Computerised speech and language therapy or attention control added to usual care for people with long-term post-stroke aphasia: the Big CACTUS three-arm RCT

Rebecca Palmer,[1*] Munyaradzi Dimairo,[1] Nicholas Latimer,[1] Elizabeth Cross,[1] Marian Brady,[2] Pam Enderby,[1] Audrey Bowen,[3] Steven Julious,[1] Madeleine Harrison,[1] Abualbishr Alshreef,[1] Ellen Bradley,[1] Arjun Bhadhuri,[1] Tim Chater,[1] Helen Hughes,[1,4] Helen Witts,[1,5] Esther Herbert[1] and Cindy Cooper[1]

[1]School of Health and Related Research, University of Sheffield, Sheffield, UK
[2]Nursing, Midwifery and Allied Health Professions Research Unit, Glasgow Caledonian University, Glasgow, UK
[3]Division of Neuroscience & Experimental Psychology, Manchester Academic Health Science Centre, University of Manchester, Manchester, UK
[4]Speech and Language Therapy, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK
[5]Speech and Language Therapy, Derbyshire Community Health Services NHS Foundation Trust, Chesterfield, UK

*Corresponding author r.l.palmer@sheffield.ac.uk

Declared competing interests of authors: All authors declare financial support from The Tavistock Trust for Aphasia. Rebecca Palmer was a National Institute for Health Research (NIHR)/Higher Education Funding Council for England-funded senior clinical academic lecturer until June 2017. She has current funding from the Stroke Association for a Doctor of Philosophy (PhD) student conducting work on fidelity to the intervention. The Stroke Association had previously funded early development work on the software used in the intervention but she was not involved in that. She was author of the intervention manual. Nicholas Latimer is supported by the NIHR (Post-doctoral Fellowship, reference PDF-2015-08-022) and is currently supported by Yorkshire Cancer Research (award S406NL). Pam Enderby has a patent on the Therapy Outcome Measures (2015) used in this trial from which she receives royalties. Audrey Bowen is funded by the Stroke Association and the NIHR Collaborations for Leadership in Applied Health Research and Care Greater Manchester. She co-authored the Communication Outcome after Stroke (COAST) and Carer COAST tools, which are patented. Madeleine Harrison receives PhD fellowship funding from the Stroke Association. Esther Herbert received a NIHR Research Methods Fellowship, outside the submitted work. Cindy Cooper sits on the NIHR Clinical Trials Unit (CTU) Standing Advisory Committee (2016 to present) and the UK Clinical Research Collaboration Registered CTU Network Executive Group (2015 to present).

Published April 2020
DOI: 10.3310/hta24190

Scientific summary

The Big CACTUS three-arm RCT

Health Technology Assessment 2020; Vol. 24: No. 19
DOI: 10.3310/hta24190

NIHR Journals Library www.journalslibrary.nihr.ac.uk

Scientific summary

Background

More than one-third of stroke survivors acquire aphasia. This language disorder affects a person's ability to understand spoken language, talk, read and write, leading to frustration, isolation, low mood and difficulty carrying out roles at work, in the family and in the wider community. People with aphasia often want more speech and language therapy than they have access to from NHS services in the long term post stroke despite evidence that improvements can continue for years with speech and language therapy.

Self-managed use of specialist aphasia computer software provides a potentially low-cost option to enable more language practice without increasing demands on limited speech and language therapy resources. Computer software can provide the opportunity for repetitive practice of meaningful language material and feedback on success to the person with aphasia (adhering to principles of experience-dependent neuroplasticity) in their homes without a speech and language therapist present. The pilot study suggested feasibility, acceptability and potential clinical effectiveness and cost-effectiveness of an approach to self-managed computerised word-finding therapy. Big CACTUS (Clinical and cost-effectiveness of aphasia computer treatment versus usual stimulation or attention control long term post-stroke) was the first trial to evaluate the clinical effectiveness and cost-effectiveness of such an approach to providing long-term aphasia therapy in a full randomised controlled trial.

