Lee Silverman Voice Treatment versus NHS Speech and Language Therapy versus control for dysarthria in Parkinson's disease (PD COMM)

Sackley, Catherine M; Rick, Caroline; Brady, Marian C.; Woolley, Rebecca; Burton, Christopher ; Patel, Smitaa; Masterson-Algar, Patricia; Nicoll, Avril; Smith, Christina H.; Jowett, Sue; Ives, Natalie; Beaton, Gillian; Dickson, Sylvia ; Ottridge, Ryan; Sharp, Leslie ; Nankervis, Helen; Clarke, Carl E; PD COMM Collaborative Group

Lee Silverman Voice Treatment versus NHS Speech and Language Therapy versus control for dysarthria in Parkinson's disease (PD COMM): a UK, multicentre, pragmatic, randomised controlled trial.

Authors

Catherine M. Sackley, Caroline Rick, Marian C. Brady, Rebecca Woolley, Christopher Burton, Smitaa Patel, Patricia Masterson-Algar, Avril Nicoll, Christina H. Smith, Sue Jowett, Natalie Ives, Gillian Beaton, Sylvia Dickson, Ryan Ottridge, Leslie Sharp, Helen Nankervis, and Carl E. Clarke on behalf of the PD COMM collaborative group.

Author's affiliations

School of Health Science, University of Nottingham, QMC, Nottingham NG7 2HA, UK. (Prof. C. M. Sackley PhD, H. Nankervis PhD)

Population Health Sciences, Addison House, King's College London, Guy's Campus, London SE1 1UL, UK. (Prof C. M. Sackley PhD, H. Nankervis PhD, Leslie Sharp)

Nottingham Clinical Trials Unit, University of Nottingham, Applied Health Research Building, University Park, Nottingham NG7 2RD, UK. (C. Rick PhD)

Birmingham Clinical Trials Unit, University of Birmingham, Birmingham B15 2TT, UK. (C. Rick PhD, R. Woolley MSc, S. Patel MSc, N. Ives MSc, R. Ottridge MPhil)

Nursing, Midwifery and Allied Health Professions Research Unit, Glasgow Caledonian University, Glasgow G4 0BA, UK. (Prof M. C. Brady PhD, A. Nicoll PhD, S. Dickson BSc)

Queen Elizabeth Hospital, NHS Greater Glasgow and Clyde, Glasgow, UK. (G. Beaton BSc)

School of Allied and Public Health Professions, Canterbury Christ Church University, Canterbury CT1 1QU, UK. (Prof C. Burton PhD)

School of Medical and Health Sciences, Bangor University, Bangor, UK. (P. Masterson-Algar PhD)

Health Economics Unit, Institute of Applied Health Research, University of Birmingham, Birmingham, B15 2TT, UK. (Prof. S. Jowett PhD)

Division of Psychology and Language Science, Faculty of Brain Sciences, University College London, London, UK. (C. H. Smith PhD)

Institute for Applied Health Research, University of Birmingham, Birmingham B15 2TT, UK. (Prof C. E. Clarke FRCP)

Department of Neurology, Sandwell and West Birmingham Hospitals NHS Trust, Birmingham, B18 7QH, UK. (Prof C. E. Clarke FRCP)

Correspondence to: Caroline Rick, Nottingham Clinical Trials Unit, University of Nottingham, , Nottingham, NG7 2RD. Email: caroline.rick@nottingham.ac.uk

Abstract

Objectives

We aimed to assess the clinical effectiveness of two speech and language therapy (SLT) approaches versus no speech and language therapy for dysarthria in people with Parkinson's disease.

Design

This was a pragmatic, UK-wide, multicentre, three-arm, parallel group, unblinded, randomised controlled trial. Participants were randomly assigned using minimisation in a 1:1:1 ratio to Lee Silverman Voice Treatment (LSVT LOUD®), NHS SLT, or no SLT. Analyses were based on the intention to treat principle.

Setting

The speech and language therapy interventions were delivered in outpatient or home settings.

Participants

Between September 2016 and March 2020, 388 people with Parkinson's disease and dysarthria were randomised into the trial: 130 to LSVT LOUD®, 129 to NHS SLT, and 129 to no SLT.

Interventions

Lee Silverman Voice Treatment (LSVT LOUD®) consisted of four, face-to-face or remote, 50-minute sessions each week delivered over 4 weeks. Home-based practice activities were set for up to 5 to 10 minutes daily on treatment days and 15 minutes twice daily on non-treatment days.

NHS Speech and language therapy (NHS SLT) dosage was determined by the local therapist in response to individual participants' needs. Prior research suggested that NHS SLT participants would receive an average of one session per week over 6 to 8 weeks. Local practices for NHS SLT were accepted, except for those within the LSVT LOUD® protocol.

Main outcome measures

The primary outcome was the self-reported Voice Handicap Index (VHI) total score at 3 months.

Results

People randomised to LSVT LOUD® reported lower VHI scores at 3 months post-randomisation than those who were randomised to no SLT (-8·0 points (99%CI: -13·3 to -2·6); p = 0·0001). There was no evidence of a difference in VHI scores between NHS SLT and no SLT (1·7 points; (99%CI: -3·8 to 7·1); p = 0·43). Patients randomised to LSVT LOUD® also reported lower VHI scores than those randomised to NHS SLT (-9·6 points; (99%CI: -14·9 to -4·4); p < 0.0001). There were 93 adverse events (predominately vocal strain) in the LSVT LOUD® group, 46 in the NHS SLT group, and none in the no SLT group. There were no serious adverse events.

Conclusions

LSVT LOUD® was more effective at reducing the participant reported impact of voice problems than no SLT and NHS SLT. NHS SLT showed no evidence of benefit compared to no SLT.

Trial registration

The completed trial registration is ISRCTN12421382.

