E-learning+ Rehab Therapy (TEAACH)

NCT04245449

Document Date 08/14/2019

## PROTOCOL TITLE:

**A novel therapy + e-learning self-management program for stroke survivors**

## PRINCIPAL INVESTIGATOR:

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## 1.0 Objectives / Specific Aims

Our central premise is that survivors must engage in more in-home paretic arm use and less non-paretic arm use because real world use drives neural plasticity more than the limited therapy visits available. We argue that survivors do not use the paretic arm outside of the clinic to maximize beneficial plasticity because post-discharge support from the rehabilitation team is limited, thus survivors do not fully understand why or how to use the paretic arm at home. Although current in/outpatient rehabilitation provides basic education about stroke and managing impairments, current rehabilitation practice does little to empower stroke survivors with knowledge or skills; specifically, knowledge of the neurobiological processes causing the impairment and the requisite skills to manage their own long-term recovery. Our unique interprofessional research team, comprised of experienced stroke rehabilitation providers and a nurse scientist, are award-winning educators and passionately believe that survivors can improve outcomes if supported with knowledge and skills.

Hence, we created a first of its kind multimodal therapy + e-learning program called **T**raining to **E**mpower **A**ctivity-dependent-plasticity-based **A**rm-use-habits in the **C**ommunity and at **H**ome (TEAACH). Here we test its implementation:

**AIM: Implement the TEAACH program**
*Rationale:* Online training to improve post-discharge self-management skills in community dwelling stroke survivors is a new concept, therefore there is a need to test the feasibility of this approach. *Method:* Twelve (n=12) survivors ≥3 months post stroke with moderate arm motor impairment, will be enrolled in TEAACH. TEAACH is a cutting-edge therapy + e-learning program designed to gradually transition the stroke survivor away from therapist-management to self-management of long term stroke recovery. TEAACH will have 3 essential components; a behavioral contract signed before the program begins to assure that its focus is explicit in survivors' minds; direct therapist contact for 3 months (3 months in-clinic therapy with online guidance); and online course activities guided by rehabilitation professionals to engage learning and peer mentorship.

**SA1: Determine the feasibility of implementing the TEAACH program:**
The primary endpoint will be a determination of the feasibility of the e-learning + therapy program. Primary outcome will be feasibility defined as (1) subjects' level of engagement in the program, (2) acceptability, (3) technological literacy, and (4) practicality. Data will be analyzed qualitatively.

**SA2: Determine the initial efficacy of TEAACH:**
Early indication of efficacy will be determined by TEAACH-related changes in measures of (1) self-confidence and social support, (2) self-management skills, and (3) paretic arm impairment and at-home paretic arm use. Changes scores will be calculated to detect a treatment effect measured from baseline (pre-TEAACH) to post TEAACH (3 months), and at 5-months to assess retention.

Impact: This project addresses a critical gap in the field because it innovatively addresses survivors' skills needed to be the self-managers of their own recovery for the long term. TEAACH has an online platform which means that it could be immediately incorporated into clinical practice, modules could be added to meet other needs such as ongoing wellness education, or it could easily be redesigned to meet similar needs in other patient populations.

# 2.0 Background

## A. SIGNIFICANCE

**A.1. Arm paresis from stroke is a long-term impairment that reduces quality of life:** Most stroke survivors, >75%, exhibit upper extremity (UE) hemiparesis, and only 15% recover fully.[1,2] The majority of daily activities require 2 hands,[3] thus paresis of one hand reduces independence[4] and quality of life.[5]

**A.2. Paretic arm movement can improve during in-clinic therapy, but survivors fail to use the paretic arm outside of the clinic**: Intensive task-practice therapies enable survivors to recover UE skill.[6-8] But, as shown in **Figure 1** patients demonstrate persistent hyper-reliance on the non-paretic arm for daily activities.[9-11]

