The effect of two speech and language approaches on speech problems in people with Parkinson's disease: the PD COMM RCT

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Scientific summary

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Scientific summary

Background

Parkinson's disease (PD) is a complex neurodegenerative disorder experienced by 6.1 million people worldwide in 2016. PD is more common in men (1.4 : 1.0) and mostly affects people over 50, with peak incidence between 85 and 89 years old. PD affects approximately 145,000 people in the UK. Symptoms of PD are classified as motor or non-motor. The initial diagnostic motor symptoms are unilateral tremor, slowness, stiffness and mild imbalance. However, as the condition progresses, more severe motor decline occurs with imbalance leading to falls and unpredictable freezing episodes, all of which are unresponsive to medication. Speech and voice problems (known as dysarthria) are common with a reported prevalence of 68%. These problems increase physical and mental demands during conversation, reliance on family and/or carers and the likelihood of social withdrawal reducing quality of life. Speech and language therapy (SLT) in the UK aims to improve communication for people with PD-related dysarthria and their families. The NHS SLT or Lee Silverman Voice Treatment (LSVT) LOUD are two SLT approaches typically available in the UK, but evidence of their effectiveness is inconclusive.

Objectives

The primary objective of the PD COMM trial was to evaluate the clinical and cost-effectiveness of two SLT approaches: LSVT LOUD and NHS SLT compared with no SLT (control) for people with PD-related dysarthria. The primary comparisons were: LSVT LOUD versus no SLT control and NHS SLT versus no SLT (control). An additional objective was to evaluate and compare the clinical and cost-effectiveness of two types of SLT (LSVT LOUD vs. NHS SLT) in people with PD.

Methods

The PD COMM trial was a UK, multicentre, three-arm parallel group, unblinded, superiority, randomised controlled trial with a 12-month follow-up. Participants were randomised at the level of the individual to treatment with NHS SLT, LSVT LOUD or no SLT (control) in a 1 : 1 : 1 ratio. Participants randomised to the no SLT (control) group could be referred for SLT at the end of trial or if it became medically necessary, during the trial. The type and dose of SLT for those in the no SLT (control) group for whom it became necessary was determined by the therapists and clinicians responsible for the care plan of the participant. Recruitment took place at 41 sites throughout the UK and sites remained open until the trial finished. This trial was conducted in the UK in outpatient and home settings.

The trial interventions were intended to be provided as follows: LSVT LOUD consisted of personalised maximum effort drills and high-effort speech production tasks. NHS SLT reflected local non-LSVT practices: content, dose and frequency determined by the therapist in response to participant's individual needs. NHS SLT was tailored to the individuals' needs as per local practice, typically consisting of 6 to 8 weekly sessions; LSVT LOUD comprised 16 sessions of individual treatment with home-based practice, over 4 weeks (16 hours dosage). Suitably trained speech and language therapists or therapist assistants administered the interventions.

People with idiopathic PD where themselves or their carer reported speech or voice problems, were enrolled. We excluded people with a diagnosis of dementia, laryngeal pathology or those who have received SLT for speech or voice problems in the previous 2 years. Speech and language therapists or assistants trained in LSVT LOUD delivered the intervention. Speech and language therapists on the trial were provided with LSVT LOUD training by LSVT Global for free if they needed it to register or

re-register as a LSVT therapist. Participants were recruited from their routine outpatient appointments in geriatric/elderly care, neurology or SLT secondary care settings. Interventions were provided through secondary-care outpatient community-based SLT departments. For some participants who had specific needs, the intervention was provided at home.

Participants were randomised at the level of the individual via a central, secure, web-based computer-generated randomisation system developed and controlled by the Birmingham Clinical Trials Unit (BCTU), thus ensuring concealment of next treatment allocation. To randomise a patient into the trial, staff delegated the task of randomising patients into the trial either logged onto the trial database or rang the BCTU randomisation telephone line. The randomisation process used a minimisation procedure. The following minimisation variables were used: age (≤ 59, 60–70, > 70 years); disease severity measured using the Hoehn and Yahr staging (1.0–2.5, 3.0–5.0) and severity of speech measured using the Voice Handicap Index (VHI) total score (≤ 33, mild 34–44, moderate 45–61, severe > 61). To avoid any possibility of the treatment allocation becoming predictable, a random element was included within the randomisation process. Once the participant was randomised into the trial, they were given a unique trial identifier and the treatment allocation was confirmed by e-mail to the site.

The primary outcome measure for the trial was patient-reported VHI total score at 3 months. The VHI measures the psychosocial consequences of voice disorders and provides an overall perception of effectiveness of voice-related communication. The VHI comprises of 30 questions (0–120 negatively scored) divided into emotional, functional and physical subscales (0–40 subscale score).