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Main Text

Introduction

Parkinson's disease is a progressive, neurodegenerative disorder leading to declining motor function and non-motor conditions such as dementia, depression, and anxiety. A common motor feature is dysarthria (often referred to as hypokinetic dysarthria), which may lead to reduced speech volume, word stress patterns and fluency; speech that is monotone in pitch with imprecise articulation; changed voice quality and breath support; and an irregular speech rhythm.[1] Parkinson's-related dysarthria negatively impacts communication, social activities, and participation, leading to stigmatisation, social isolation, and reduced quality of life.[2-5] Dysarthric symptoms vary in their response to increased dopaminergic medication[6] and can become worse with subthalamic stimulation surgery.[7]

Speech and language therapy (SLT) for people with Parkinson's-related dysarthria aims to maximise communication through exercise interventions targeting motor skills, approaches to support communication between the person with Parkinson's disease and their family, and the use of alternative or augmentative aids to facilitate communication. Several SLT approaches are available to people with Parkinson's disease throughout the UK National Health Service (NHS), though variations in methods and dosage are evident.[8] Lee Silverman Voice Training (LSVT LOUD®), for example, an approach developed in the USA[9-11], that is partially available in the UK, is an intensive intervention that targets increased vocal loudness through vocal exercises and functional speech tasks. It is unusual in that it is highly protocolised.

Prior to conducting this trial, a Cochrane systematic review which included data from two of the three available randomised controlled trials (n = 41) showed that participants randomised to SLT demonstrated increased vocal loudness with two speech samples (5·4dB and 11·0dB) compared to people that had no SLT.[12] The small number of trials, limited sample sizes, and high risk of bias due to inadequate or poorly reported randomisation and allocation concealment, meant that there was insufficient evidence to determine the effectiveness of SLT for Parkinson's-related dysarthria compared to no therapy. Another review[13] which compared different SLT approaches found insufficient evidence to recommend any particular SLT approach over another. Overall, there have been 25, mostly small, RCTs of SLT interventions published. These trials showed some improvement in outcome measures of vocal loudness when speaking and reading. However, few trials measured communication participation, and only two small RCTs reported outcomes at 12 months and one at 24 months (see Appendix 1 - supplementary background information).

Following our PD COMM pilot trial of SLT in Parkinson's disease,[14] we developed the UK-wide trial to assess the effectiveness of two current SLT approaches in a pragmatic context in response to an NIHR-HTA commissioned funding call. Pragmatic trials are designed to reflect the realities of clinical practice.[15] We aimed to assess the clinical effectiveness of two SLT approaches versus no SLT for dysarthria in a pragmatic randomised controlled trial with a large number of people with Parkinson's disease, using patient-reported outcome measures reflecting the impact of dysarthria on participants' lives. The three options of LSVT, NHS SLT or no SLT reflects a common treatment scenario within the NHS. We used the PRECIS-2[16] tool to assess the impact that trial design decisions would have on applicability. The trial was registered in the ISRCTN registry: ISRCTN12421382.

Methods

Design

This was a multicentre, three-arm parallel group, unblinded, superiority, randomised controlled trial with concurrent process and economic evaluations conducted in the UK. The process and economic evaluations will be reported in detail elsewhere. Participants were recruited consecutively, with no selection, and randomised at the level of the individual in a 1:1:1 ratio to LSVT LOUD®, NHS SLT, or no SLT (control). Participants randomised to no SLT could be referred for SLT at the end of trial or during the trial, if deemed medically necessary. If SLT was required for any participant in the no SLT group, then the type and dosage was determined by the therapist responsible for their care. If a participant was non-adherent with their randomly allocated treatment, this did not constitute a reason for withdrawal from the trial. Participants were followed-up at 3, 6 and 12 months post-randomisation as this was reflective of the assessment time periods in the NHS post-treatment. The trial sites and their staff were NHS locations in England, Scotland and Wales which were already providing an SLT service. There were changes to the protocol (Appendix 2 – Table A). The trial was approved by the West Midlands - Coventry & Warwickshire Research Ethics Committee (15/WM/0443).

Participants

People were eligible to be included in the trial if they had a diagnosis of idiopathic Parkinson's disease as defined by the 1988 UK Parkinson's disease Brain Bank Criteria[17] and if they (or their carer) reported problems with their speech or voice.

Persons excluded from the trial were people with Parkinson's disease who had dementia, as clinically defined by their specialist clinician; a history of vocal strain or previous laryngeal surgery, evidence of laryngeal pathology including vocal nodules[9]; or receipt of SLT for Parkinson's-related dysarthria in the previous 2 years.

These criteria reflect the population who would be provided with SLT due to voice or speech problems on the NHS, except for previous SLT in the last 2 years which would normally not exclude a patient from receiving SLT and possibly those with dementia assessed as able to comply with treatment. The additional exclusions were 1. To ensure there was no carry over from previous SLT based on previous work by Ramig et al[18] and 2. Out of concern that patients who had dementia would not be able to comply with the intervention following feedback from the PD COMM Pilot trial.

Randomisation and masking

A central web-based randomisation system was developed and held at the Birmingham Clinical Trials Unit (BCTU). Randomisation used a minimisation process with age (≤ 59, 60–70, > 70 years), disease severity using the Hoehn and Yahr staging[19] (1·0–2·5, 3·0–5·0) and severity of speech using the Voice Handicap Index (VHI)[20] total score (≤ 33, mild 34–44, moderate 45–61, severe > 61) as the minimisation variables. A random factor was included within the minimisation algorithm to avoid the treatment allocation becoming predictable.

After providing written informed consent, and completion and collection of all baseline data, the person with Parkinson's disease could be randomised into the trial. To ensure concealment of the next treatment allocation, the local collaborator accessed the secure, central, web-based randomisation system hosted at the BCTU to obtain the intervention group that the participant was randomised to. To avoid overloading local services and/or delays between randomisation and a participant starting treatment, local availability of SLT was confirmed prior to randomisation. Due to the nature of the interventions, the trial was not blinded.