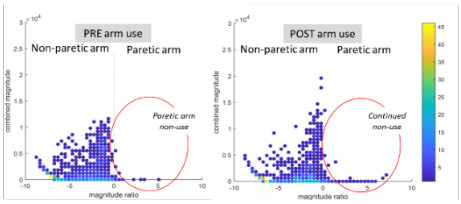



**Figure 1:** A stroke survivor (38 yo male, baseline FMA-UE score = 21/60) enrolled in our NIH/NINDS SBIR project. He played a custom designed computer game at home for 6 weeks. The effect of the therapy program on home/community non-paretic and paretic arm use was quantified with wrist worn accelerometers worn for 48 hours. The results are presented as Bimanual Activity Plots. Each data point indicates arm activity, with the data point's color indicating the activity duration (warm colors = longer duration). The combined magnitude (y-axis) quantifies the intensity of an activity, while the magnitude ratio (x-axis) indicates the contribution of each arm to the activity. A magnitude ratio value = 0 (dotted vertical line) indicates equal non-paretic and paretic arm use. The PRE intervention plot to the left shows nearly exclusive use of the non-paretic arm for daily activities. The POST intervention plot to the right shows minimal increases in paretic arm use for uni- and bimanual tasks.

**A.3. Non-paretic arm use is a behavioral compensatory strategy:** The natural response to impairment of one arm is to compensate by using the other arm for critical life activities. Survivors learn compensatory strategies from rehabilitation therapists[12] and a variety of self-help resources.[13]

**A.4. Over reliance on the non-paretic arm is a behavioral manifestation of an underlying activity-dependent maladaptive plasticity that harms paretic arm recovery**: Repeated behaviors are supported through increasingly more efficient neural networks.[14] Rodent stroke models link non-paretic limb use to increased neural excitability in the non-lesioned hemisphere through a growth response in the basilar dendrites of pyramidal neurons[15] which triggers new inter-cortical trans-callosal connections[16] resulting in synaptic reorganization in areas that should be associated with paretic arm use.[17-19] In other words, non-paretic limb use elicits activity-dependent plasticity processes that hijack neural reorganization of motor networks that otherwise could support paretic limb recovery [20] Human TMS studies show that an imbalance between the hemispheres and continued maladaptive processes are strengthened by ongoing use of the non-paretic arm. By continuing to exclusively use the non-paretic arm survivors are impeding their own paretic arm recovery (**Figure 2**).

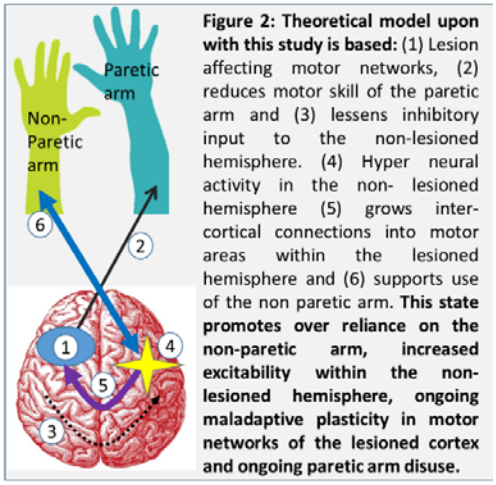



**Figure 2: Theoretical model upon with this study is based:** (1) Lesion affecting motor networks, (2) reduces motor skill of the paretic arm and (3) lessens inhibitory input to the non-lesioned hemisphere. (4) Hyper neural activity in the non- lesioned hemisphere (5) grows inter-cortical connections into motor areas within the lesioned hemisphere and (6) supports use of the non paretic arm. **This state promotes over reliance on the non-paretic arm, increased excitability within the non-lesioned hemisphere, ongoing maladaptive plasticity in motor networks of the lesioned cortex and ongoing paretic arm disuse.**

**A.5. With paretic arm recovery as the goal, survivors must extensively use the paretic arm to reverse maladaptive plasticity and drive beneficial plasticity:** Therapy alone does not elicit a high enough movement dose for beneficial plasticity[21] because the duration of therapy programs[22] and sessions[23] are limited. To effectively actualize restorative plasticity within the constraints of our current healthcare system, more paretic arm use must happen in the home because therapy alone is not/cannot be enough. **Our hypothesis is that patient self-directed in-home paretic arm use drives neural plasticity more than the limited therapy visits available** (**Figure 3**). However, there are very few effective in-home programs[24] except the "transfer package"[28] element of a Constraint Induced Therapy (CIT)[8] program.[25] The transfer

