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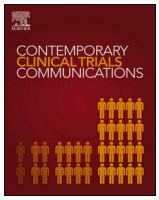

TEleRehabilitation foR Aphasia (TERRA) phase II trial design

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ABSTRACT

Background and purpose: Despite comprehensive evidence that supports the utility of aphasia therapy in persons with chronic (≥6 months) stroke-induced aphasia, the amount of therapy provided to patients in the United States is typically far less than what is likely necessary to maximize recovery. Two potential contributors to this discrepancy are limited access to rehabilitation services due to the availability of providers and logistical difficulties with transportation. One way to increase access to aphasia therapy is to rely on telerehabilitation.

Methods: The TEleRehabilitation foR Aphasia (TERRA) trial is a prospective, randomized, rater-blinded, multicenter phase II non-inferiority trial to evaluate telerehabilitation for aphasia therapy in persons with chronic post-stroke aphasia. Participants are randomized (1:1) to receive either aphasia remote therapy or in-clinic therapy for 30 total days of treatment (15 days of a semantically focused approach and 15 days of a phonologically focused approach) for 45 min per day. A total of 100 adults (ages 21–80) with a history of left hemisphere ischemic or hemorrhagic stroke incurred at least 12 months prior to study enrollment will be randomized. The trial will be conducted at the clinical research facilities at two sites: the Medical University of South Carolina and the University of South Carolina.

Conclusions: This paper details the design of the TERRA trial, which aims to test whether aphasia therapy delivered by a remote speech-language pathologist through videoconferencing (i.e., via telerehabilitation) is not clinically worse than in-clinic therapy for individuals with chronic post-stroke aphasia to provide an opportunity to move to a definitive phase III trial.

1. Introduction

A recent trial conducted by Breitenstein and colleagues [1] showed that aphasia therapy improves speech production and communicative quality of life in persons with chronic (>6 months) stroke-induced aphasia. Several comprehensive meta-analyses, as well as numerous smaller studies, support this finding and further emphasize the overall positive effects of aphasia therapy [2,3]. Despite comprehensive evidence that supports the utility of aphasia therapy, the amount of therapy provided to patients in the United States is typically not adequate to maximize recovery [4]. There are a few important reasons underlying this discrepancy. For example, considerable emphasis is placed on acute and subacute stroke recovery with less therapy focus on the chronic period, when recovery is typically incremental. Also, access to rehabilitation services can be limited by the availability of providers (e.g., rural regions) or by limited access to transportation to clinic facilities caused by physical disabilities post-stroke.

One way to increase access to aphasia therapy is to develop comparable telerehabilitation services to treat language deficits (otherwise known as aphasia remote therapy; ART). Providing ART would vastly increase the availability of speech-language pathology services and may have the potential to decrease the cost of treatment. To date,

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telerehabilitation in stroke has primarily focused on physical therapy, with only a handful of smaller studies involving aphasia therapy [5]. A few studies have started to explore the feasibility and effectiveness of ART, both clinician-supervised therapy and unsupervised therapy (computerized therapy) [6–10]. However, no properly powered trials have been conducted comparing clinician-supervised aphasia therapy via telerehabilitation to clinician-supervised therapy provided in the clinic.

If ART is found to be equally effective as in-clinic aphasia therapy and will be reimbursed by third-party payers, it may reduce the overall cost of rehabilitation as well as provide therapy access to a large number of patients who are currently underserved. However, a crucial step toward changing policies regarding telerehabilitation reimbursement is first to demonstrate its efficacy. Our prior work has focused on personalized predictors of response to phonologically- or semantically-focused aphasia therapy [11,12]. So far, we have demonstrated that therapy for individuals with chronic aphasia can effectively improve communication [13]. An important next step is to test whether the same kind of therapy yields similar results when provided via ART.

2. Methods and design

TEleRehabilitation foR Aphasia (TERRA) is an NIH-funded multisite, prospective, controlled, randomized, rater-blinded phase II clinical trial with the goals to assess the comparable efficacy of ART to in-clinic therapy (I-CT), and to assess whether participant attitudes and cognitive-linguistic factors influence acceptance and outcome of aphasia therapy administered via telerehabilitation. It takes place at the Medical University of South Carolina (MUSC) and the University of South Carolina (USC). Written, informed consent is obtained from each participant or their legally authorized representative using the IRB-approved consent process.