Procedures

Key members of the site research team were required to attend either a meeting or a teleconference covering aspects of the trial design, protocol procedures, adverse event reporting, collection and reporting of data, and record keeping. Trial therapists were registered with UK regulatory body the Health and Care Professions Council (HCPC), which sets standards for education, training and practice.

The interventions were provided, and trial data collected through secondary care outpatient community-based SLT departments. Where there were specific needs, or where the SLT service routinely offered it, this happened at home.

LSVT LOUD®

Delivered over four weeks, LSVT consisted of four, face-to-face or remote, 50-minute sessions each week. Sessions consisted of repetitions of maximum sustained "ah" phonation for as long as possible and then using high and low pitch glides held for 5 seconds, each in a good quality loud voice, followed by 10 self-generated functional sentence repetitions.[11] Functional movement exercises using a speech production hierarchy that progressed from reading single words to phrases, sentences, paragraphs and finally conversations, followed and were tailored to individual participant's goals. A fundamental part of LSVT LOUD is retraining of auditory sensory feedback.

Participants were set home-based practice activities for up to 5 to 10 minutes daily on treatment days and 15 minutes twice daily on non-treatment days.[11] Twenty one centres had access to the LSVT Companion software[21] providing an option of remote delivery. Only speech and language therapists or therapist assistants trained in LSVT LOUD® could deliver the intervention.[22]

NHS SLT

Generic NHS SLT is poorly defined within the published literature with no widely accepted standards for content and dosage of intervention. Therefore, local practices for NHS SLT were accepted, except for those within the LSVT LOUD® protocol. Some isolated techniques, such as vocal loudness exercises, may be common to both SLT approaches but the distinction between trial interventions could be preserved with the individualised treatment approach, the broader range of NHS SLT strategies and techniques, the intensity of delivery regimen and overall dose. NHS SLT dosage was determined by the local therapist in response to individual participants' needs. Prior research suggested that NHS SLT participants would receive an average of one session per week over 6 to 8 weeks.[8]

Outcomes

The primary outcome was the VHI[20] total score at 3 months post randomisation. Both vocal assessments and participant reported outcomes were trialled in the PD COMM pilot trial[14]. The participant assessed VHI score was chosen due to the prohibitive additional time involved in vocal assessments, the potential for vocal assessments to skew the results in favour of LSVT LOUD due to the focus on vocal loudness, and the trial's focus on participants' self-perception of functional communication using voice/speech. It is also commonly used in clinical practice with people with Parkinson's.

The VHI is a patient reported measure of the impact of communication difficulties, and has a score ranging from 0 to 120[20] (with a low score being positive). Secondary outcomes included the VHI Subscales; Parkinson's Disease Questionnaire-39 (PDQ-39)[23]; Questionnaire on Acquired Speech Disorders (QASD; also known as Living with Dysarthria)[24]; EuroQol5D [25] (5-level version); ICEpop CAPabilities Measure for Older Adults (ICECAP-O)[26]; resource utilisation; adverse events (AEs);

Hoehn and Yahr[19] stage, and carer quality of life (Parkinson's Disease Questionnaire–Carers; PDQ-carer).[27]

Adverse Events

As the adverse events in people with Parkinson's disease are well-known, only SLT-specific adverse events or serious adverse events related to vocal strain or abuse were reported for this trial. Vocal strain could be identified by patients reporting symptoms and therapists noticing clinical signs such as hoarseness. Deaths, if not deemed a serious adverse event according to the trial definition, were reported to the sponsors (BCTU) to ensure further trial data collection forms were not sent out. Data on adverse events was sought for all three trial arms.[28]

Statistical analysis

The primary comparisons in PD COMM were: (1) LSVT LOUD® versus no SLT; and (2) NHS SLT versus no SLT. We also compared LSVT LOUD® versus NHS SLT. The intention to treat principle was used for all primary analyses for both primary and secondary outcomes. All estimates of differences between groups are presented with two-sided, 99% confidence intervals, which was a deviation from the protocol, which stated 95% confidence intervals, to allow for adjustment for multiple comparisons... Statistical analysis was undertaken using the statistical software packages: SAS software, version 9.4 and Stata version 17.

To estimate differences in the VHI total score at 3 months between the two arms of interest, a linear regression model was used with the VHI baseline score and the minimisation variables: age and severity of PD (Hoehn and Yahr) included in the model as covariates. Various supporting (e.g. per-protocol) and sensitivity analyses (e.g. to assess impact of missing data) were undertaken for the primary outcome. Subgroup analyses were also performed for the primary outcome to assess whether the treatment effect differed according to age, baseline voice severity, and Parkinson's disease severity.

Continuous secondary outcome measures (e.g., PDQ-39) were analysed using linear regression models adjusting for relevant baseline score and the minimisation variables (baseline VHI, age and severity of PD). The primary analysis of the secondary outcomes was at 3 months as per the primary outcome. Secondary analyses assessed the outcomes at both 6 and 12 months using linear regression analysis as per the primary analysis, and also using repeated measures models that included all data across the 3, 6 and 12 month assessment points. Adverse events and Hoehn and Yahr stage at 12 months were summarised descriptively. Medication doses were recorded, and we calculated levodopa dose equivalents for all medication using the accepted formula.[29] Where the participant had a non-professional carer, they were also invited to join the trial and complete the PDQ-Carer questionnaire at 3, 6, and 12 months.

