Caregiver Collaborative Integrated Therapy in Sub-Acute Stroke Protocol-Remote

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Research Design and Methods

A leading cause of serious, long-term disability in the United States,[1] stroke has a particularly pernicious impact on individuals and families. Approximately 4.8 million stroke survivors (SS) require assistance from family members who are often untrained and ill prepared for the burdens associated with stroke rehabilitation.[2, 3] Family care partners (CP) are key contributors to stroke recovery, but their efforts can lead to a high level of CP burden and depressive symptoms, reduced quality of life (QOL) and increased stress in the context of high levels of family conflict surrounding the recovery process.[4, 5] Rehabilitation therapy interventions have primarily targeted SS outcomes without specifically addressing the well-being of the CP.[6] Our group has pioneered creative approaches for engaging CPs in rehabilitation activities within the family which have great potential to improve physical and psychosocial health for both the CP and SS.

We have developed a theory-based, family-centered intervention, **Care**partner and **C**ollaborative **I**ntegrated **Th**e**r**apy (**CARE-CITE**),[7] designed to engage CPs during SS upper extremity (UE) functional task practice in the home. Residual UE impairments occur in up to 80% of SSs [8] and are a primary factor in loss of functional independence. CARE-CITE guides the CP in collaborative goal setting and providing autonomy support (characterized by empathy, choice and reducing use of controlling language) for the SS to promote motivation and creative problem solving in UE self-management.

The goal of this study is to implement CARE-CITE paired with usual and customary UE care sooner after stroke when SSs are in outpatient rehabilitation and in the sub-acute stroke (1-3 month) recovery period. We will examine CARE-CITE during this early stroke recovery phase and gather evidence to ascertain the theorized mechanisms of effect. This new information will inform future intervention development, testing, and translation to improve stroke outcomes sooner during the rehabilitation process.

The scientific premise underpinning this research is that a theory-based, family-centered intervention *focused* on skill building, improved family context, and problem-solving will improve SS physical function and quality of life while reducing CP negative outcomes during outpatient rehabilitation. The research design is a mixed methods, two-group (2:1) exploratory pilot study comparing intervention (CARE-CITE with usual customary care (n=24 dyads) to an attention control with usual customary care (n=12 dyads)**.**

Aim 1: To evaluate effects of web-based CARE-CITE at home during subacute stroke recovery on both CP and SS health outcomes and QOL. *Hypotheses: **1.1**. CPs receiving CARE-CITE will have reduced depressive symptoms and improved QOL at 2-month post intervention compared to the control group. **1.2.** SSs receiving CARE-CITE will have improved upper extremity function and QOL at 2-month post intervention compared to the control group.*

Aim 2: To examine the effect of web-based CARE-CITE on the family context and processes related to stroke rehabilitation. *Hypotheses: **2.1**. CPs receiving CARE-CITE will have less family conflict and provide greater autonomy support at 2-month post intervention compared to the control group. **2.2.** SSs receiving CARE-CITE will have improved perceived autonomy support and UE self-efficacy at 2-month post intervention compared to control group.*

Exploratory Aim. Use qualitative methods to complement the interpretation of effects on processes and outcomes from Aims 1 and 2. At 3 months post intervention, we will evaluate CPs' perceptions of the benefits, challenges and experiences with the intervention and explore changes in their perceived QOL, family conflict, and autonomy support.

- **General Overview of Proposed Methods:** We propose a mixed methods, convergent design[9] with a two-group experimental approach with separate quantitative and qualitative analyses followed by integration of the findings. We will block randomize (2:1) 36 dyads to treatment or control. All SS will be 1-3 months post stroke and living at home to capture family dyads who are still in sub-acute post stroke outpatient rehabilitation therapy. The intervention will last 4 weeks. Baseline and 3-month post-intervention assessments will include questionnaires, measures of recovery, and semi-structured interviews (**Table 2)**. **Methodological Modification:** All study interactions with participants (including screening, evaluations and interventions) will occur remotely via phone call or HIPPA compliant Zoom platform currently being used by Emory Healthcare for telehealth clinic visits.

Study Participants: All Emory Hospital stroke admissions will be screened based upon study

inclusion/exclusion criteria and contacted by the research coordinator, if eligible. Participant eligibility will be confirmed via telephone and virtual screen, and initial virtual evaluation will follow. All self-report written CP and SS questionnaires will be delivered to participants' homes for completion. Completed questionnaires will be returned via self-addressed stamped envelope or study staff will arrange for pick-up from the participant's home. The evaluator will review questionnaires for completeness and conduct a virtual evaluation to complete SS upper extremity assessments and address any missing CP data. All potential dyads will read/sign Emory IRB approved consent/HIPAA forms. Evaluations and training sessions will be video-recorded for standardization procedures to ensure study rigor and reliability. Video or audio recording is optional and not required for participants to participate in the study. Participants will have the option to consent to these recordings. A medical screen from participant's physician will be obtained prior to enrollment. Patients will agree to allow researchers to review their medical records for data collection.