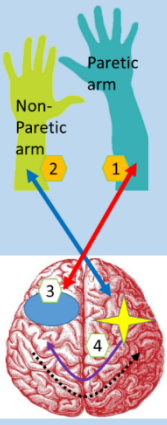
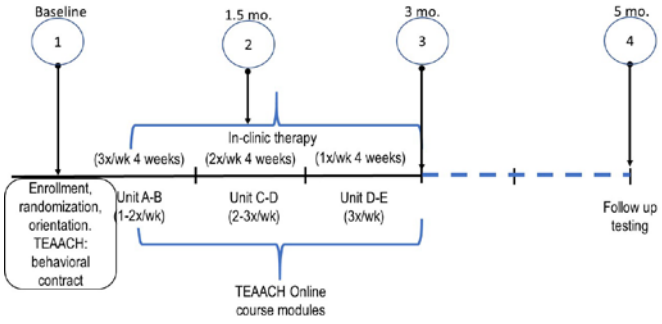



**Figure 3: Scientific basis of the proposed project:** The TEAACH program enables survivors' to acquire the understanding of activity dependent plasticity and problem solving skills needed to (1) drive at-home paretic arm use, (2) so that paretic arm use is balanced with non-paretic arm use. (3) Increased paretic arm use elicits beneficial activity dependent plasticity of the motor networks within the lesioned hemisphere (4) including beneficial plasticity of the trans-callosal connections to/from the non- lesioned hemisphere. **This state, survivor-driven relentless at-home paretic arm use, affords enough paretic arm use to elicit activity dependent plasticity and lasting changes in neural networks supporting long term paretic arm recovery.**

package is a set of behavioral techniques designed to explicitly address clinic-to-home skill transfer including behavioral contracts and therapist-led daily conversations to identify and overcome perceived barriers to at home arm use.[25,26] However, CIT is resource-heavy and is not clinically feasible. A new model of patient-driven in-home therapy is needed.

## 3.0 Intervention to be studied (if applicable)

The **3-month** intervention studied is called **T**raining to **E**mpower **A**ctivity-dependent-plasticity-based **A**rm-use-habits in the **C**ommunity and at **H**ome (TEAACH). TEAACH has two components: An Online Educational Course and an In-Clinic Rehabilitation Therapy Program.




The TEAACH design and testing timepoints are indicated in the **figure to the left**. Subjects will be tested (see below) at enrollment (Baseline, evaluation timepoint 1, E1)), at the midpoint of the therapy + online program (1.5 months, E2), immediately following the in-clinic therapy + online program (3 months, E3), and 2 months after the program for follow up (5 months, E4).

**TEAACH e-learning:** 3-months of online educational modules include neuroscience education (based on an effective pain educational model[37]) to improve patient self-efficacy, and strategy-training[38] to improve patients' problem-solving abilities for at-home arm use. The course is live on the MUSC MoodleCE platform.

**TEAACH in-clinic therapy:** 24 in-clinic sessions; 3 times/week for 4 weeks (month 1), 2 times/week for 4 weeks (month 2) and 1 time/week for 4 weeks (month 3) with 200 movement repetitions per session. In our RCTs, this therapy dose required ~1.0-1.5 hours/session. A critical element of TEAACH is the focus on linking in-clinic therapy to out-of-clinic real world paretic arm use via MoodleCE Learning Activities.

| | month 1 | month 2 | month 3 | month 4 | month 5 | month 6 | month 7 | month 8 | month 9 | month 10 | month 11 | month 12 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| N=12 | TEAACH Group 1 (n=4) | | | | | | | Group1 f/u tests | | | | |
| | | | TEAACH Group 2 (n=4) | | | | | | | Group2 f/u tests | | |
| | | | | | TEAACH Group 3 (n=4) | | | | | | | Group3 f/u tests |

Enrollment: Subjects will begin TEAACH in groups of 4 (ideally. However, as per enrollment logistics, the groups may range from 3-5 subjects). The purpose of group enrollment is to afford opportunity for peer-to-peer interactions within the online learning environment. Peer interactions are strongly beneficial for behavioral change and learning.[39] As shown in **the above timeline,** each group of subjects enrolled will form their own "section" of the online Moodle course. New subjects, in groups of 4, will be enrolled every 2 months forming a separate course section. The purpose of forming new course sections is to assure that the course does not have to pause to allow new enrollees to "catch up." Also, overlapping sections allows peer mentoring by having participants who are at a certain stage of health behavioral change mentor other participants who are at another stage of change. Mentor/mentee activities have been built into the course activities.