Sample size

As the minimal clinically important change (MCIC) score for the VHI, our primary outcome, has not yet been established, a 10-point difference in VHI between both types of SLT and no SLT (control) as observed in the PD COMM pilot trial[30] was used to inform the sample size calculations. Using a two-sided t-test and the upper standard deviation of 26·27 obtained from the pilot trial (effect size 0·38) with 80% power and $\alpha = 0{\cdot}01$; 163 participants per arm were required. A sample size of 546 participants in total (182 participants per arm) was planned, anticipating 10% attrition.

Process evaluation

For the intervention process evaluation, individual participant data were extracted from treatment record forms and therapy notes for a subset of trial participants. A piloted data extraction form, designed with reference to TIDieR and dysarthria management guidelines descriptions,[31] supported the categorisation of therapy descriptions across both SLT interventions. One researcher completed the data extraction forms and a second independently checked a sample. Interviews with patients were also completed to explore experiences of the implementation of trial interventions.

Trial oversight

Independent Trial Steering (TSC) and Data Monitoring Committees provided oversight and included members with Parkinson's disease. Interim data analyses of the primary outcome and adverse events were supplied in confidence to the data monitoring and ethics committee (DMEC). The DMEC could recommend discontinuation of the trial to the TSC if the recruitment rate or data quality were unacceptable, or if any issues were identified which may compromise participant safety.

Patient and Public Involvement

The NIHR HTA Commissioning stream works with stakeholders including patients and the public to prioritise questions to commission. The PD COMM group worked with the local Parkinson's UK branch and several individuals who contributed to the development, design, interpretation, oversight, reporting and dissemination of the study.

We fully accept that the PPI was significantly less than we would do today, however was not considered unusual at the time particularly given the nature of the commissioned call and the significant input of the participants and PPI group in the pilot trial.

Dissemination Statement

Once the results are published, we plan to disseminate the results widely, both on our University websites, our X (formerly Twitter channel: @PDCOMM_trial) and with Parkinson's UK. Much of our previous research is in the NICE guidelines for Parkinson's and, given this is the largest clinical trial in Speech and language therapy for Parkinson's with robust results on the clinical and cost-effectiveness in the NHS, we would expect it to form a significant part of future NICE guidance.

Role of the funding source

This trial was funded by the National Institute for Health Research, Health Technology Assessment (NIHR HTA) Programme, project number HTA 10/135/02. LSVT LOUD® training was provided by LSVT Global. The funder and LSVT Global had no role in the PD COMM trial design, data collection, data analysis, data interpretation, or writing of the report.

Results

Over the 42-month recruitment period from 26th September 2016 to 16th March 2020, a total of 388 people with Parkinson's-related dysarthria were randomised from 41 of the 42 recruitment centres:

130 participants to LSVT LOUD®, 129 participants to NHS SLT and 129 participants to no SLT (Figure 1). The COVID-19 pandemic impacted on the provision of SLT services for people with Parkinson's disease and, following discussions with the TSC and the funder, the trial was closed to recruitment in November 2020 after a period of recruitment suspension and prior to achieving the recruitment target (388 recruited; 71% of target). In total, 109/130 participants started LSVT LOUD®, 119/129 participants started NHS SLT and 120/129 participants did not receive SLT, as intended, for the no SLT group. Reasons for withdrawal from the trial varied and included: SLT too intense, Parkinson's deteriorated, other commitments, and wanted SLT.

Figure 1: Trial flowchart

Participants were mainly male (286/388; 74%), about half were 70 years or older and just under two thirds had mild (≤2·0) Parkinson's disease (Table 1). Data collection form return rates were high throughout the trial: primary outcome; 99% of baseline forms returned and 86% or more returned at each time point. Total time that SLTs recorded spending on the interventions was three times greater for LSVT LOUD® and delivered over more sessions (mean 1216 minutes [SD 454]; median 16 sessions) than NHS SLT (404 minutes [SD 234]; median 5 sessions) over a shorter period (LSVT LOUD® mean 7 weeks [SD 7]; NHS SLT 11 weeks [SD 11]) (see Appendix 2, Table B). The Companion software was used for 7 LSVT LOUD® participants from 5 sites with a range of 3 to 8 sessions per participant. Some therapy-related activities were similar in time allocation across interventions (goal setting, information provision and advice, liaison and onward referral). In contrast, active therapy time per participant differed with a mean of 752 minutes [SD 287] for LSVT LOUD® plus 15 minutes [SD 45] for other therapy given to the LSVT LOUD® group compared with 149 minutes [SD 113] of therapy in the NHS SLT group, reflecting LSVT LOUD®'s greater therapy intensity (hours per week) and frequency (days per week) (see Appendix 2, Table B).

Table 1: Participant demographics

From the intervention content process evaluation on a subset of therapist-completed trial participant records, most SLT interventions were delivered by qualified speech and language therapists on a one-to-one basis in outpatient settings; some participants received therapy in a group (NHS SLT) or remotely via computer software (LSVT LOUD®); or from a therapy assistant (across SLT interventions) (See Appendix 2, Table B). As expected, LSVT LOUD® activity was only reported in the LSVT participant therapy records, including the use of LSVT worksheets[32]. NHS SLT mainly described impairment-based and compensatory therapy, but also application of augmentative and alternative communication strategies, functional therapy, and generalisation. Both interventions used sheets, lists, pictures, reading passages and magazines to practise speech production techniques learned in therapy. The treatment content reports demonstrated variability and the likely tailoring of interventions to individual participants' needs. Many LSVT LOUD® records reported tailoring by level of difficulty and functional relevance, but such tailoring was less frequently reported in NHS SLT (see Appendix 2, Table B).

Participants were considered adherent if they attended at least 14 of 16 LSVT LOUD® sessions, if they completed their NHS SLT sessions within 3 months of randomisation, or if they received no therapy in the no SLT group. LSVT LOUD® adherence was similar (59%; 77/130) to NHS SLT (54%; 70/129), though not as high as for the no SLT group (93%; 120/129). Participants in the no SLT (control) arm were considered non-adherent if they reported receiving SLT over the course of the 12 month follow-up, with an exception for dysphagia-only SLT. Patient interview data demonstrated considerable determination to engage with the trial interventions successfully, although some

patients indicated they found the intensity of LSVT LOUD to be challenging. The support of family members, and adjustment of personal and family routines were key to facilitating participation.