Objectives

The aim was to provide definitive evidence of whether or not self-managed computerised speech and language therapy for word-finding for persisting post-stroke aphasia in addition to usual care was clinically effective and cost-effective, when compared with usual care alone or attention control. The main research objectives were to establish whether or not:

1. self-managed computerised speech and language therapy for word-finding (computerised speech and language therapy) increases the ability of people with aphasia to retrieve vocabulary of personal importance
2. computerised speech and language therapy improves functional communication ability in conversation
3. patients receiving computerised speech and language therapy perceive greater changes in social participation in daily activities and quality of life
4. computerised speech and language therapy is cost-effective for persistent aphasia post stroke
5. any effects of computerised speech and language therapy are evident 12 months after therapy has begun.

This trial also sought to investigate:

6. functional use of treated words in conversation
7. generalisation to retrieval of untreated words
8. carer perception of communication effectiveness and the impact on carers' quality of life
9. negative effects of computerised speech and language therapy.

Methods

Design

Big CACTUS was a pragmatic, superiority, individually randomised, single-blind (blinded outcome assessors), parallel-group randomised controlled adjunct trial.

Setting

The trial was conducted in 21 NHS speech and language therapy departments across the UK. Participants were treated by speech and language therapists working in routine clinical practice.

Participants (eligibility and recruitment)

Participants were eligible if they were aged > 18 years and had aphasia subsequent to stroke(s) at least 4 months prior to randomisation. Participants were required to have word-finding difficulties (demonstrated by a score of 5–43 out of 48 on the Naming Objects test of the Comprehensive Aphasia Test) and to have sufficient cognitive and visual ability to use the computer software. They were excluded if they had a premorbid speech and language disorder caused by a neurological deficit other than stroke, required treatment in a language other than English or were currently using a computer program aimed at improving word-finding.

Eligible participants were identified from current and past speech and language therapy caseloads and from voluntary sector support groups. Speech and language therapists used a consent support tool to identify the support required for each individual to provide informed consent. This also identified those who were unable to provide consent with support and required a carer declaration of belief that they wished to take part (or a relative to provide consent in Scotland).

Interventions

Participants were randomised to one of three groups. All groups received usual care.

Usual care

This was the usual speech and language therapy being provided to each individual (for some, this entailed no speech and language therapy input). Therapy was provided by qualified speech and language therapists or speech and language therapy assistants face to face in either one-to-one or group sessions.

Computerised speech and language therapy

The computerised speech and language therapy intervention focused on the treatment of word-finding, a difficulty experienced by most people with aphasia. The approach evaluated had four key components:

1. Specialist aphasia software – StepByStep© version 5.0 (Steps Consulting Ltd, Acton Turville, UK) was chosen as it allowed for tailoring and selection of personally relevant words, and provided feedback on whether or not words produced were correct, adhering to principles of experience-dependent neuroplasticity.
2. A speech and language therapist assessed the participant and selected and tailored the software exercises and word-finding cues according to the language profile on the baseline language assessment. The speech and language therapist supported the participant to select 100 words of personal relevance for practice and trained and supported a volunteer/speech and language therapy assistant to provide support to the participant.
3. Self-managed, independent practice of the therapy exercises at home by the participant was recommended for 20–30 minutes per day over a 6-month period.
4. A volunteer/speech and language therapy assistant provided monthly support including encouraging practice, moving on to harder exercises, practice using the new words in functional contexts and adding new words if needed.

The speech and language therapists attended 1 day of training on how to use and tailor the software. They were given an intervention manual.

Attention control

This group aimed to control for the additional activity and attention received in the computerised speech and language therapy group. Puzzle books were provided each month according to level of difficulty needed and participant interests. Participants were encouraged to complete one puzzle per day for the 6-month period. A member of the research team telephoned the participant for a supportive chat once a month.

Randomisation

Participants were randomised to one of the three groups using a fixed 1 : 1 : 1 allocation ratio by a centralised web-based randomisation system. The randomisation schedule was generated using stratified block randomisation stratified by centre and severity of word-finding difficulty at baseline.