Eligible participants with chronic aphasia are randomized into one of two arms: aphasia therapy administered via telerehabilitation (ART) or to aphasia therapy administered in clinic (I-CT) using the minimal sufficient balancing method [14] to control the imbalance in the distribution of Western Aphasia Battery-Revised Aphasia Quotient (WAB-R AQ) [13]. The therapists delivering ART and I-CT are the same.

Each participant receives 3 weeks of phonologically focused treatment and 3 weeks of semantically focused treatment. The treatment order is randomized for each participant using the big stick design [16]. Outcome measures will be assessed immediately post-treatment for each round of treatment, as well as at 6 months post-treatment [Fig. 1].

2.1. Aims

The primary aim for TERRA is to test whether aphasia therapy delivered by a remote speech-language pathologist (SLP) through videoconferencing (ART) is non-inferior to I-CT. Secondary objectives of TERRA are to address the following questions.

1. How do participant cognitive-linguistic abilities, as well as their experiences with and attitudes toward computer/technology affect the use of ART?
2. What is the role of brain health and other personal/health characteristics in treated aphasia recovery?
3. How can models of word production predict response to aphasia therapy?

2.2. Study population

Participants include individuals with a history of at least one left-hemisphere stroke and the presence of chronic aphasia. See Table 1, below, for inclusion and exclusion criteria.

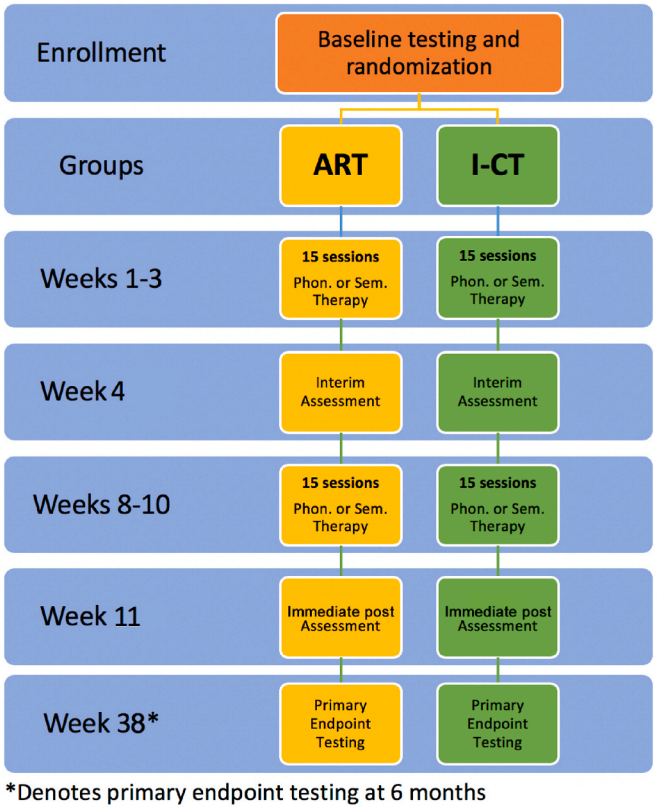

Fig. 1. Study timeline.

Table 1
Inclusion and exclusion criteria for TERRA.

Inclusion	Exclusion
Left-hemisphere ischemic or hemorrhagic stroke incurred at least 12 months prior to randomization	Previous neurological injury or disease affecting the brain (e.g., traumatic brain injury, dementia)
English as primary language for at least the past 20 years	Severely limited speech production (severe unintelligibility) that interferes with adequate participation in the therapy provided (i.e., WAB-R Spontaneous Speech score of 0–1)
Provide informed consent either independently or through a Legally Authorized Representative (LAR)	Severely limited auditory comprehension that interferes with adequate participation in the therapy provided (i.e., WAB-R Comprehension score of 0–1)
21–80 years of age	History of right-hemisphere stroke
Compatible with magnetic resonance imaging (MRI) on a 3-T (3T) scanner (e.g., no metal implants, not claustrophobic)	History of bilateral, cerebellar or brainstem stroke

2.3. Randomization

Eligible participants are randomized to one of two arms through a "real-time" randomization procedure implemented on the trial website for the Data Coordination Unit system at MUSC, WebDCU™. The procedure balances overall treatment distribution as well as the distribution of one important baseline covariate: baseline aphasia severity (WAB-R AQ). The arm assignment will be based on the current status of the WAB-R AQ distribution, as well as the overall balance of treatment assignment. Independent of the treatment arm assignment, the therapy sequence (semantically-focused approach first or phonologically-focused approach first) is also randomized using WebDCU™.