Orientation to the Moodle Learning Platform and the Behavioral Contract: At the baseline evaluation session (E1), subjects will be oriented to the TEAACH program and its expectations

via an in-person orientation session. They will be shown how to access the Moodle Online Course through the MUSC secure network using either a computer, tablet or phone. Although we intend to have participants use their own preferred device and wifi connection, the budget includes monies for 10 tablets to afford opportunity for subjects without technology to participate. Security: The MUSC MoodleCE platform is behind the MUSC firewall and will allow password protected access only to the research team and participants enrolled in TEAACH. The investigative team has extensive experience with the Moodle platform. Once oriented to the TEAACH program subjects will sign a behavioral contract (akin to the course syllabus) that clearly outlines the program goals, scientific premise and expected behaviors. A behavioral contract is considered a critical element of a "transfer package" method to enhance real-world use of the paretic arm.[37]

Theory guiding TEAACH e-learning design and implementation: Every aspect of the course has been thoughtfully designed for consistency with current theories of health behavior change (Transtheoretical Model)[60] and methods of instructional design (Constructivism operationalized as the revised Blooms Taxonomy).[61] To our knowledge we are the first to fit theories from the typically disparate fields of health behavior and education into a framework guiding a stroke rehabilitation program. Stroke survivors do not use their paretic arm during non-clinic times, a learned behavior with a maladaptive plasticity substrate. Increased use of the arm to elicit a beneficial activity-dependent plasticity to support further arm recovery requires that the survivor undergo a behavioral change, from paretic arm *dis-use* to paretic arm *use*. New patterns of behavior must be learned, i.e., must be taught. The Transtheoretical Model of Health Behavior

