treatment period c. Barriers to treatment delivery per protocol (focus groups)	a. and b. yes d. no, will be analysed as part of the qualitative study
7. Assess training and support needs for NHS staff delivering the intervention	a. Feedback on training delivered (focus groups) b. Support offered / accepted (e.g. log of calls and emails to central support lines)	No, this will be analysed as part of the fidelity analysis

Feasibility Objectives	Feasibility Outcomes	Included in quantitative analysis to be conducted by NCTU
8. Evaluate treatment fidelity when delivered through NHS services	a. Measures of treatment fidelity including: i. Adherence to intervention manual ii. Uptake of activities b. Feedback from participants and staff (focus groups)	No, this will be analysed as part of the fidelity and qualitative analysis
9. Determine the services and interventions provided as usual care and evaluate methods for measuring this	a. Post-diagnostic care pathway b. Services available c. Uptake of services	No, this will be analysed as part of the health economic analysis.
10. Assess follow-up and outcome completion rates	a. Response rate to follow-up assessment b. Questionnaire completion rates c. Amount of missing questionnaire data at item and scale levels	Yes
11. Determine the relevance and acceptability of a range of clinical outcome measures and selection of the primary outcome for the main trial	a. Completion rates and reasons for non-completion / missing data b. Estimates of clinically important differences, variance and sensitivity to change for the clinical outcome measures c. Direct questions to participants regarding relevance of measures	Yes
12. Evaluate the utility and acceptability of resource use questionnaires for use in an economic evaluation alongside a future RCT	a. Completion rate and reasons for non-completion / missing data	No, this will be analysed as part of the health economic analysis.
13. Comparative micro-costing of PRIDE intervention and usual care	a. Staff time and resources for delivery of PRIDE intervention b. Other service use	No, this will be analysed as part of the health economic analysis.
14. Estimate the sample size required for a definitive study	a. Primary outcome selection b. Variability in the outcome c. Withdrawals and losses to follow-up	No, this objective will be met after consideration of the other feasibility outcomes described above.

Feasibility Objectives	Feasibility Outcomes	Included in quantitative analysis to be conducted by NCTU
15. Determine the resources required for a full trial	a. Sample size, recruitment rate (number of sites / recruitment period), staffing and resources (for recruitment, treatment and follow-up)	No, this objective will be met after consideration of the other feasibility outcomes described above.

Clinical outcomes

Clinical outcomes will be measured to assess the relevance and acceptability of these outcomes for use in a future definitive RCT and to obtain information to inform selection of the primary outcome measure for a future trial. In addition to asking participants to complete a range of clinical outcome measures, participants will also be asked to rate the relevance and acceptability of these measures to their experience.

The following clinical outcomes will be assessed at baseline and at follow-up visits completed at 3 and 6 months post-randomisation (see Table 2).

Table 2: Summary of the clinical outcome measures

Outcome measures	Scale, description and source	Derivation of scores			
			Base-line	3 months	6 months
<i>Participants</i>					
Activities of Daily Living	- Measured using the Lawton Instrumental Activities of Daily Living (IADL) Scale (Lawton and Brody 1969) - Performance is measured across eight domains	- Each domain has between three and five response options describing ability. These are scored as 0 (less able) or 1 (more able). - Domain scores summed to produce summary score from 0 (low function) to 8 (high function).	✓	✓	✓
Health related quality of life	- Measured using EuroQoL Quality of Life Questionnaire – 5 Domains, 5 Levels (Euroqol Group 1990) - Consists of two parts: a descriptive system and a visual analogue scale (VAS) asking about health on that day - The 5 level descriptive system will be used as part of the health economic analysis - The VAS will be analysed as part of the quantitative analysis conducted by the NCTU	VAS scores range from 0 (worst health can imagine) to 100 (best health can imagine)	✓	✓	✓