2.4. Intervention: aphasia therapy

The primary goal of TERRA is not to test the effectiveness of aphasia therapy. Rather, the goal is to test whether there is comparable efficacy of the mode of therapy delivery (ART vs. I-CT). For that reason, it was appropriate to select therapy approaches that are typically employed and compare the outcome of those approaches based on delivery modality. Given that we have already shown statistically significant improvement in naming using the semantically-focused and phonologically-focused therapy regimen [9], we employed the same approaches in TERRA.

The therapy approaches were grouped based on whether they primarily targeted semantic versus phonological processing. The semantically or phonologically-focused approaches are utilized in two separate therapy phases, for 15 days of treatment (45 min/day) each. We previously observed that naming performance was improved after using this therapy regimen in clinic (i.e. 15 days of treatment for 45 min/day in two phases) [12]. It is important to note that the therapy approaches used in TERRA are not selected to match the individual impairment profiles of the participants. Rather, one of our goals is to understand whether participants respond differently to semantic or phonological therapy and whether their impairment profile predicts what therapy approach works better. Each of the therapy types is described in detail below.

2.4.1. Semantically-focused therapy tasks

We use three types of semantically-focused therapy tasks. The first, Semantic Feature Analysis (SFA), has a relatively long history as a therapy approach for aphasia [17,18]. For each pictured stimulus, the participant is prompted to name the picture. Then, he or she is encouraged to produce semantically related words that represent features similar to the target word (e.g., superordinate category, use, action, physical properties, location, and association). For example, to elicit a location feature, a clinician might say, "Where do you typically find this object?" If the participant is not able to name the target item once each word feature has been produced, the clinician will say the target word. Regardless of naming accuracy on the last item, therapy continues on to the next stimulus item. Because both nouns and verbs have been used for SFA-focused activities, stimuli for SFA tasks in TERRA utilize both.

The second semantic therapy approach is the Semantic Barrier Task. This approach includes features of the Promoting Aphasics' Communication Effectiveness (PACE) approach [19]. It relies on a stack of picturable stimuli, which are split between the participant and clinician and placed face up on a table. A visual barrier is placed between the clinician and the participant so they cannot see each other's pictures. The goal of the task is for one participant (e.g., person with aphasia) to describe each card so that their conversation partner (e.g., clinician) can guess the picture on the card. Participants are only allowed to describe the semantic features of the target, and the clinician models the kinds of cues that are allowed. Participants are encouraged to use both verbal as well as non-verbal (e.g., gesturing, drawing, writing) means of communicating the target word. The clinician and participant take turns describing pictures.

The third approach, Verb NEtwork Strengthening Therapy (VNeST), is a semantic therapy approach that targets the lexical retrieval of verbs and their thematic nouns [20,21]. The objective of VNeST is for the participant to generate verb-noun associates with the purpose of strengthening the connections between the verb and its thematic roles. VNeST can be modified to fit participants with very limited speech output (e.g., choosing a cue card, using sentence completion, etc.).

2.4.2. Phonologically-focused therapy tasks

Three phonologically-focused approaches, also with sound research pedigrees, will be used. The first is the Phonological Components Analysis task (PCA), which was modeled after semantic feature analysis [22]. It requires the participant first to attempt to name a given picture and then to identify the phonological features of the target words (e.g., first sound, syllables, last sound, association, and rhyme). Once the features have been identified, participants are prompted to attempt to name the picture again. Then, the therapy moves on to the next item in a stack of targeted imageable nouns and verbs.