Inclusion/exclusion criteria: All SSs will be 1-3 months post ischemic or hemorrhagic event[10], discharged from inpatient neurologic rehabilitation to their home, have minimal to moderate UE deficits (actively initiate 20 degrees of wrist and 10 degrees of finger extension), no severe cognitive deficits (Mini-mental test[11] >24), no physician determined major medical problems that would limit participation in outpatient therapy, and a CP living in the home.[10, 12] CPs must >21 years old, able to read and write English and have no significant cognitive deficits (Mini-mental test >24). CPs will be defined as those individuals who are a spouse/partner or family member dwelling in the same household, the family member most involved in stroke recovery, and self-identify as the primary caregiver of the SS.[4, 13] CPs must be familiar with using a computer and accessing websites, or be familiar with using a tablet (available for loan if no computer available).

We plan to recruit 12 dyads into the usual care attention control group and 24 dyads into the CARE-CITE group. The larger intervention group will contribute precision to the pilot-based estimates of mean changes and variability for key outcomes, while also improving the lessons to be learned about feasibility to inform future implementation for a larger-scale trial. Given the PI's extensive and successful recruitment experience for other prior stroke studies, a recruitment rate of 2-3 dyads per month is a realistic estimate for the proposed time period. An attrition rate of ~8% is projected based on the literature;[14-16] thus, we will enroll 40 dyads to achieve a complete sample of 36.

Intervention group: CARE-CITE: While the SS is receiving usual and customary outpatient UE rehabilitation, the CARE-CITE intervention will occur over 4 weeks. The primary CARE-CITE components will be education via web platform. The research interventionist will conduct a virtual in-home visit via Emory Zoom platform at orientation and during week 4, and telephone follow ups. The research interventionist will work in tandem with the outpatient rehabilitation treatment team to coordinate care plans and patient goals.
1) Visit 1: Virtual Orientation (3 hours). The research interventionist will meet virtually with CP and SS to review collaborative goals setting, evaluate UE movement limitations, and identify functional activity preferences. Together, they will begin development of a progressive therapeutic exercise plan for home-based functional task practice, determine activities for each goal and measurable milestones to accomplish during the treatment period, creating a framework to improve joint responsibilities for self-management skills.
2) CP completes 6 online CARE-CITE modules (15-30-minute sessions each). During the week following Visit 1, the CP will access the website to complete 6 online modules. Modules include demonstration videos and instructive content covering following areas: principles of functional task practice (i.e., activities of daily living such as eating, grooming, or leisure/vocational activities), adaptation of tasks, and importance of progression of challenging tasks to drive neuroplasticity (i.e., increasing numbers of practice repetitions or weight of objects lifted). Examples are provided to address potential SS frustration and improve adherence. Underpinning the content is the concept of autonomy support, with examples of fostering empathy (e.g., the CP using non-dominant hand during activities), problem solving (guidance for adaptation of functional activities at home to increase success or challenge), instruction in the use of non-controlling language with role playing situations and the importance of creating choice in activities. For example, in one vignette to demonstrate problem solving, a CP interacts with the SS during a meal using non-controlling language to offer choice for task modifications for manipulating food with the weaker hand. The SS becomes frustrated with the challenging task, and the CP demonstrates options for dialogue that foster collaborative problem solving.
3) Weekly teleconference/Zoom check-in. Each week during the 4-week intervention, the research interventionist will complete a structured 10-minute phone call with CP to answer questions and assist with problem solving.
4) Visit 2: Virtual Home visit (3 hours). At the end of week 4, the same research interventionist will conduct a virtual home visit to review progress with milestones and advancement of activity goals.

5) "CARE-CITE Booster" session – 4 weeks after the intervention period, the research interventionist will make a brief 10-minute telephone booster call to reinforce CARE-CITE content, ask the CPs to identify two challenging areas during SS practice activities, and CP opportunities to use principles of autonomy support.

Attention Control group: SS and CP will receive customary care outpatient rehabilitation therapy but no CARE-CITE intervention. The CP will receive a CP support brochure with general caregiving information including website resources to mimic web interaction of intervention group (e.g., stroke caregiver resource site). The research coordinator will handle all communication. The CP will receive the same number of structured weekly phone calls and the "booster call" to answer any questions, assess helpfulness of the information and ascertain if there was any use of the web resources or social support groups.