Secondary outcomes were: the VHI subscales; the Parkinson's Disease Questionnaire-39, a validated, health-related quality-of-life measure specific to PD; the Questionnaire on Acquired Speech Disorders, self-reported participation restriction related to speech and communication; the participant-rated EuroQol5D (5-level version) which provides a simple descriptive profile and a single index value for health status; the ICEpop Capabilities Measure for Older Adults (ICECAP-O), a measure of capability in older people for use in economic evaluations; a disease-specific participant resource usage questionnaire; carer quality of life, measured using the PD Questionnaire – carer; and adverse events.

For participants in either SLT arm, any vocal strain or abuse believed to be associated with treatment was identified by the therapists at the participants' SLT session and was reported in the adverse event log. All participant-reported resource usage forms completed for the trial were checked to ensure that no vocal strain or abuse had occurred in outpatient appointments with ENT specialists. At the 12-month clinical visit, the medical professional also checked whether any adverse events had occurred since entering the trial.

There were two nested studies within this trial: a process evaluation and an economic evaluation. A process evaluation of the content of the interventions examined participants' and therapists' reported content of a subset of the two SLT interventions. Individual participant therapy data recorded by participants and therapists during the PD COMM trial were extracted from treatment record forms and therapy notes. Extraction category headings were piloted and reflected the Template for Intervention Description and Replication intervention reporting guidelines, with ongoing refinement as extraction progressed and components of the interventions were identified which were inadequately accounted for in the initial framework. The process evaluation of the implementation of the interventions used normalisation process theory which is highly attuned to the challenges of complex interventions as it encourages looking at systems as a whole. We considered that its conceptual framework would assist the interpretation and synthesis of data and analysis to explain what implementation processes took place and the interactions and gaps between the PD COMM interventions, the changing context, speech and language therapists and their practice.

A within-trial economic evaluation in the form of cost–utility analysis was conducted from the perspective of the NHS. The primary results were expressed in terms of cost per quality-adjusted

life-year (QALY) gained at 12 months for the three trial comparisons. Additional secondary analyses were performed from the NHS, personal social services perspective, broader societal perspective and using the capability approach, which uses broader measures of capability well-being.

Results

The mean age of participants in PD COMM was approximately 70 years old, and 74% were male (286/388). The mean duration of PD was between 5 and 6 years, with a broad range from newly diagnosed to over 30 years, and the majority (61%) were in Hoehn and Yahr stage of 2 or less (< 5% were in Hoehn and Yahr stage 4 or more). The participants mostly lived with a significant other (83%) or lived alone (14%). The levodopa equivalency of the medication the participants were taking at baseline was similar in the two SLT intervention groups (551.4 and 557.2 mg/day) but was slightly higher (597.6 mg/day) in the no SLT (control group). The majority of carers recruited into the trial were the spouses of the participants (177/194).

Lee Silverman Voice Treatment LOUD was delivered over a median of 16 sessions and a mean of 6.6 (SD 6.5) weeks. The dose of the treatment was 1216 (SD 454) minutes, which consisted of 963 (SD 330) minutes of SLT content [mean SLT content per session: 63 (SD 10) minutes], with 752 (SD 287) minutes dedicated to LSVT LOUD [mean LSVT content per session: 54 (SD 7) minutes]. NHS SLT was delivered over a median of five sessions over a mean of 11.4 (SD 11.4) weeks. The duration of NHS SLT was shorter than LSVT LOUD, totalling a mean of 404 (SD 234) minutes, with 298 (SD 171) minutes dedicated to SLT content. Mean active therapy time for NHS SLT was 149 (SD 113) minutes. The mean individual session length was similar to that of LSVT LOUD at a mean of 55 (SD 16) minutes.

The negatively scored VHI at 3 months was the primary outcome (lower scores reflect a better voice-related quality of life). The analyses were performed based on the intention-to-treat (ITT) principle using a linear regression model to estimate differences between each of the three comparisons. Data were available at 3 months in 106, 102 and 98 in the LSVT LOUD, NHS SLT and no SLT (control) group, respectively. At 3 months, the VHI total score for the LSVT LOUD group was 8 points lower than for the no SLT (control) group [−8.0, 99% CI (−13.3 to −2.6); $p = 0.0001$]. For NHS SLT, at 3 months, the VHI total score was 1.7 points higher than the no SLT (control) group [1.7, 99% CI (−3.8 to 7.1); $p = 0.4$]. In the third comparison, the LSVT LOUD group was 9.6 points lower than the NHS SLT group [−9.6, 99% CI (−14.9 to −4.4); $p < 0.0001$]. The main per-protocol analysis population included only those participants who both adhered to treatment and completed the 3-month VHI outcome assessment within the 1-month time window. This analysis gave similar results to the main ITT analysis: LSVT LOUD versus no SLT: −9.7, 99% CI (−16.0 to −3.4); NHS SLT versus no SLT: 1.1, 99% CI (−5.6 to 7.8); and LSVT LOUD versus NHS SLT: −10.8, 99% CI (−17.8, −3.8). Similar results were also seen for the two other per-protocol analyses. Various sensitivity analyses were undertaken to assess the impact of missing data. Different assumptions were made about the reasons for missing data to investigate the impact, if any, on our analysis of the primary outcome. All these analyses gave results that were in agreement with the primary ITT analysis.