Outcome measures	Scale, description and source	Derivation of scores			
			Base-line	3 months	6 months
Quality of life	- Measured using DEMQOL (Smith, Lamping et al. 2005) - Assesses five domains of quality of life including health and well-being, cognitive functioning, social relationships and self-concept.	- Scale consists of 28 items about the last week with 4 response options (a lot, quite a bit, a little and not at all). - Items are scored as 1 = a lot, 2 = quite a bit, 3 = a little and 4 = not at all apart from 5 positive questions which are scored in reverse. - Items are summed to produce a total score ranging from 28 to 112, higher scores indicating better quality of life. - Missing items are imputed with person-specific mean of completed items provided at least 50% of items are complete (i.e. 14 items).	✓	✓	✓
Mood	Measured using the Geriatric Depression Scale (GDS) – short form (Sheikh and Yesavage 1986)	15-items about the last week with responses of yes or no. - Items scored as 1 when response indicates depression and 0 otherwise (10 items indicate the presence of depression when answered positively, and 5 items when answered negatively). - Item scores summed to produce a total score ranging from 0 to 15,	✓	✓	✓

Outcome measures	Scale, description and source	Derivation of scores			
			Base-line	3 months	6 months
		with higher scores indicating more severe depression.			
Cognition	Measured using the Standardised Mini Mental State Exam (S-MMSE) (Molloy and Standish 1997)	- Brief assessment of cognition testing orientation (time and place), repetition, verbal recall, attention and calculation, language and visual construction - The total test score is the sum of the correct responses ranging from 0 to 30 with a lower score indicating more cognitive impairment. - An adjusted score can be calculated for people who are physically unable to do some of the tasks on the MMSE (IHPA Australia).	✓	✓	✓
Wellbeing	- Control, Autonomy, Self-realisation and Pleasure (CASP) questionnaire (Hyde, Wiggins et al. 2003) - Assesses quality of life in older people across 4 domains; control, autonomy, pleasure and self-realisation.	19 items with four response options (often, sometimes, not often and never) - Items scored on a 4 point Likert scale as shown on the CASP website (https://casp19.com/casp-scoring-and-properties/). - Items scores summed to produce a total score ranging from 0 to 57,	✓	✓	✓

Outcome measures	Scale, description and source	Derivation of scores			
			Base-line	3 months	6 months
		with higher scores indicating better quality of life. The 12 item version of the CASP will also be used as this has been found to have a better factor structure for people with dementia than the 19 item version (Stoner, Orrell et al. 2019). In the 12 item version, items 3 (control subscale), items 6 and 8 (autonomy subscale), items 13 and 14 (pleasure subscale) and items 16 and 17 (self-realisation subscale) are not used.			
Quality of relationships	Measured using Impact on Participation and Autonomy Questionnaire for older people (IPAQ-O) social relations subscale (Hammar, Ekelund et al. 2014)	- Social relations subscale has 5 items with 5 response items - The response options on the PRIDE CRF were very good, good, fair, poor, very poor from the original IPAQ (Cardol, de Haan et al. 2001) rather than amended response options for the IPAQ-O (totally agree, partly agree, neither agree nor disagree, disagree, and totally disagree). - The response options will be scored as on the original IPAQ: very good =	✓	✓	✓

Outcome measures	Scale, description and source	Derivation of scores			
			Base-line	3 months	6 months
		1, good = 2, fair = 3, poor = 4 and very poor = 5. - Item scores summed to produce a total score ranging from 5 to 25 with higher score indicating more restriction in participation. - The mistake in the response options will be acknowledged in a footnote in the results tables and in the publication.			
Positive emotions	- Measured using the Positive Psychology Outcome Measure (PPOM) (Stoner, Orrell et al. 2018) - Two subscales: hope and resilience	16-item scale measuring aspects of positive psychology with an eight item hope subscale and an eight item resilience subscale - Each item is rated on a 5-point Likert scale (0 = not true at all, 1 = rarely true, 2 = sometimes true, 3 = often true, 4 = true nearly all the time). - Items scores summed to produce a total score ranging from 0 to 64 and subscale scores ranging from 0 to 32, higher scores indicate better wellbeing.	✓	✓	✓

Outcome measures	Scale, description and source	Derivation of scores			
			Base-line	3 months	6 months
Social engagement	Measured using the number of social contacts and leisure activities in the preceding 2 weeks.	Questions asked: - How many times over the last 2 weeks have you met up with friends or family? (e.g., family or friends visiting, you visiting them, attending a social club) - How many times over the last 2 weeks have you participated in any leisure activities? (e.g., hobbies)	✓	✓	✓
Global change in wellbeing and independence	Participants will be asked to provide a rating of their perceived change using a 5-point ordinal scale.	Questions asked: - Compared to 3/6 <i>[depending on time since randomisation]</i> months ago when you started in the PRIDE study, how would you rate your general wellbeing now? Response options: much better, a bit better, no change, a bit worse, much worse. - Compared to 3/6 <i>[depending on time since randomisation]</i> months ago when you started in the PRIDE study, how independent do you feel now? Response options: much more independent, a bit more independent, no change, a bit less independent, much more independent.		✓	✓