Procedures: The research coordinator will make a virtual screening appointment at via HIPPA compliant Emory Zoom telehealth platform for interested participants. If screening criteria are met, an electronic informed consent (via RedCAP data management system) will be obtained from the CP and SS. Following baseline data collection obtained via a virtual evaluation by the research evaluator (licensed physical therapist), participants will be randomized to groups using a random number generator. The research interventionist (licensed physical therapist) will schedule dyads in the intervention group for the orientation virtual home visit and the second virtual home visit and complete weekly phone calls. The research coordinator will schedule all dyad data collection appointments and complete attention control group dyads phone calls. All dyads complete a virtual evaluation for the 3-month post-test visit. *To increase rigor and minimize bias*, data collectors will be blinded to group assignment/study hypotheses and will be trained in study procedures (e.g. Mini-mental test administration) by the PI [Blanton], with regular assessments of competence every 4 months. The PI will train the research interventionist in delivering the intervention and provide supervision by reviewing all in home visits. To minimize missing data, all participants will be sent email / text / mail reminders for upcoming appointment dates. Using the web platform, we will be able to track the frequency and time on each web module. All dyads will receive $100 for study participation at the end of the 3-month follow up.

Instruments: Variables and measures have all been tested in this population previously. Each standard tool has evidence of established reliability and validity in this patient population as referenced in **Table 2**.

Table 2. R21 Measures collected at baseline and 3 months post-intervention

VARIABLE	MEASURES	Description	Reliability/Validity
CP Depression	CES-D	20-item, Likert-type scale	Established validity, internal consistency, reliability [17]
CP Quality of life	SF-36	36-item Likert-type scale, mental health domain	Sensitive indicator CP mental health[18, 19]
SS Quality of Life	Stroke Impact Scale (SIS)	59-items, 8 domains function	Test-retest reliability ICC = 0.70 to 0.92;Internal consistency alpha coefficient of 0.83-0.90 [20]
SS Upper Extremity Function	Wolf Motor Function Test (WMFT) (dropped from remote study) Motor Activity Log (MAL)	15 item speed measures;2 item strength; low score/faster speed 30-item questionnaire, Likert-type scale; high score/high quality UE use	Inter-rater reliability r=.97; valid in the stroke population[21]
CP/SS Autonomy Support Environment	Family Care Climate Questionnaire FCCQ-CP/FCCQ-SS	14-item, Likert-type scale. Higher scores/higher autonomy support perception	Internal consistency >. 70; Construct validity supported-higher FCCQ-SS scores related to SS lower perception of criticism, higher family emotional involvement-higher satisfaction with family support ($p \leq .05$)[22]
CP Family Conflict	Family Caregiver Conflict Scale (FCCS) about Stroke Recovery	15-item, Likert-type scale; Higher scores/higher conflict	Established content/construct validity in stroke CP; reliability Cronbach's alpha =.93[23]
SS UE Self Efficacy	Confidence in Hand and Movement Scale (CAHM)	20-item (scale 0-100)UE confidence for functional tasks; high scores/high confidence	Reliable and valid with moderate relationship with WMFT 3-9 months post stroke[10]

Additional secondary outcome measures will be collected for CP-Family Assessment Device (FAD) Scale (baseline only), CP Caregiver Strain Index (CSI), CP Bakas Caregiving Outcomes Scale (BCOS), SS Fugl-Meyer Assessment (FMA) (baseline only), SS Neuro-QoL Short Form v1.1 - Satisfaction with Social Roles and Activities, CP BRICS NINR Depression scale (PROMIS Depression- Short Form 6a), SS Neuro-QOL SF v1.0 - Upper Extremity Function (Fine Motor, ADL).

Additional clinical data about SS (such as medications, concurrent medical problems, pre-morbid handedness, side affected by stroke) and about the CP (co-morbidities and medications) will be collected to fully describe the sample and explore relationships using correlation analysis. The CP adherence to the intervention will be assessed by monitoring CP review of the CARE-CITE modules through Google Analytics, and completion of module feedback questionnaires including specific examples of ways they used the educational information (e.g., "provide an example of how you used autonomy support with your loved one"). Participants will have the option to wear bilateral, wrist-worn accelerometers (Actigraph) to assess upper extremity performance in the home environment for a period of 1-3 days at time of the baseline and 3-month follow-up evaluations.