Table 2: Primary and key secondary outcomes at 3 months

For the VHI total score at 3 months (primary outcome), LSVT LOUD® was 8 points lower (i.e., better) than for no SLT (-8.0 points [99%CI -13·3, -2·6] p = 0.0001). There was no evidence of a difference between the NHS SLT and no SLT groups (1.7 points [99%CI -3·8, 7·1] p = 0·43). The VHI total score for LSVT LOUD® was nearly 10 points lower than for NHS SLT (-9·6 points [99% CI -14·9, -4·4] p < 0·0001) (Table 2). Pre-planned supporting and sensitivity analyses of the primary outcome (see Appendix 2, Table C) were conducted and supported the results of the primary outcome analysis. Secondary analyses of the primary outcome, VHI total score at 6 and 12 months and over the whole 12 months using a repeated measures analysis gave similar results to that observed in the primary analysis at 3 months (Table 3).

Table 3: Secondary analyses of primary and key secondary outcomes

Exploratory hypothesis generating subgroup analyses for the primary outcome found there to be evidence of an interaction between the severity of the impact of voice problems (VHI) and treatment (test for interaction p=0·007), but not for Parkinson's severity (p=0.7) or age (p=0.7). Generally, the intervention effect increased as the baseline VHI score increased; for example, for LSVT LOUD® greater benefits were observed amongst those reporting more severe VHI scores at baseline (Appendix 2, Table D).

For all subscales (emotional, functional and physical) of the VHI (secondary outcomes), the scores were lower (i.e., better) for LSVT LOUD® compared to both no SLT and NHS SLT at both 3 months and for the overall trial period, with significant benefits observed for the emotional and functional subscales. There was no evidence of a difference between NHS SLT and no SLT at any timepoint across all three VHI subscales (Tables 2 and 3).

At 3 months, QASD scores (secondary outcome) were lower (i.e., better) with LSVT LOUD® compared with no SLT and NHS SLT. There was no evidence of a difference between NHS SLT and no SLT (Table 2). Similar results were seen at 6 and 12 months, and over the whole trial follow-up period (Table 3).

The PDQ-39 (secondary outcome) assesses eight domains (mobility, activities of daily living, emotional wellbeing, stigma, social support, cognition, communication, bodily discomfort) and overall quality of life. At 3 months, the largest differences were observed in the communication domain for LSVT LOUD® versus no SLT: -6.2 points (99%CI: -11.9. -0.6, p=0.004) which exceeded the MCID for this domain (Tables 2 & 3, and see Appendix, Table E). For the ICECAP-O and the EuroQol5D utility and visual analogue scores (secondary outcomes), no evidence of a difference was found for any of the comparisons at any time point (Tables 2 & 3).

The carer quality of life summary index score (secondary outcome) was lower (i.e., better) for both LSVT LOUD® and no SLT when compared to NHS SLT at 3 months (Table 2). Differences in favour of LSVT LOUD® and no SLT when compared to NHS SLT were also observed in the anxiety & depression subscale at 3 months (see Appendix 2, Table F).

At 12 months, the median Hoehn and Yahr stages were similar to baseline, and the amount of treatment (reported using levodopa equivalency) had increased since baseline (see Appendix 2, Table G). No serious adverse events were reported in this trial. Adverse events were reported in 36/130 (28%; 93 AEs) participants in the LSVT LOUD® group, 16/129 (12%; 46 AEs) participants in the NHS SLT group and none in the no SLT group. Most adverse events reported were vocal strain, with a

higher number in the LSVT LOUD® group (80 events) compared with the NHS SLT group (45 events). Part of therapy is supporting people to use their voice without strain, and only two participants from the LSVT LOUD® group crossed over to NHS SLT following a vocal strain adverse event. One participant who experienced a dry aching throat following LSVT LOUD® completed only 9 sessions.

Word count for main text (inc. headings 3876)

Discussion

Statement of principal findings

LSVT LOUD® was more effective at reducing the participant-reported impact of voice problems for people with Parkinson's-related dysarthria than NHS SLT and no SLT after 3 months. These results remain robust when the potential effects of non-adherence to treatment and the impact of missing data were investigated. The continued benefit of LSVT LOUD® on dysarthria over the 12-month trial period compared to NHS SLT and no SLT is encouraging, but it remains possible that re-intervention may be required should the treatment effect wear off or as their Parkinson's disease progresses and their dysarthria deteriorates. A benefit was also observed in communication-related quality of life (using the PDQ-39) for patients randomised to LSVT LOUD® which exceeded the MCIC of 4.2.[33] The higher rate of vocal strain with LSVT LOUD® treatment was mostly a minor, transient issue at an acceptable rate in relation to the level of benefit, although it reinforces the need for management by suitably skilled therapists. The higher costs of delivering the intensive LSVT LOUD® face to face by a qualified SLT, and alternative methods of adapting delivery that could support a more sustainable service delivery, will be considered in the economic analysis which will be published separately. However, given the relative benefits, the PD COMM trial results support the adoption of LSVT LOUD® as an effective SLT intervention option for Parkinson's-related dysarthria.

NHS SLT reflected mixed-theoretical therapeutic intervention tailored to the individual by the therapist. In PD COMM, there was no clear evidence of benefit for NHS SLT compared to both no SLT and LSVT LOUD® after 3 months. The confidence intervals are, however, moderately wide which may reflect variability in the intervention offered. NHS therapy was delivered at a much lower intensity and did not demonstrate benefit over control. Therefore, these results should not be interpreted as evidence of no beneficial effect for all NHS SLT theoretical approaches, across all dosages. Further research is required to understand the effectiveness of specific aspects of the intervention including dosage.