The second, Phonological Production Task [23,24], is a phonologically-based therapy that focuses on the identification of phonological features using the same 60 targeted imageable nouns and verbs used in the PCA. It requires the participant first to sort the target pictures into two stacks, one-syllable and more than one-syllable words. The participant is to tap out each syllable in the target word, and they have 5 min to complete as many as possible. Various levels of cueing from the therapist can be provided as needed. The last 10 min of this treatment moves on to identifying a hierarchy of phonological features using a pair of the targeted imageable nouns/verbs. Once the targeted feature is identified for each of the words, the participant is required to blend the syllables/sounds together, forming a novel word.

The third approach, the Phonological Judgment Task [11], relies on the computerized presentation of verbs and nouns where participants are required to judge whether pairs of words include similar phonological features. The task is comprised of five conditions that entail determining if a set of words: a. includes the same number of syllables; b. includes the same initial syllable; c. includes the same final syllable; d. which word has more syllables; and e. rhyme. Participants respond to each condition by pressing one of two response buttons on the computer screen or on a button box, depending on the task requirements and instructions.

2.5. Intervention: aphasia remote therapy

No commercial software packages are available that allow for SLP administration of the therapy approaches included here. Therefore, the TERRA investigators created software that allows an SLP to administer therapy using a teleconferencing style portal, which includes the presentation of all therapy materials and enables the SLP and participant to watch each other in real-time. The ART app is a custom-built therapy delivery software that integrates real-time media streaming (audio and video) with the ability to administer therapy as well as computer-based testing remotely.

Upon enrollment, all participants randomized to ART are provided a touch-screen laptop. In cases where the participant does not have internet access, the laptop can be configured to connect to the internet automatically, with minimal effort from the participant, using a wireless hotspot. The therapy "app" is installed on the laptops, and each laptop is assigned a unique alphanumeric key, akin to a subject identifier, which allows SLPs to communicate selectively with and target that specific machine for a given therapy session. A program that allows secure remote access of the laptop is installed on the laptops so that SLPs/technical staff can assist participants with startup and troubleshooting once the devices have been deployed.

During the week of baseline testing, participants, and their caregiver (if appropriate), receive training on how to maintain the laptop computer, how to set up a space for optimal therapy sessions (e.g., a quiet room with ample lighting on their face), and how to charge the laptop. The laptop is continuously accessible via the internet. SLPs are, therefore, able to start the therapy app remotely and play 'alert' sounds/notifications to signal that the therapy session is about to start. For backup purposes, if the participant fails to show up on time for their scheduled appointment, the SLP will place a phone call to them no later than 10 min after the scheduled start time.

The therapy app was designed primarily to be able to administer the six different therapy components in TERRA [Fig. 2] to participants receiving remote treatment. The left side of the screen consists of two video boxes. The upper left box will always contain a video of the remote agent (participant), while the lower left box will always contain a video

Fig. 2. A picture of the laptop running the TERRA therapy app. The therapist (middle, left) is administering therapy to a participant (top, left) using the PCA task.

of the local agent (SLP). Care was taken to make sure the "buttons" where participants touch the screen to make selections are sufficiently large and easily manipulated during the therapy tasks.

2.6. Baseline assessments

All individuals with chronic aphasia are screened for inclusion in the study. Once deemed eligible, participants will complete baseline testing and neuroimaging. The assessment timeline is outlined in Table 2. Baseline assessments occur at least 1-year post-stroke. Assessments will occur over a 4-day period, depending on the testing needs of the participant. Participants are administered the WAB-R [15] to confirm the absence of severely limited speech production and severely limited auditory comprehension and, therefore, eligibility. A high-resolution structural MRI is administered to confirm only left hemisphere lesion, or, if there are contraindications to scanning, the lesion etiology is confirmed based on a previous scan and/or a detailed radiology report.