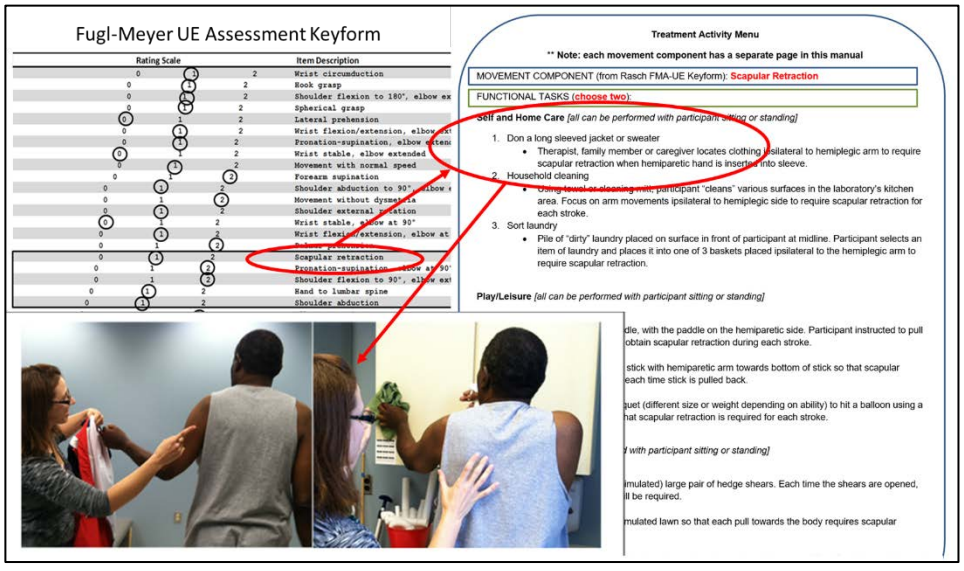
**Table 2: TEAACH Course Organization**

| Stage of Behavioral Change<br>Transtheoretical Model | Instructional Design Processes<br>Blooms Taxonomy | TEAACH Online Course Unit (dose) | Learning Objectives<br><br>At the conclusion of this unit of instruction the stroke survivor will…. | Examples of Moodle Course Features and Learning Activities: |
|---|---|---|---|---|
| **Precontemplation and initial contemplation**: unaware of the need to self-manage arm recovery | **Remembering**: facts, definitions, lists | **A** (1 activity per week for 1 month) | … demonstrate the ability to log into and interact within the Moodle course<br>… list several ways that a stroke changes the brain and body<br>… define "recovery" | **Assignment:** with therapist and course instructor assistance learn to use the Moodle course<br>**WebX Classroom:** Stroke 101<br>**WebX Mentee Meeting:** Led by survivors<br>**Moodle Wiki:** begin collection of web pages, definitions and resources that is added to throughout the course |
| **Contemplation:** become aware of need | **Understanding**: interpreting, summarizing | **B** (2 activities per week for 1 month) | … discuss the reasons why having a stroke causes arm paresis<br>… define activity-dependent plasticity and give examples<br>… report successful paretic arm use to the group. | **WebX Classroom:** Learned Arm Disuse<br>**Assignment:** review baseline assessment results with therapist<br>**Assignment:** with therapist assist, use paretic arm for new task<br>**Discussion Board:** group discussion on motivations for using and not using the paretic arm<br>**Quiz - Automatic Feedback:** survivors' reflect on own learning |
| **Preparation:** initial skill acquisition | **Applying**: implementing, executing | **C** (3 activities per week for 1 month) | … discuss the link between using the "good" arm and recovery of the "bad" arm<br>… implement guided training strategy with progressively less assistance | **WebX Classroom:** Use It or Lose It: principles from neuroscience<br>**WebX Mentee Meeting:** Survivors enrolled in another section will lead the meeting<br>**Moodle Workshop:** survivors post video of self using paretic arm and receive peer assessment. |
| **Action**: overtly engaged in skill acquisition | **Analyzing**: organizing, classifying, differentiating | **D** (3 activities per week for 1 month) | … analyze at-home activities in order to use the paretic arm independently<br>… discus reasons why using the paretic arm is easier/harder at-home vs. in therapy | **WebX Classroom:** How often do stroke survivors use the paretic arm compared to people who have not had a stroke?<br>**Readings:** arm use and recovery<br>**Discussion Board:** report at-home paretic arm use to the group and discuss |
| | **Evaluating**: checking, recommending | **E** (3 activities per week for 1 month) | …. recommend "tips and tricks" for using the paretic arm at-home to others in the course based on your own successes | **WebX Classroom:** Non paretic arm use vs. Paretic arm use<br>**WebX Mentor Meeting** with survivors enrolled in other sections: lead mentoring discussion.<br>**Video Forum:** asynchronous video chat about ongoing successes and struggles for at home paretic arm use. |
| **Maintenance**: sustained self-management skills | **Creating**: generating, planning | **F** (1 activity per week for 1 month) | … design new challenges for using the paretic arm<br>… generate plans for increased at-home arm use | **WebX Classroom:** Assuring long term success<br>**Moodle Chat:** real-time synchronous discussions about goals and plans for long term success.<br>**Quiz - Automatic Feedback:** survivors' reflect on own learning |

Change[60] defines 5 stages of behavioral change, which applied to stroke survivors are; (1) precontemplation, a stage in which stroke survivors are unaware of the negative neural consequences of ongoing paretic arm disuse, they await the rehabilitation team's intervention to provide a "cure", and thus have no reason to drive their own long term recovery; (2) contemplation: through the interactions with study team and peers, survivors become aware of the need to self-manage paretic arm recovery but may be ambivalent and lack self-confidence; (3) preparation: as the course and in-clinic therapy sessions begin, survivors take small steps toward self-management as they begin to develop skills and intentional behaviors; (4) action: as the course gets underway the survivor overtly engages in paretic arm use both in-clinic and at home as he/she acquires the new skills needed to manage arm use; (5) maintenance: the survivor demonstrates sustained self-management skills, is able to use his/her paretic arm in daily life activities. The educational theory of Constructivism,[61] operationalized in the revised Bloom's Taxonomy, provides an overall framework from which to develop learning activities to progress survivors through the 5 stages of change. Constructivist theorists propose that learning is optimized when the learner seeks to accomplish a clear goal then engages in a problem-solving process to achieve that goal. As the learner iteratively engages in this problem solving process, he/she receives feedback from him/herself, instructors and peers about his/her skill or understanding which empowers the learner to construct his/her own knowledge.[62] The revised Booms Taxonomy operationalizes Constructivism principles with verbs to indicate progressively more complex problem solving learning processes. Bloom's taxonomy guided TEAACH learning objectives and learning activities.

TEAACH MoodleCE Course Organization: **The table above** presents the course organization. There will be 6 instructional units (A-F) incorporated into this 3-month e-learning course. Each unit is tailored to a stage of behavioral change. Columns 1-3 illustrate how course units relate to stages of behavioral change and instructional design processes. Example learning objectives (column 4) and learning activities (column 5) show the link to the corresponding stage of behavioral change. Each unit's learning activities will leverage various features of the Moodle platform to address the unit objectives through engaging learning activities to (a) develop survivors' knowledge of concepts and facts about stroke recovery and (b) enable acquisition of survivors' problem-solving skills for paretic arm use.