Outcomes

The trial had co-primary outcomes looking for change in both impairment and activity. Impairment was defined as the ability to use vocabulary of personal importance, measured by naming pictures of 100 words chosen for use in therapy. Activity was defined as functional communication ability in conversation measured by 10-minute videos of conversations structured around topics of personal importance, rated using the activity scale of the Therapy Outcome Measures. A key secondary outcome was change in participants' own perception of communication-related social participation and quality of life using the Communication Outcomes After Stroke patient-reported outcome measure. All outcome measures were undertaken at baseline prior to randomisation, 6 months post randomisation (end of treatment – primary time point) and at 9 and 12 months post randomisation. Further secondary outcomes included health-related quality of life and resource use to estimate the cost-effectiveness of computerised speech and language therapy compared with usual care and activity/attention control. An unofficial accessible variant of the EuroQol-5 Dimensions, five-level version, was developed for this trial so that participants were able to rate their own quality of life for quality-adjusted life-year estimation. The standard EuroQol-5 Dimensions, five-level version, was also completed by proxy by carers.

Additional outcomes included the use of treated words in the videoed conversations; generalisation of the therapy to untreated words using the Object Naming test of the Comprehensive Aphasia Test; and carer perception of communication effectiveness and impact on their own quality of life using the Carer Communication Outcomes After Stroke. Negative effects of the computerised speech and language therapy were recorded using a questionnaire for computerised speech and language therapy participants, and through collection of adverse events and serious adverse events for all groups.

Blinding

The trial was single blind as participants knew their allocated treatment group. However, all outcome measures at all time points were conducted by speech and language therapy assessors who were blind to the treatment group.

Sample size

The trial aimed to recruit 285 participants (95 per group) to address both co-primary objectives with 90% power for a 5% two-sided test adjusted for a 15% drop-out rate. A 10% mean difference in change in word-finding and a Therapy Outcome Measures effect size of 0.45 were assumed to be minimal clinically important differences to detect. This sample size had 83% power to address the key secondary objective on change in Communication Outcomes After Stroke for a 5% two-sided test assuming a 7.2% mean difference in change as clinically worthwhile.

Analysis

The analysis of the primary outcome measures was based on a modified intention-to-treat principle detailed in the full report. A multiple linear regression model adjusted for stratification factors was used. A sensitivity analysis was conducted exploring the impact of missing data and heterogeneity of treatment effect across predefined subgroups (word-finding severity, time post stroke and comprehension ability).

The primary health economic analysis was a model-based cost–utility analysis adopting a lifetime time horizon and an NHS payer perspective. Cost-effectiveness is expressed in terms of the incremental cost-effectiveness ratio, that is cost per quality-adjusted life-year gained. Secondary analyses included within-trial analysis, a broader perspective (including volunteer costs) and analysis of subgroups.

Results

A total of 995 potential participants were screened, of whom 288 (29%) consented and 278 (28%) were randomised, slightly lower than the target of 285 but sufficient to address the co-primary and key secondary research questions with intended statistical power owing to the drop-out rate (9%) being lower than anticipated (15%). A total of 240 participants were included in the modified intention-to-treat analysis: usual care, $n = 86$; attention control, $n = 71$; and computerised speech and language therapy, $n = 83$.

The mean age of participants was 65.4 years (range 23–92 years) and 61% of participants were male. Forty-four per cent of participants had mild word-finding difficulties (Comprehensive Aphasia Test Naming Objects score of 31–43), 30% had moderate difficulties (score of 18–30) and 26% had severe difficulties (score of 5–17). Participants were 2 years (median) post stroke (range 4 months to 36 years). The characteristics of groups were broadly similar at baseline.

Computerised speech and language therapy participants practised computer exercises for 28 hours (mean). The quality of delivery of computerised speech and language therapy in terms of tailoring the software and provision of support to the participants was good. However, 85% of participants were assisted to practise using their new words in functional contexts for only 45 minutes (median) in total over 6 months. Similar mean amounts of usual care were received by all groups across the 6-month intervention period (computerised speech and language therapy, 3.2 hours; usual care, 3.8 hours; and attention control, 3.2 hours).