A battery of cognitive-linguistic assessments is administered for the purpose of patient description, including an examination of mid-to high-frequency object naming via the in-house assessment confirmation of usefulness of treatment via the "Treated Naming 40" [25], which only assesses naming of treated words. A lack of change on Treated Naming 40 would be suggestive of no specific response to therapy. Also assessed in the battery is non-verbal abstract problem solving and inductive reasoning as well as non-verbal working memory via the Weschler Adult Intelligence Scale (WAIS) IV [26], the presence of apraxia of speech via the Apraxia of Speech Rating Scale (ASRS) Version 3 [27,28], verb processing and production/comprehension of canonical and non-canonical sentences via the Northwestern Assessment of Verbs and Sentences (NAVS) [29], semantic processing of nouns via the Pyramids and Palm Trees Test (PPTT) [30], the ability to distinguish the lexical and conceptual contributions to non/verb and action/object dissociation via the Kissing and Dancing Test (KDT) [31], the ability to repeat via the Philadelphia Repetition Test (PRT) [32], and the ability to produce simple two-word combinations with appropriate morphology via the Morphosyntactic Generation (MorGen) Test [33]. Participants are also assessed for quality of life and sustained attention via the Stroke and Aphasia Quality of Life Scale (SAQOL-39) [34] and the Continuous Performance Test (CPT) [35], respectively. We also collect baseline characteristics, including:

Table 2
TERRA schedule of evaluations.

Assessment	Baseline	Inter-Treatment Evaluation	1 Month Post-Treatment Evaluation	6 Month Post-Treatment Evaluation
Informed consent, collection of individual demographic and baseline characteristics, randomization	X			
MRI/fMRI	X	X	X	X
Saliva sample for genotyping	X			
WAB-R	X			X
PNT	X	X	X	X
SAQOL-39	X			X
Cinderella story telling	XX	X	X	X
Cookie Theft picture description	XX	X	X	X
Broken Window picture description	XX	X	X	X
Treated Naming 40	X	X	X	X
WAIS IV sub-tests	X			
CPT	X			
ASRS	X			
NAVS	X			
PPTT	X			
KDT	X			
PALPA sub-tests	X			
PRT	X			
Neglect assessment	X			
MorGen	X			
CAS	X			
Aphasia Friendly Telehealth Usability Questionnaire (TUQ) [43]			X	
SLP TUQ			X	
Participant satisfaction survey			X	

- Socio-demographic information, including age, sex, race/ethnicity, handedness, education level, and occupation
- Medical history and current medication information
- Genotyping for brain-derived neurotrophic factor (BDNF), forkhead box P2 (FOXP2), apolipoprotein E (ApoE4), and Pals1-associated tight junction (PATJ) via a saliva sample
- A select set of sub-tests from the Psycholinguistic Assessments of Language Processing in Aphasia (PALPA) [36].
- Visual field cut and visual neglect screening
- Computer use assessment via the Computer Attitude Scale (CAS) [37].

Discourse samples are taken twice at baseline to assess words produced per minute (WPM), a component of the TERRA primary outcome measure (further discussed in the Outcomes section). Three discourse tasks are administered.

1. Broken Window picture sequence description [38].
2. Cinderella story-telling [39].
3. Cookie Theft picture description from the Boston Diagnostic Aphasia Examination [40,41].

The ability to correctly name nouns, the other component of the primary outcome, is measured using the Philadelphia Naming Test (PNT) [42].

2.7. Outcomes

The primary outcome measure for this trial is a composite of the improvement at 6-months post-therapy for correct naming (on the PNT) and WPM produced during discourse tasks. The composite improvement score is referred to as the Speech Production Outcome Score (SPOTS) and is the combined t-score for change in correct naming on the PNT and change in average WPM during discourse.

The secondary outcomes for this trial include the change from baseline to 6 months in the individual components of the primary outcome (correctly named PNT items and WPM), SAQOL-39 mean score, and WAB-R AQ.

2.8. Blinding

The participants and the SLPs administering the treatment and assessments are not blinded to the treatment arm, but the raters of the outcome measures are blinded to treatment assignment, study timepoint, and treatment type (semantically or phonologically focused). The raters are centrally located at USC and do not have contact with the onsite SLP that administers treatment of the participants. Offline scoring is performed on videotaped behavioral assessments with no time stamps.