TEAACH In-Clinic Therapy: Subjects will receive 24 in-clinic Targeted Task Practice rehabilitation sessions; 3 times/week for 4 weeks (month 1), 2 times/week for 4 weeks (month 2), 1 time/week for 4 weeks (month 3) with 200 movement repetitions per session which, in our recently completed RCT of this intervention, required ~1.0-1.5 hours/session, consistent with the literature.[57] The content of the therapy sessions will be individualized according to each participants' score on the Fugl-Meyer Assessment of the Upper Extremity Keyform according to the procedures followed in our



previous VA Merit Award, and that we have published.[58] We call this therapy approach Targeted Task Practice. The distinguishing feature of this intervention is that the Fugl-Meyer Assessment of the Upper Extremity (FMA-UE) Keyform is used to individualize the content of therapy sessions to assure that all task-practice will occur at the optimal level of difficulty for each patient. The procedure for using the keyform to individualize treatment sessions is **illustrated above** as a 4 step process which is also detailed in a recent publication.[58] (1) First, the FMA-UE[54] will be administered in a standardized manner and videotaped. The therapist will score the FMA-UE by circling item ratings on the keyform. (2) Second, the therapist will identify the transition zone by following the consistent pattern of ratings at the bottom of the keyform upwards until it deviated to the next lower adjacent rating (e.g., from a rating of 2 to 1, or from a rating of 1 to 0). This deviation will mark the lower boundary of the transition zone which is defined as the first 5 consecutive items for which 3 of these items received the next lowest rating. These 5 items represent the expected next steps in the subject's transition from a current skill level to a greater skill level,[58] therefore they will be the movements to target in the task practice therapy sessions. (3) Third, to assure the functional relevance of the rehabilitation program the 5-transition zone paretic arm motions will be practiced within the context of functional activities so that they will not be disconnected from their functional application. In our previous Merit project, we developed a detailed study-specific Treatment Activity Menu which links each of the 30 FMA-UE voluntary movement items to functional tasks that primarily require the item's arm movement. We will use this manual in the proposed study. The therapist and subject will collaborate to identify 2 functional activities from the Treatment Activity Menu for each of the 5 target movements identified by the keyform transition zone (total of 10 functional activities). An example of this menu is shown in the figure. As shown, the menu links the FMA-UE item "scapular retraction" to the functional tasks "Donning a long-sleeved jacket" and "household cleaning" because the tasks naturally require repetition of the targeted movement. (4) Finally, as shown in the photos, subjects will perform 20 repetitions of each movement target within each functional activity for a total of 200 repetitions/session. The number of repetitions is based on work indicating its feasibility, safety and effectiveness.[46] The process of scoring the keyform, locating the transition zone, identifying targets and choosing functional activities required ~15 minutes in our previous studies. To assure systematic task difficulty progression throughout the in-clinic program, subjects will be reassessed with the FMA-UE keyform weekly to identify new therapy targets and functional activities. The expectation is that as ability increases, the keyform transition zone will shift upwards to identify 5 new, slightly more difficult targets.

Assurance of patient safety during in-clinic sessions: Therapy sessions will be conducted by a licensed occupational therapist. Heart rate and blood pressure will be recorded before, during and after each session and the study therapist will closely monitor the subject for possible pain or fatigue. In previous work we demonstrated that the functional tasks practiced in a session were at a difficulty level that matched or slightly exceeded the subjects' movement ability level,[59] therefore we do not expect that the patient will show movement compensations. To further assure that movement compensations do not emerge and cause pain or injury, aspects of each task such as object weight, speed of performance or surface heights will be manipulated by the therapist.

A critical element of TEAACH is the focus on linking in-clinic therapy to out-of-clinic real world paretic arm use via MoodleCE Learning Activities: In-clinic therapy for TEAACH subjects will incorporate "guided training" methods into the task practice therapy sessions to elicit survivors' self-reflection and self-efficacy. Guided training[63] is an emerging, effective method to train independent problem-solving abilities via self-instruction, self-monitoring, self-evaluation, and self-rewarding. The therapist will teach a "goal-plan-do-check" process, which will then be practiced throughout therapy. Specifically, before the start of each functional task, with the