The mean improvement in word-finding at 6 months was 1.1% (standard deviation 11.2%), 2.4% (standard deviation 8.8%) and 16.4% (standard deviation 15.3%) based on 86, 71 and 83 participants in the usual care, attention control and computerised speech and language therapy groups, respectively. On average, computerised speech and language therapy improved word-finding by 16.2% more than usual care (95% confidence interval 12.7% to 19.6%; $p < 0.0001$) and by 14.4% more than attention control (95% confidence interval 10.8% to 18.1%), indicating that the effect was not attributable only to activity/attention. Most of this effect was maintained at 9 and 12 months. Computerised speech and language therapy improvement in word-finding was broadly consistent regardless of time post stroke.

However, improvements in functional communication were negligible and very similar across groups. The mean difference in change between the computerised speech and language therapy group and the usual-care group was −0.03 (95% confidence interval −0.21 to 0.14; $p = 0.709$) and between the computerised speech and language therapy group and attention control group was −0.01 (95% confidence interval −0.20 to 0.18). Similarly, there was insufficient evidence to suggest that computerised speech and language therapy improved participants' perceptions of their communication ability and participation or its impact on their life. The computerised speech and language therapy group mean improvement in Communication Outcomes After Stroke was only 0.5% (95% confidence interval −3.1% to 4.1%) and 3.8% (95% confidence interval −0.0% to 7.5%) compared with usual care and attention control, respectively.

On average, there was no improvement in treated words used in conversation across groups. However, close to 1 out of 10 participants in the usual-care and attention control groups used at least five more treated words in conversation at 6 months than at baseline, compared with approximately 3 out of 10 participants in the computerised speech and language therapy group. In addition, there was insufficient evidence to suggest that improved word-finding of treated words generalises to untreated words.

Subgroup analyses indicated that the effect of computerised speech and language therapy on word-finding was slightly higher for participants with mild word-finding difficulties and for those with verbal comprehension within normal limits.

Small differences were seen in carers' perception of communication effectiveness: 4.6% in favour of computerised speech and language therapy compared with usual care (95% confidence interval 0.3% to 9.0%) at 6 months, and 5.1% in favour of computerised speech and language therapy compared with attention control (95% confidence interval 0.5% to 9.7%). The differences were not maintained at 9 and 12 months. Improvement in carers' quality of life in the computerised speech and language therapy group compared with the usual-care group was 5.3% (95% confidence interval −1.1% to 11.7%), but only 0.3% (95% confidence interval −6.4% to 6.9%) compared with the attention control group at 6 months.

Negative effects of computerised speech and language therapy were low: 27% of participants in the computerised speech and language therapy group reported fatigue or anxiety at some point, which translates to one event per person per year. Differences in the incidences of adverse events and serious adverse events were similar between groups.

The computerised speech and language therapy was a low-cost intervention, at £733 per person. The cost of delivering the same average amount (28 hours) of therapy face to face would be £1400. The primary cost-effectiveness analysis estimated an incremental cost per participant of £732.73 (95% credible interval £674.23 to £798.05) and an incremental quality-adjusted life-year gain of 0.017 (95% credible interval −0.05 to 0.10) for computerised speech and language therapy compared with usual care, resulting in an incremental cost-effectiveness ratio of £42,686 per quality-adjusted life-year gained. For computerised speech and language therapy compared with attention control, the incremental cost-effectiveness ratio was £40,164 per quality-adjusted life-year gained. Subgroup analyses resulted in incremental cost-effectiveness ratios of £22,371 and £28,819 per quality-adjusted life-year gained for computerised speech and language therapy compared with usual care in participants with mild or moderate word-finding difficulty, respectively. Using EuroQol-5 Dimensions, five-level version, quality-of-life scores reported by carers on behalf of patients instead of scores derived from the unofficial accessible version of the EuroQol-5 Dimensions, five-level version, resulted in an incremental cost-effectiveness ratio of £28,819 for computerised speech and language therapy compared with usual care.