2.9. Treatment and assessment fidelity

Our treatment and assessment fidelity procedures, developed for previous studies from our group, are outlined in Spell et al. [44] To ascertain treatment fidelity, we follow the guidelines from the NIH Behavior Change Consortium [45] with respect to study design, training, treatment delivery, treatment receipt, and treatment enactment. All personnel who have contact with participants are trained to ensure that all exchanges are ethical, respectful, and successful communication strategies are employed. This includes training for communication during initial recruitment and participant identification, for the informed consent process, and for participant retention. It also includes training in assessment administration procedures and treatment procedures. This training helps to reduce variability introduced by clinicians communicating or carrying out procedures with different styles than others. Treatment fidelity is optimized by monitoring multiple components, specifically clinician training, treatment delivery, and treatment receipt, through face-to-face and video-recorded treatment sessions. This is an ongoing process, not only occurring at the onset of the project but rather continually performed over the entire project duration to ensure that treatment implementation is consistent throughout the trial duration. The study coordinator, who is an SLP, observes a randomly selected treatment session and evaluates treatment delivery and receipt for each participant. A treatment fidelity log is maintained for each SLP who delivers treatment. As with the assessment fidelity plan, immediate feedback is provided when a speech-language pathologist deviates from a treatment protocol. When an SLP deviates from a treatment protocol, she or he is given feedback immediately. Each SLP will have one or two semantic and one or two phonological treatment sessions evaluated for each participant enrolled.

Assessors are SLPs who complete training for baseline and informed consent. Illustrating the relationships between the assessments that the clinicians are administering and the specific project goals emphasizes the importance of the assessment process and adherence to prescribed procedures. This development of clinician "meta-competence" or "buy-in" is thought to be important in treatment fidelity and is intuitive in assessment as well – understanding the "why" facilitates investment in the "how," or adherence to procedures [46,47]. In addition, highlighting the opportunities most susceptible to drift or contamination serves to bring the information to the forefront so that it can be actively avoided. Finally, clinician attrition is likely to be less observed in clinicians who are invested in the project goals and feel as if their contribution is important. The following assessment training procedures are implemented.

1. Independent reading of the assessment manual
2. Video observation of expert administration of each test, administered to persons with varying types and severity of aphasia
3. A small group training session that includes manual review, highlighting of similarities and differences between administration procedures via discussion and video observation, and supervised role-play with feedback
4. Supervised assessment sessions with expert feedback
5. Yearly small group training as needed. These training procedures guard against clinician-to-clinician variability, drift, and contamination. Each SLP will have 1–2 assessments evaluated for fidelity per participant with a rotating list to make sure all assessments are observed for each SLP

To ascertain and quantify assessment fidelity for the naming and discourse outcome measures, the study coordinator conducts an annual review of 10 % of assessment sessions for each rater (each rater's assessment load for these measures overlaps 50 % with that of another rater). From these, intra- and inter-rater reliability are explored using intraclass correlation coefficients. In addition, an assessment-fidelity log is maintained for each speech-language pathologist, which includes whether they adhere to the assessment administration protocol and whether they enact the assessment and engage the participant. Approximately 10 % of all sessions are observed by the study coordinator. When a speech-language pathologist deviates from an assessment protocol, they receive immediate feedback.

2.10. Statistical analysis

2.10.1. Statistical hypotheses

Let θ be the treatment group difference (ART minus I-CT) as measured by SPOTS, in which a larger value of θ favors ART. The statistical hypotheses are H_0: $\theta \leq -\delta_0$ vs. H_A: $\theta > -\delta_0$ where δ_0 is the non-inferiority margin.

2.10.2. Sample size considerations

SPOTS is calculated by first standardizing the change from baseline for each component (PNT and WPM) by subtracting the sample mean and dividing by sample SD. Then the standardized change scores are summed together. Lastly, the sum is multiplied by 10 and added to 0 to create a "t-score". The t-score SD is greater than 10, by design, since it involves the sum of two dependent random variables.

For this trial, the non-inferiority margin is defined as approximately half of the SD of the SPOTS calculated using data from the POLAR trial (t-score mean = 50, SD = 13.2; not published). Assuming SD = 13.2, δ_0 = 6.6, power = 90 % and alpha = 0.15, the sample size needed is 50 participants per group. This sample size takes into account 5 % loss to follow-up. In prior studies, missing data have been very minimal (<5 %), and we anticipate a similar level of study completion here.

2.10.3. Primary analysis

The primary analysis will test the non-inferiority hypothesis using a two-sample, one-sided *t*-test, testing whether the expected therapy difference is less than the non-inferiority margin defined here as $\delta_0 = 6.6$. If the null hypothesis of inferiority (H_0: $\theta \leq -\delta_0$) is rejected, this is preliminary evidence that ART should be studied further but not definitive evidence of non-inferiority. If the preliminary analysis indicates the data is highly non-normal, then the primary analysis will be based on a bootstrapped *t*-test.