Outcome measures	Scale, description and source	Derivation of scores			
			Base-line	3 months	6 months
	Supporters will also be asked to independently provide a rating of their perceived change for the person with dementia from their perspective, during the course of the study, using the same 5-point ordinal scale	Questions asked: - Compared to 3/6 months ago <i>[depending on time since randomisation]</i> when your friend/relative started in the study, how would you rate their general wellbeing now? - Compared to 3/6 months ago <i>[depending on time since randomisation]</i> when your friend/relative started in the study, how independent do you feel they are now?		✓	✓
<i>Supporters</i>					
Health related quality of life	Measured using the EuroQoL Quality of Life Questionnaire – 5 Domains, 5 Levels - Consists of two parts: a descriptive system and VAS - The 5 level descriptive system will be used as part of the health economic analysis - The VAS will be analysed as part of the quantitative analysis conducted by the NCTU	VAS scores range from 0 (worst health can imagine) to 100 (best health can imagine).	✓	✓	✓

3. INTERIM ANALYSIS

No formal interim analyses are planned.

4. GENERAL ANALYSIS CONSIDERATIONS

4.1. Analysis sets

The table below describes the analyses sets.

Outcome	Analysis set
Feasibility outcomes	Feasibility outcomes relating to consent and randomisation will use the number of patients screened as the analysis set.
Clinical outcomes	Data for participants and supporters presented according to allocated group regardless of adherence with the allocated intervention.

All analyses will be for participants with outcome data collected. There will be no imputation for missing data.

4.2. Timing of final analysis

All outcomes will be analysed collectively after database lock.

4.3. Statistical software

Analyses will be performed using Stata version 16.0 or above.

4.4. Derived variables

Derivations for the clinical outcomes are described in Table 2.

4.5. Procedures for missing data

Follow-up completion, completion of questionnaires during the follow-up visits and amount of missing data for each item within each questionnaire are feasibility outcomes and will therefore be summarised descriptively overall and by allocated group.

Baseline characteristics between those followed-up and not follow-up at 3/6 months will be compared to investigate how similar these are across the treatment arms to assess possible attrition bias in data collection.

For missing data within questionnaires tool specific guidance will be used, if available, as described in Table 2. Otherwise missing items in questionnaires will be imputed by the participant mean of the completed responses (rounded to one decimal place) (Bell, Fairclough et al. 2016).

As this is a feasibility study and clinical outcomes will be analysed descriptively, there will be no imputation of data for participant/supporters who are not followed up.

5. DESCRIPTION OF SITE AND PARTICIPANT CHARACTERISTICS

5.1. Trial recruitment

The number of NHS sites approached about the trial, who returned the site selection questionnaire, who were deemed able to deliver the study and agreeing to participate will be summarised as part of assessing the acceptability to clinicians of the trial procedures. Reasons for non-participation will be described.

For sites that take part, the number of days between the site initiation visit and opening to recruitment and days between opening and randomisation of the first participant will be tabulated to inform a larger trial. To assess the pool of potential participants for a larger trial, the number of potentially eligible patients within the site at the time of opening and number of new potentially eligible patients registered during the site recruitment period will be tabulated (if available). The number of patients invited to take part in the trial and expressing an interest in the trial will be summarised by site.

Recruitment will be tabulated by site and by route of identification (NHS services – invited in clinic or by invitation letter, Join Dementia Research or self-referral) to show the number screened, the number assessed as eligible prior to consent, the number giving consent and the number randomised. Reasons for not consenting after screening (including reasons for not being eligible prior to consent) and reasons for not randomising after consent will also be tabulated by site and route of identification.

Age and gender will be presented descriptively for the screened patients according to recruitment status (i.e. eligibility, consent and randomisation) to ascertain adequacy of inclusion/exclusion criteria and likely generalisability of the trial to the required targeted population.