Conclusions

The computerised speech and language therapy intervention provided additional hours of speech and language therapy to people with persistent aphasia at a low cost. Computerised speech and language therapy led to significant improvements in word-finding ability that were maintained irrespective of time post stroke. Word-finding improvements did not generalise to conversation or participant perceptions of communication participation and quality of life. Cost-effectiveness results suggest that computerised speech and language therapy is unlikely to be considered cost-effective for the whole population investigated, given typical current National Institute for Health and Care Excellence cost-effectiveness thresholds. Subgroup analyses are prone to increased uncertainty; however, the intervention may be more cost-effective for people with mild and moderate word-finding difficulties.

The computerised speech and language therapy intervention can be offered as part of speech and language therapy provision to achieve repetitive word-finding practice and improve the ability to find new words. This research suggests that it is important to use words of personal relevance in therapy owing to limited generalisation to untreated words, and that there needs to be a focus on supporting

the generalisation of new words into functional use. Further research recommendations in order of priority include:

1. investigating ways to assist with generalisation of newly learned vocabulary into use in conversation and other functional communication contexts
2. identification of what was practised, and whether or not all of the exercises set up by the speech and language therapist were used
3. exploration of further cost and time efficiencies
4. exploration of who to target the intervention towards
5. implementation of an optimised computerised speech and language therapy approach as part of NHS speech and language therapy provision
6. validation of the accessible variant of the EuroQol-5 Dimensions, five-level version.

Trial registration

This trial is registered as ISRCTN68798818.

Funding

This project was funded by the National Institute for Health Research (NIHR) Health Technology Assessment programme and will be published in full in *Health Technology Assessment*; Vol. 24, No. 19. See the NIHR Journals Library website for further project information. The Tavistock Trust for Aphasia provided additional support to enable people in the control groups to experience the intervention after the trial had ended.

Health Technology Assessment

HTA/HTA TAR

ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

Impact factor: 3.819

Health Technology Assessment is indexed in MEDLINE, CINAHL, EMBASE, The Cochrane Library and the Clarivate Analytics Science Citation Index.

This journal is a member of and subscribes to the principles of the Committee on Publication Ethics (COPE) (www.publicationethics.org/).

Editorial contact: journals.library@nihr.ac.uk

The full HTA archive is freely available to view online at www.journalslibrary.nihr.ac.uk/hta. Print-on-demand copies can be purchased from the report pages of the NIHR Journals Library website: www.journalslibrary.nihr.ac.uk

Criteria for inclusion in the *Health Technology Assessment* journal

Reports are published in *Health Technology Assessment* (HTA) if (1) they have resulted from work for the HTA programme, and (2) they are of a sufficiently high scientific quality as assessed by the reviewers and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

HTA programme

Health Technology Assessment (HTA) research is undertaken where some evidence already exists to show that a technology can be effective and this needs to be compared to the current standard intervention to see which works best. Research can evaluate any intervention used in the treatment, prevention or diagnosis of disease, provided the study outcomes lead to findings that have the potential to be of direct benefit to NHS patients. Technologies in this context mean any method used to promote health; prevent and treat disease; and improve rehabilitation or long-term care. They are not confined to new drugs and include any intervention used in the treatment, prevention or diagnosis of disease.

The journal is indexed in NHS Evidence via its abstracts included in MEDLINE and its Technology Assessment Reports inform National Institute for Health and Care Excellence (NICE) guidance. HTA research is also an important source of evidence for National Screening Committee (NSC) policy decisions.

This report

The research reported in this issue of the journal was funded by the HTA programme as project number 12/21/01. The contractual start date was in January 2014. The draft report began editorial review in July 2018 and was accepted for publication in October 2019. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the reviewers for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

This report presents independent research funded by the National Institute for Health Research (NIHR). The views and opinions expressed by authors in this publication are those of the authors and do not necessarily reflect those of the NHS, the NIHR, NETSCC, the HTA programme or the Department of Health and Social Care. If there are verbatim quotations included in this publication the views and opinions expressed by the interviewees are those of the interviewees and do not necessarily reflect those of the authors, those of the NHS, the NIHR, NETSCC, the HTA programme or the Department of Health and Social Care.

Published by the NIHR Journals Library (www.journalslibrary.nihr.ac.uk), produced by Prepress Projects Ltd, Perth, Scotland (www.prepress-projects.co.uk).