2.10.4. Secondary analysis

The mean difference (95 % CI) for each secondary outcome will be reported. The mean differences will be reported unadjusted and adjusted for any observed baseline differences.

2.10.5. Exploratory analysis

We will also assess whether participant and clinician attitudes (as measured by the TUQ), biographical factors, and baseline cognitive-linguistic factors influence acceptance (as measured by the proportion of subjects who completed at least 80 % of therapy) and outcome of aphasia therapy (as measured by SPOTS) for those participants who were assigned to the ART group. We assume there are three latent factors: 'perceived ease of use', 'perceived usefulness,' and 'usage intention'. First, an exploratory factor analysis of the TUQ will be performed to assess the latent factor structure. In order to evaluate the Technology Acceptance Model, which incorporates Cognitive-Linguistic factors and Biographical factors (TAM + C-L-B model), structural equation modeling will be used to gauge different paths on ART outcome and adherence separately. PROC CALIS in SAS software will be used to assess the correlation, and potential influence of different paths. A minimum of 5–15 subjects per variable are recommended for structural equation modeling. Given the sample size in the group randomized to ART, this would correspond to 3 to 10 variables, which could be included. Most variables are continuous or quasi-continuous and will be assumed to be jointly multivariate normal. The normality assumption will be assessed (via Shapiro-Wilk's test for normality) prior to performing the model.

Finally, to address Aim 3, building on the prior work of our group in the development of quantitative models of word-level speech production, we will use a multinomial processing tree model to provide therapy response predictions based on estimates of participants' latent abilities in lexical, phonological, and semantic processing, as inferred from their naming response types [48].

3. Discussion

At present, and despite the best evidence that supports the utility of aphasia therapy, the amount of therapy provided in the U.S. is often much less than needed. This is attributable to the lack of emphasis on chronic stroke recovery and access to rehabilitation services. One approach to increase access to rehabilitation services is to rely on tele-rehabilitation. Providing ART could vastly increase the availability of SLPs and may also potentially decrease costs. The few studies of ART published so far have been underpowered and provide limited evidence regarding the utility of ART in comparison to I-CT. Before moving to a definitive phase III trial, it is important to determine whether ART is non-inferior to I-CT.

TERRA is the first phase II, non-inferiority trial of ART that is exclusively administered by an SLP. Participants with chronic aphasia are randomized to either ART or I-CT, relying on the same therapy approach used in the recently completed POLAR study [9]. The outcome measure focuses on speech production and combines correct naming on the PNT [41] and WPM during discourse. The primary endpoint is a change in the outcome measure at 6 months compared to baseline. The non-inferiority margin is set so that if ART leads to less than 50 % improvement than the improvement following I-CT, it will be considered inferior for therapy delivery.

There is also very little known about what factors may influence the efficacy of telerehabilitation for aphasia therapy. Relying on the TAM model [49], TERRA will assess personal attitudes towards general technology use at baseline. Attitudes toward the use of ART after completion of the therapy phase will also be assessed and related to the acceptance and effectiveness of ART. Finally, participants' cognitive-linguistic status and biographical factors are tested at baseline, before therapy is initiated, to start to explore which participants may have difficulty with telerehabilitation and may be poor candidates in the future phase III trial.

CRediT authorship contribution statement

Christy Cassarly: Writing – review & editing, Writing – original draft, Methodology, Conceptualization. **Alexandra Basilakos:** Writing – review & editing. **Lisa Johnson:** Writing – review & editing, Conceptualization. **Janina Wilmskoetter:** Writing – review & editing. **Jordan Elm:** Writing – review & editing, Methodology, Conceptualization. **Argye E. Hillis:** Writing – review & editing. **Leonardo Bonilha:** Writing – review & editing, Conceptualization. **Chris Rorden:** Writing – review & editing. **Gregory Hickok:** Writing – review & editing. **Dirk-Bart den Ouden:** Writing – review & editing, Methodology, Funding acquisition. **Julius Fridriksson:** Writing – review & editing, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Conceptualization.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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