Strengths and weaknesses of the study

In terms of trial limitations, most participants were in the early stages of Parkinson's disease with mild speech impairment, which may not reflect the PD SLT population as a whole.[34] We did not collect sufficient screening data to assess this. Differences in access to therapy and intervention format could not be concealed from participants, making trial blinding unfeasible. Trial outcomes were participant- or carer-completed questionnaires. Thus, participants' and carers' knowledge and expectations about their treatment allocations, particularly to no treatment, may have contributed to an elevated risk of performance bias.

The disadvantage of many previous trials of PD-related dysarthria has been the use of sound pressure level (i.e. speech volume) without including participant reported outcome measures (PROM). The use of a PROM is an advantagen as the VHI measures how the participant perceives the impact their voice problems are having on their daily activities and their quality of life, which is a more meaningful measure of communication for them.[12 13] Future trials of new interventions may benefit from developments in the field of clinically relevant PROMS[35], which explore participation rather than impairment outcomes.

Variation in speech and language therapist experience levels, particularly with respect to being newly trained in LSVT LOUD® specifically for the trial, presents a risk that this trial may not have captured the full potential of the SLT approaches. Whilst there is a difference in the duration of

treatment between the two active treatment populations, the treatment could have been stopped at any point within the 3-month window from randomisation. This means both interventions could have finished near to the primary outcome data collection point and both interventions could have happened in a short time period. Finally, due to the COVID-19 pandemic, the trial closed early (suspended March 2020, closed November 2020) to recruitment, and thus did not recruit to the planned sample size and some follow-up data was lost as the post could not be accessed within the time frame. However, we do not believe this would have changed the trial's overall conclusions and clinical implications. Our meta-analysis of the PD COMM pilot and full trial data supports this (Appendix 2 – Figures 2, 3 and 4).

Meaning of the study: possible explanations and implications for clinicians and policymakers

This is the first large scale pragmatic trial comparing two commonly used SLT approaches against each other and against no therapy. There is a robust signal that, after 3 months, LSVT LOUD® is effective compared to no SLT for the reduction of Parkinson's disease dysarthria-related problems, which persists throughout the 12 months from starting treatment. This, combined with the lack of evidence of effectiveness of NHS SLT as it was provided in this trial, means there is a pressing need to discuss optimal use of speech and language therapy resources for people with Parkinson's disease.

Unanswered questions and future research

Evidence from stroke-related language rehabilitation suggests that effective therapeutic interventions were associated with dosage (total hours), frequency (number of days per week), and intensity (hours per week) regimens beyond a specific threshold. Thus SLT may have a dose effect, and treatment threshold is relevant and may interact with participant characteristics such as severity.[36] The PD COMM trial was not designed to provide evidence about the relative benefits of NHS SLT versus LSVT LOUD® at equal doses or different dose combinations.

Attention should, however, be paid to factors beyond the treatment content when determining the make-up of future SLT services: the current availability of speech and language therapists, access to outpatients, home and remote visits, software, costs, and frequency of treatment required. This trial also encourages a closer look at the impact of SLT provision on carers, and further research involving outcomes for carers could optimise future SLT care for people with Parkinson's disease.

Contributors

CMS – was the Chief Investigator on this study and the pilot study. Cath contributed to the conceptualisation, data curation, formal analysis, funding acquisition, investigation, methodology, project administration, resources, software, supervision, validation and writing – review and editing.

CR- Caroline Rick contributed to the design of the trial, funding acquisition, interpretation of the data and oversaw the running of the trial.

MB – Marian Brady contributed to the conception, design and obtaining funding for the trial, oversaw Scottish recruitment site set-up and data collection, data analysis and interpretation for the main trial data, the therapy data process evaluation and contributed to drafting and critical revision of the manuscript

RW - inputted into the design of the trial, oversaw the running of the trial, performed the interim and final data analyses, interpreted the data and contributed to writing the report.

CB – contributed to obtaining funding for the trial, study design, data analysis and interpretation for the main trial and the process evaluation, and the writing of the manuscript.

SP – designed the trial, contributed to obtaining funding for the trial, oversaw the running of the trial, developed and led on the statistical aspects of the study, supervised and performed the interim and final data analyses, interpreted the data and contributed to writing the report.

PMA – made contributions to the acquisition of data and the management and ongoing oversight of the trial. PMA read, edited and approved the manuscript.

AN - supported Scottish site start up and recruitment and data acquisition, led on therapy data analysis (reported in detail elsewhere), and read, edited and approved the manuscript

CS – contributed to developing the project, provided specialist input, interpreted the data and writing the report.

SJ – contributed to the conceptualisation, funding acquisition, methodology, supervision, and writing – review and editing.

NI – designed the trial, obtained the funding for the trial, provided statistical oversight of the study, oversaw the final data analyses, interpreted the data and contributed to writing the report.

GB – reviewed and contributed to the delivery of the trial in clinical settings, data collection methods, clinical interpretation of the data, reviewing and approving the manuscript.

SD – supported Scottish site start up and recruitment, data acquisition, therapy data analysis, interpretation and contributed to the revision and approval of the final manuscript.

RO – contributed to the supervision and oversight of the project's administration, data collection, and writing – review and editing

HN – drafted the manuscript and contributed to the writing – editing and review.

CEC – contributed to the trial concept, design, funding, interpretation and paper writing.

Declaration of Interests

Patricia Masterton- Algar - None

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Avril Nicoll – Employed part time as a researcher on PD COMM trial and received free LSVT LOUD® training (online) from LSVT Global as part of their role in the trial.

Helen Nankervis, Sylvia Dickson - Employed part time as a researcher on PD COMM trial.