Data Management and Planned Analysis: All quantitative data storage will be maintained through the Emory HIPPA compliant REDCap database. Standard data cleaning, identification of missing data, identification of outliers, and internal consistency reliability for standardized scales will be completed. Initial data analysis will include descriptive statistics to describe the sample and summarize major study variables. **For Aim 1**, we hypothesize that for dyads receiving CARE-CITE, CPs will display reduced (improved) CES-D depression and improved SF-36 (QOL) scores and SS will have higher scores on the MAL (improved use of arm function), SIS (QOL), and reduced scores on the WMFT (faster UE speed of movement) consistent with moderate to large effect sizes at 3-months as compared to baseline and more favorable changes in these scores after 3-months as compared to the attention control group. **For Aim 2**, we hypothesize that for dyads receiving CARE-CITE, both members will have higher autonomy support (FCCQ-CP; FCCQ-SS), CP will have reduced FCCS (family conflict) and SS will display higher CAHM (UE self-efficacy) as compared to baseline and to the control group. The first component of the primary analysis will involve the construction of 95% confidence intervals in order to summarize changes from baseline to 3-months within each group. We will also report the results of paired t tests or nonparametric Wilcoxon signed rank tests to assess changes from baseline to two months post intervention within each group. Similarly, we will compare mean or median changes of the outcomes targeted in Aims 1 and 2 across the two groups using two-sample t tests or Wilcoxon rank sum tests, respectively. Recognizing the pilot nature of the study, these inferences will be viewed primarily as descriptive rather than as definitive hypothesis testing efforts. To address the multidimensional nature of the data, we will examine inter-correlations among the study variables, including variables that may influence response to the intervention. As needed, we will use linear regression models to augment the primary analyses in order to assess the extent of association between patient characteristics and mean changes and whether observed differences in mean changes across groups persist after controlling for such variables. The **biological variables** of CP age, sex, gender and relationship of CP to SS (e.g. spouse, adult child) and other participant characteristics such as SS other health problems will be examined and potential relationships explored to gain insight into possible confounding factors. ***Potential limitations:*** While CP of any sex/gender will be recruited, most CPs are female, which may limit interpretations of any sex/gender differences found.

Exploratory Aim Methods: At the end of 3-month post-intervention evaluation we will invite the 24 CPs in the intervention group to participate in focused individual interviews to better understand their perceptions of how CARE-CITE impacted health outcomes, QOL, and family conflict and autonomy support. We will use a semi-structured interview guide (developed by the study team and reviewed by content and qualitative experts – See Appendices) that addresses both outcomes and process aspects of CARE-CITE. For example, questions will focus on: how the dyad incorporated autonomy supportive strategies; benefits/ challenges of using autonomy supportive approaches; conflicts in CP and SS working together and how CP perceive the intervention impacted SS function. An open-ended question will be included for CP to share additional feedback about CARE-CITE. Virtual interviews (~45-60 minute each) via HIPPA compliant Emory Zoom telehealth platform will be conducted by the PI and a research assistant (RA). Dr. Lutz (qualitative methods expert) will provide oversight to the PI and RA for qualitative interviews and analysis. Interviews will be audio-recorded and transcribed verbatim by a professional transcriptionist for accuracy. **Data Analysis:** Data collection and analysis will occur simultaneously. Dr. Lutz, Dr. Blanton and the RA will analyze transcripts line-by-line, using thematic analysis, to identify salient themes.[24] Transcripts will be reviewed for themes: autonomy supportive interactions (e.g. empathy, offering choice, problem solving) or non-autonomy supportive interactions (guilt inducing, lack of empathy, controlling language); types and opportunities to work together on recovery activities; and perceived effects on outcomes (functional recovery, depression, and QOL). As themes are identified in early interviews, they will be verified with new CPs to substantiate their relevance; the interview guide will be adapting accordingly. Comparisons of themes will be made within and across interviews.[24-26] CP responses will be compared for similarities and differences in the challenges and benefits of the intervention. Data saturation is expected to occur between 15-24 participants.[27] QSR NVivo 11 qualitative data management software[28] will aid in analyzing the data making comparisons within and across texts, and comparisons to the quantitative measures. Using guidelines by Fetters, et. al.,[9] triangulating qualitative and quantitative data will occur at the study end by merging data, based on methods described by Creswell, et al.,[29] including the use of side-by-side joint displays. Dyad and CP quantitative data (e.g. change in family conflict, autonomy support and caregiver depression scores will be compared for concordance or discordance with themes identified in the interviews to better understand mechanism of the intervention. *Approaches to ensure rigor of the data analysis and interpretation*: 1) Team members will keep memos to record findings and track analytical interpretations providing an audit trail with supporting documentation from interviews and data analysis. 2) The team will meet monthly to discuss the ongoing data analysis and data collection. 3) Provisional

findings from early interviews will be discussed with the entire team for feedback on the interpretations and to help develop additional interview questions.

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