Analyses of the 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.

For the secondary outcomes, LSVT LOUD participants reported lower VHI emotional and functional subscale scores at 3 months than participants with no SLT (control) [−3.0, 99% CI (−5.1 to −0.9); $p = 0.0003$]; [−2.9, 99% CI (−4.8 to −1.1); $p < 0.0001$], while there was no evidence of a difference between NHS SLT and no SLT (control) groups. Similarly, LSVT LOUD participants described lower emotional, functional and physical subscale scores compared to NHS SLT participants [−3.2 99% CI (−5.3 to −1.1); $p < 0.0001$]; [−2.9, 99% CI (−4.7 to −1.1); $p < 0.0001$]; [−2.2, 99% CI (−4.1 to −0.3);

p = 0.003] at 3 months. There was no evidence of a difference between the other treatment comparisons at 3 months.

For the Questionnaire on Acquired Speech Disorders (QASD) results, the LSVT LOUD scores were lower (i.e. better) than no SLT (control) [−5.4, 99% CI (−9.8 to −1.0); *p* = 0.002] and lower than for NHS SLT [−4.3, 99% CI (−8.7 to 0.1); *p* = 0.01], although this was a borderline difference, at 3 months. There was no evidence of a difference in the scores for NHS SLT compared to no SLT (control) at 3 months. For the participant-reported quality-of-life measure Parkinson's Disease Questionnaire-39 (PDQ-39), there were lower scores for LSVT LOUD compared to no SLT (control) in the communication subscale [−6.2, 99% CI (−11.9. −0.6); *p* = 0.004] at 3 months. There was no evidence of any difference in the three trial comparisons for the PDQ-39 or ICECAP-O scores at 3 months.

The carer quality-of-life score (Parkinson's Disease Questionnaire–Carer) was higher (i.e. worse) after NHS SLT compared to no SLT (control) at 3 months [6.2 99% CI (0.1 to 12.3); *p* = 0.009]. The LSVT LOUD score was lower (i.e. better) than the NHS SLT score overall, using repeated measures [−6.3, 99% CI (−11.8 to −0.7); *p* = 0.004] with a borderline significant difference at 3 months [−5.6, 99% CI (−11.6 to 0.4); *p* = 0.02]. The anxiety and depression subscale and the stress subscale supported these results. For LSVT LOUD compared to no SLT (control) there was no evidence of a difference at any time point for the overall score or the subscales.

Participants reported positive engagement in the trial processes and with both active interventions. Therapists reported they were prepared for their engagement with the trial and intervention implementation, regardless of their professional history or pre-trial practice regimes. The LSVT LOUD intervention provided a clear structure for clinical work in contrast to the need to 'pull together' the NHS SLT intervention.

In regard to economic evaluation of the interventions, the results suggest that LSVT LOUD was associated with an incremental cost-effectiveness ratio (ICER) of £197,772 per QALY gained and £77,017 per QALY gained compared to no SLT (control) and NHS SLT, respectively. Using the capability outcome measure, the cost of achieving an additional year of full capability (YFC) for the LSVT LOUD group was £87,899 compared with no SLT (control) and £46,210 compared with NHS SLT. The ICERs using the year of sufficient capability (YSC) as the measure of outcome were £121,706 and £51,344 per YSC gained for LSVT LOUD versus no SLT (control) and NHS SLT, respectively. For all three outcomes, NHS SLT was dominated by no SLT (control) as it was less effective and more costly and was therefore not cost-effective. At NICE, threshold of £20,000 per QALY, the cost-effectiveness acceptability curves show that the probability of LSVT LOUD being cost-effective was 0% and 3% compared to no SLT (control) and NHS SLT, respectively. The probability of NHS SLT being cost-effective versus no SLT (control) was 2%. Considering the higher willingness-to-pay threshold of £30,000 per QALY, LSVT LOUD still had a low probability being cost-effective compared with NHS SLT and no SLT (control), with a probability of being cost-effective of 14% when compared with NHS SLT.

Conclusions

This is the first large-scale pragmatic randomised controlled trial comparing two SLT approaches and no treatment. LSVT LOUD is beneficial compared to no SLT (control) for reduction of PD-related speech impacts, which persists for at least 12 months from starting treatment. There is lack of evidence of effectiveness for NHS SLT, as currently provided, for PD-related speech or voice impacts. Both LSVT LOUD and NHS SLT were not cost-effective compared with no SLT (control). While LSVT LOUD was more effective than NHS SLT and control (no SLT) in terms of QALYs, it was also associated with higher costs due to the intensive delivery of the intervention. Alternative delivery models, with fewer supervised sessions allowing for more unsupervised sessions or engaging therapy assistants in the

delivery of some sessions, may reduce LSVT LOUD intervention costs sufficiently to approach cost-effectiveness.

Study registration

This study is registered as ISRCTN12421382.

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