Leslie Sharp- None

Data Sharing

All requests for access to PD COMM data should be submitted to the corresponding author for consideration by the CI. Access to anonymised patient level data with a data dictionary may be granted following review, no earlier than 6 months after this publication with no end date. Proposals for data access will need to describe how the data will be used. Transfer of data will be by a secure method and only after approval by the Trial investigator team.

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The PD COMM Collaborative Group

The Birmingham Clinical Trials Unit co-ordinated the trial: Pui Au, Ravinder Dhaliwal, Nicolas Folidis, Jane Futterer, Max Hughes, Natalie Ives, Ryan Ottridge, Smitaa Patel, Luke Price, Caroline Rick, Naveed Saeed, Lauren Sturdy, Sarah Tearne, Neil Winkles, Rebecca Woolley.

The PD COMM Collaborative Group Participating centres and PD COMM Collaborative Group members (*indicates current principal investigator and # indicates former principal investigator at that centre)

1. Aneurin Bevan University Health Board: A Church*, A Davey, C Gallagher, A Conroy, S Bailey, B Done, D Davies

2. Basildon and Thurrock University Hospitals NHS Foundation Trust: S Sveinbjornsdottir*, M Kasti[#], K Allen, J Colnet, J Riches, L Kittridge, L Morris, C Waszkiewicz
3. Bath and North East Somerset Community Health and Care Services; V Lyell*, V Page, N Bassford, H Rayner, E Henderson, L Wilson, C Sandham, S Thomas, Z Lampshire
4. Betsi Cadwaladr University Health Board: S Abraham*, JV Hindle[#], S Jones, P Martin-Forbes, C Watkins, JA Roberts, E Newcombe, L Bibby, L Matthews, J Roberts, S Thomas, H Hawthorne, K Clewley, S Lord, Ji Roberts, G Bretag, S Noble, J Stockport, T Chaudhury, G Davies, N Agnew, L Waggett, C Jones, G Owen, Ju Roberts
5. Blackpool Teaching Hospitals NHS Foundation Trust: D McGhee*, H Mcclure, A Ling Zhi Teo, R Wheeldon, C Wilkinson, M Oprea, G Van Duyvenvoorde, N Wilson, L Evans, R Belshaw, A Clarke, M Turner, C Thompson, A Hancock, R Brady, P Thet, A Pseftinakou, E Ward, S Hankinson
6. Brighton and Sussex University Hospitals NHS Trust: R Saha*, J Aram, D Mullan, J Newman, K Micabel, H Robinson, K Chick, J Gaylard, J Cochrane, R Gass, R Rose, S Plumb, K Stewart
7. Cardiff and Vale University Health Board: E Christopher Thomas*, A Kissick, P. Wright, B Mohamed, S Mahon, T Williams, S Appleton, N Elliott, L Evans, J Ridley, L Knibbs
8. Central London Community Healthcare NHS Trust: A Funaki*, P Daly, J Hackworth, K Timms, L Evison, A Bajracharya, M Kalani
9. East Cheshire NHS Trust: M Silverdale*, K Andrews, A Davies, R Bedford, A Jones, D Mournfield, L Howieson, V Price, J Hunter, A Baggs, L Evans, R Norton, M Holland, K Pointon, M Young, N Keenan, C Dean
10. Gloucestershire Hospitals NHS Foundation Trust: S Kulkarni*, S Bobeldijk, S Beames, J Cavanagh, S Sudlow, C Loveridge, P Townshend
11. Great Western Hospitals NHS Foundation Trust: G Lennox*, R Whittaker, D Nelson, S Pegler, C Drayson, P Turner, J Stockwell, R Elliott-Jones, C Pensotti
12. Guy's and St Thomas' NHS Foundation Trust: T Andrews*, E White, E Turner, T Burnay, C Hickey, S Warner, K Marlew
13. Harrogate and District NHS Foundation Trust: R Buccoliero*, C Isles, C Stemp, J Guy, C Bennett, P Randall, L Ware, J Cann, A Hubbard, A Dunn
14. Homerton University Hospital NHS Foundation Trust: L Sautin*, S Grobler#, S Adjei#, A Hankin, D Ovayolu, M Dobbs, O Joyce, R Humphreys, A Jha, C Holbrook, K Rowsell, F Johnson, H Thornley, S Conway
15. Hywel Dda University Health Board: C James*, M Hughes, S Murrow, K Pope, C MacPhee, E Williams, R Hughes, A Evans, A Richmond, K Pilborough, K Campbell, S Elizabeth Davies, A Taylor, S Thomas, D Asandei, E Garrard, H Thomas
16. Lancashire Teaching Hospitals NHS Trust: T Majeed*, J Dawber, S Furey, A Oppetit, J Birt, M Hare, V Fleming, A Timoroksa, H Al-Nufoury, S Sharp, L Freimann, K Morgan, K Rushton, C Maxwell
17. Leeds Teaching Hospitals NHS Trust: I Mavroudis*, J Alty[#], E Richfield, J Harrison, V Smith, T Joyce, J Bamford, S Jamieson, J Cosgrove, S Butterworth, E Sacre, L Makawa, P Duggan-Carter, C Arnold, K Brown, P Mpofu, C Joyce, S Henderson, C Wiseman, L Hyne, B Stevens, A Wood, D Holland, V Smith
18. London North West Healthcare NHS Trust: J Juada*, S Molloy[#], C Pavel, M Dhanarante, T Adedoyin, C Rowbottom, L Little, R Choudhury, L Prados, A Kelly, R Eggers, T Saifee, P Poku, L Niepage, R Cullen
19. Manchester University NHS Foundation Trust: D Ahearn*, A Fountain, A Curran