To assess the ability of NHS sites to deliver the trial and the intervention, the number of research staff and facilitators involved in the trial will be tabulated with turnover during the trial. In addition for the intervention facilitators, job role and grade will be summarised.

5.2. Participant flow

The flow of participants through the trial will be summarised in a Consort flow diagram which will show the numbers of people with dementia who were invited or expressed an interest in the trial, the number screened, route of identification, the number who consented, the number who were excluded prior to consent with reasons, the numbers who consented but were not randomised with reasons, the total number randomised and the number allocated to each group and follow-up visit completion at 3 and 6 months (with reasons if the visits was not completed). For the PRIDE intervention group, the number of participants who received at least one sessions and the reason if no sessions were attended will also be presented.

Recruitment rates and follow-up rates will be presented with 95% confidence intervals.

The summaries described in section 5.1 and 5.2 address the feasibility objectives relating to determining the feasibility of recruitment to a large scale RCT, refining the eligibility criteria and determining the acceptability to patients of randomisation and the trial procedures.

5.3. Baseline characteristics

The following baseline characteristics will be summarised in each of the two allocated groups and overall:

- o Demographic variables: Age at randomisation, gender, ethnicity, educational attainment, living arrangements, marital status and whether the participant has facilities available for use of the web based manual.
- o Dementia information: type of dementia, whether any medication is taken for dementia and the Clinical Dementia Rating (CDR) Scale score at baseline.
- o Clinical outcomes for the participant collected at baseline (see Table 2).
- o Supporter information: whether the participant wished to take part in the trial with a supporter, whether a supporter consented to participate, supporter relationship with the participant, length of time in the supporter role and supporter EQ-5D-5L health status VAS score at baseline.

Continuous data will be summarised in terms of the mean, standard deviation, median, lower quartile, upper quartile, minimum, maximum and number of observations. Categorical data will be summarised in terms of frequency counts and percentages.

6. ASSESSMENT OF STUDY QUALITY

6.1. Randomisation

Participants are allocated to intervention or control on a 1:1 ratio using a minimisation algorithm with a probabilistic element. The minimisation variables are study site, sex, age (< 80 or ≥ 80) and medication for dementia (any versus none). The number of participants in each allocated group and minimisation variable category will be presented as part of the baseline characteristics.

6.2. Adherence

The PRIDE intervention comprises a manual which is worked through with the support of a trained facilitator during up to three sessions of between 60-90 minutes, held over approximately two months.

Adherence to the PRIDE intervention will be summarised by tabulating (overall and by site):

- o attendance at each session
- o reason if sessions were not attended
- o number of sessions attended
- o type of manual used (paper, electronic, both, neither)
- o days from randomisation to each session
- o supporter attendance at session and reason if supporter not in attendance

to determine the acceptability to patients of the trial intervention.

6.3. Follow-up and discontinuations

For the baseline visit, the number of times that the researcher visited the participant to complete the assessments/questionnaires, the total number of minutes spent with the participant and days from the visit to randomisation will be summarised overall and by allocated group.

Three and six month follow-up visit completion will be summarised overall and by allocated group with reason if the visit was not done, days to the visit from randomisation, number of times that the researcher visited to complete the visit and total number of minutes spent with the participant. For completed visits, researcher unblinding will also be summarised.

For participants with a supporter who consented to the trial, supporter questionnaire return at 3 and 6 months will be summarised overall and by allocated group with the reason if the questionnaire was not returned. Days to questionnaire completion and whether the questionnaire was completed in-person (at the visit with the participant) or returned in the post will also be summarised.

It is possible for the participant supporter to change during the trial, for example due to the original supporter wishing to withdraw from the trial and the participant nominating an alternative supporter or the participant no longer wishing to participate with a supporter. Therefore, changes in supporter during the trial and the reason for the change will be summarised overall and by allocated group.

At each time point the completion of the clinical outcome measures (as described in Table 2) will be summarised overall and by allocated group in the following categories: fully completed, partially completed and not completed. The reason will also be summarised if not completed. The amount of missing data for each item in the clinical outcome measure will also be summarised overall and by allocated group at each time point.

6.4. Protocol deviations

A protocol deviation is a divergence or departure from the expected conduct of a study as defined in the protocol.

Protocol deviations entered onto the protocol deviations log of the electronic case report form by NCTU staff will be summarised, with the number and type by allocated group (eligibility, informed consent, minimisation error or other). In addition, the number and percentage of participants with at least one protocol deviation will be summarised. A listing of all protocol deviations will also be presented.