20. NHS Ayrshire and Arran: A Watt*, M Wilson, A Anderson, M Graham, J Taylor, P Hewat, N Pamment, L Dunlop, C McLaughlin, R Corr, A Vollam, F Litman, L Lowdon, F Burnett, J Dorans
21. NHS Dumfries and Galloway: S Donaldson*, H Moores-Poole, C Angus, S Coull, R Davy, A Gilmour-Graham, T Mcilroy, A Kendall, H Dent, J Candlish
22. NHS Forth Valley: S Pal*, E Messeder, D Thomson, V Johnston, P Raby, S Kinnear, P Faunce Smith
23. NHS Greater Glasgow and Clyde: S Wishart*, D Grosset, J Burns, A Louise Cunnington, E Newman, C Vennard, C Dalton, T Murphy, G Ralph, A Ritchie, C Nelson, A McEntee, P Fowley, H Hare, G Beaton, Z Muir, P Seenan, K Grosset,
24. NHS Highland: M Wilson*, D McDonald, J Finlayson, A Donaldson, S Sutherland, S Bramley, C Dunn, M Wallis, S Hewitt, N Dickinson, R Fusi
25. NHS Lanarkshire: H Morgan*, A Falconer[#], L Peacock; A McAlpine; C McBrearty; A Lowe; N Findlay; A Adams; C Tearney; J Picken; K MacKenzie; L McCallum; L Smith; M Sidney; P Downie; L Donnelly; R McAllister; S Campbell; S Maclachlan; L Shearer; K Campbell, P McCahill, K Costello, C McCready, R Bellian, C O'Donnell
26. NHS Lothian: G Duncan*, S Marrinan, M Dewar, J Kerr, L Killin, A Peters, A Stewart, B Daniels, A Darbyshire, I McCoy, U Duff, F Young, S Orr, C Telford, D Fraser, S Borthwick, H Bailey, L Karbownicki, E McLeod, A Degnan, S Aitken
27. NHS Tayside: D Sutherland*, E Sammler, L Whyte, C Young, L Gillies, L Gall, J Dallas, L Cassidy, E Letham, V Salisbury, L Anderson, C Hutton, S Waggett, D Anderson, A McGee, L Patterson
28. Norfolk and Norwich University Hospitals NHS Trust: S Cooper, G Mamutse, A Niruban, A Bath, A Wiltshire, M Harmer, C Wright, J Graham, K Richardson, J Tyler
29. Norfolk Community Health and Care NHS Trust: L Isaacs*, N Crow, S Pinnell, W Neale, L Maloney, R weller, K Young, C Squire, R Campbell, L Denmark
30. North Bristol NHS Trust: A Whone*, H Findlay, Y Hernandez, H Findlay, K King, L Gethin, S Ticehurst, A Swift, J Short, J Dean, C Westcott, S Cottrell, D Kruszynska, M Rolinski, S Dunn
31. Northern Lincolnshire and Goole NHS Foundation Trust: S Kamath*, Q Ma, J Hall, R. Wilson, H Goodhand, K Mellows, L Jayne Cottam, T Behan, J Gibson, E Lomas, J Kirk, L Smith, J Benson
32. Pennine Acute Hospitals NHS Trust: J Raw*, P Mulligan, A Ansari, R Irving, A Javed, S Hussain, L Johnson, R Joseph, J Brooke, J Melville, J Stockley, D Ganderton, A Cherriman, D Moth, S Thinnesen
33. Powys Teaching Health Board: J Price*, C Douglas, C Cooter, J Bushell
34. Royal Devon University Healthcare NHS Foundation Trust: R Sheridan*, C Browning, K Polverino, T Malone, S Jackson, A Foden, R James, L Roberts
35. Sandwell and West Birmingham Hospitals NHS Trust: C Clarke*, D Nicholl, A Majeed, MT Oo, K Blachford, A Boughey, J Kaur, S Kaur, M Awan, S Rahman, J Round
36. St Helens And Knowsley Hospitals NHS Trust: D Gandecha*, S Williams, S Dealing, H Moss, L Talbot, K Chadwick
37. Taunton and Somerset NHS Foundation Trust: S Cooper*, R Sophia, J Allen, S Cox, C Moreira, D Sharratt, E Foster, H Hurren, J Watson, S Northover, D Green, A Treloggen, C Pawley, K Beesley, K Milne, L Howard, S Craw, A Lewis, A Whitcher, C Vickers, T Russell, A Sykes, H Meikle, N Loraine, J Silver, B Donnelly-Ford, A Ancell
38. Torbay and South Devon NHS Foundation Trust: R Nashed[*], M Stone, C Marshall, J Garfield-Smith, G de Selincourt, S Mills, V Queen, L Thornton, H Griffin, M Farrow-Jones, E Sturdy, P Fitzell, K Almedilla, F Fitzsimmons, M Allison, F Rogers, B Reed

39. The Walton Centre NHS Foundation Trust: M Steiger*, H Treloar, L Roebuck, M Taylor
40. University Hospitals Birmingham NHS Foundation Trust: M Pinkney*, S Jones[#], S Muzerengi, M Johnson, S Stafford, E Parmar, J Albutt, S Kaur, M Awan, S Rahman, K Leahy, F Moore, S Hanif, J Woodford
41. University Hospitals Bristol NHS Foundation Trust: M Sritharan*, T Allain[#], A Daniell, K Kunsteinaite, S Slade, F Pimbblet, C Killourhey
42. Wye Valley NHS Trust: E Wales*, C Hughes, L Mercer, K Stock, M Evans, S Boyd, L King, G Horsfield, J Birch, S Anderson, Z Roberts, C Evans, N Stapleton, U Magennis, R Vernall, C Wallace, S Turner

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31. Taylor-Goh S. Royal College of Speech & Language Therapists Clinical Guidelines. 1st Edition ed. Oxon: Speechmark Publishing Ltd 2005.
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