7. ANALYSES RELATING TO FEASIBILITY OBJECTIVES

Relevance of clinical outcomes

One of the feasibility objectives is to determine the relevance of a range of clinical outcome measures. At each time point for each clinical outcome (apart from IADL and sMMSE as these are

assessed rather than questionnaire based), participants are asked “the questions in this section asked about things that are relevant to me” with response options of strongly agree, agree, neither agree nor disagree, disagree and strongly disagree. The number of participants responding as strongly agree or agree will be tabulated for each clinical outcome and time point.

Global changes

The participant rating and supporter rating of change in participant general well-being and independence will be summarised overall and by allocated group at each follow-up time point. Participant and supporter rating of change will also be cross tabulated and presented in a scatter plot to look at the consistency of the two external criteria for judging improvement.

The following clinical outcomes will be considered as candidate primary outcomes for a larger trial and their responsiveness and minimal important change (MIC) will be evaluated:

- o Activities of daily living measured using the Lawton IADL scale
- o Quality of life measured using the DEMQoL
- o Wellbeing measured using CASP (Score from 19 item version and 12 item version)

For each of the candidate primary outcomes listed above, change from baseline at 6 months according to the global change question response category from both participants and supporters will be summarised using the mean and standard deviation.

Responsiveness to change

For each candidate primary outcome, we will determine the correlation between the change score and the rank of the global change at 6 months using Spearman’s coefficient, where we hypothesised that there will be moderate-to-high correlations between change score and the global change if they measure the same construct. Secondly, we will use a receiver operating characteristic (ROC) curve analysis to plot the sensitivity versus 1-specificity for multiple cut-off points of the change in the outcome measure at 6 months against the external criterion (global change dichotomised into improvers vs. non-improvers (Table 3)). An area under the ROC curve (AUC) and 95% CI will be calculated for each curve to assess the ability of the instruments to discriminate between participants who are considered to be improved and participants who are not considered to be improved according to the external criterion.

Minimal Important Change (MIC)

For each of the candidate primary outcomes listed above, estimates of the minimal important change (MIC, defined by the COSMIN panel (Mokkink, Terwee et al. 2012) as the smallest change in score in the construct to be measured which patients perceive as important will be calculated using anchor-based methods:

- o The between patient score change method (Copay, Subach et al. 2007). The MIC will be calculated as the difference between the mean change in the group with a response of a bit better/a bit more independent and the group with a response of no change on the global change question.

- o Sensitivity and specificity based approach. Participants will be grouped into improvers and non-improvers based on the global change questions (see Table 3). Receiver operating characteristic (ROC) curves for the change from baseline to discriminate between improvers and non-improvers will be plotted and the area under the curve calculated. The estimate of the MIC using this method will be defined as the change from baseline that maximises the Youden Index: sensitivity + specificity – 1 (Perkins and Schisterman 2006).

Table 3: Classification of improvers/non-improvers from global change questions

	Improvers	Non-improvers
Well-being	Much better A bit better	No change A bit worse Much worse
Independence	Much more independent A bit more independent	No change A bit less independent Much less independent

8. ANALYSIS OF EFFECTIVENESS

Clinical outcomes will be summarised descriptively by allocated group for each time point.

It is not an objective of the feasibility study to obtain definitive estimates of the intervention effect on clinical outcomes and this feasibility trial is not powered to detect clinically relevant differences between groups. However differences in mean between groups with confidence intervals for the candidate primary outcomes described above at 6 months will be calculated to show the possible range of treatment effects. Differences between groups will be estimated using linear mixed models including fixed effects for sex, age, any medication for dementia and baseline score and a random effect for the recruiting site. Adjusted differences in means will be presented with 95%, 85% and 75% confidence intervals in a forest plot to explore the strength of the preliminary evidence (Lee, Whitehead et al. 2014).

9. ANALYSIS OF SAFETY

Adverse events and serious adverse events are not being collected for this trial and there are also no specific safety endpoints. Therefore no analysis of safety will be conducted.

10. FINAL REPORT TABLES AND FIGURES

See separate dummy table document: 1504PRIDE dummy Tables for final analysis final v2.0 (22-Jan-2020).

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