assistance of the therapist as needed, participants will instruct themselves what to do (set goal) and how to do it with the paretic arm (develop a plan). The subject does the task and then checks whether the plan worked. For example, if the task is to "set the table" the subject would identify the goal (put the plates there, and the cups there) and how to accomplish it (by reaching forward and straightening my affected arm). After doing it, the therapist will prompt the participant to register if they (1) used the paretic arm, (2) used it in the specified manner (targeted motions), (3) could do it better or differently the next time, and (4) give one's self a pat on the back if it was done well. This process will be repeated iteratively throughout in-clinic sessions and progressively faded over the 3 months in-clinic program. MoodleCE assignments will reinforce guided training. For example, a discussion board activity will ask participants to reflect on one's skill implementing the guided training strategy, a mentor meeting will center sharing one's own successes/challenges in implementing this strategy, and a video forum will show examples of this process in action.

## 4.0 Study Endpoints (if applicable)

**Primary Endpoint:** The primary endpoint will be determined in Specific Aim 1, the baseline to post intervention feasibility of the e-learning + therapy program. Outcome measures will include baseline to post intervention changes in participant scores on assessments of health literacy and technological literacy as well as their overall qualitative experiences.

## 5.0 Inclusion and Exclusion Criteria/ Study Population

**Inclusion Criteria:** (1) paresis of one arm/hand because of ischemic or hemorrhagic stroke >2 mo. and <3 yrs prior; (2) moderate arm impairment defined as a baseline Fugl-Meyer Assessment of the Upper Extremity[31] score of at least 32±2 points but no more than 47±2 points (out of 60 points[32]) based on published impairment categories[33]; (3) Montreal Cognitive Assessment[34] score ≥22 to assure that the cognitive capacity to benefit from this learning-based intervention; (4) the ability to read English; (5) the ability to communicate as per the therapists' judgement at baseline testing; (6) are 21-90 years of age; (7) have a wi-fi connection in the home and either a computer, smartphone or tablet.

**Exclusion criteria:** (1) lesion or injury to brainstem or cerebellum because lesions in these locations may interfere with learning; (2) other neurological disease that may impair motor or learning skills (e.g., Parkinson's Disease); (3) pain interfering with reaching; (4) uncorrected vision making it difficult to read information on a computer, tablet or phone.

## 6.0 Number of Subjects

N=12

## 7.0 Setting

All in-person testing, and therapy research activities will occur in Dr. Michelle Woodbury's College of Health Professions upper extremity motor function research laboratory located in the CHP Research Building at 77 President Street. Dr. Woodbury's research laboratory is in the same building as the other research laboratories in the MUSC NIH Center of Biomedical

Research Excellence (COBRE) in Stroke Recovery. The e-learning course will occur on the MUSC MoodleCE Learning Management System.

## 8.0 Recruitment Methods

Participants with stroke will be recruited from the MUSC NIH Center for Biomedical Research Excellence (COBRE) in Stroke Recovery stroke research recruitment registry called RESTORE (approved MUSC IRB #37803). The Registry currently contains the contact information for ~800 individuals with stroke who have provided consent to be contacted for potential participation in research studies. Importantly, the Center supports a dedicated project coordinator who enrolls 5-10 new participants into the registry per month and supports information technology resources needed to maintain/update the Registry's infrastructure as needed.

## 9.0 Consent Process

The study project coordinator will work closely with the COBRE in Stroke Recovery's recruitment core. The study project coordinator will query the COBRE research registry according to the inclusion criteria for the present proposal. He will identify potential participants that meet inclusion criteria and inform the PI, Co-I, or study therapist who will contact participants by phone to determine if they want to participate in the current study. If they wish to participate they will be scheduled for a time for the PI, Co-I, research therapist or project coordinator to obtain informed consent for the study proposed. Consent will be obtained after reviewing the protocol and consent form with each potential subject. If a potential subject is deemed unable to participate in informed consent as per the judgement of the PI, co-I, study therapist or project coordinator, consent will be obtained from a legally authorized representative with the patient present. For patients consenting themselves, every attempt will be made to have a relative present during the informed consent. All recruitment and informed consent procedures will be approved by the MUSC IRB.

## 10.0 Study Design / Methods

**Study Design**: This is a longitudinal cohort design.

**Research Methods**: <u>All study procedures are for research purposes</u>, that is, there are no non-research evaluations or interventions.

**Intervention Methods and Location:** The e-learning and stroke rehabilitation therapy intervention to be studied is described above in section 3.0. All in-person procedures will occur either in the PI's stroke rehabilitation research laboratory (College of Health Professions, 77 President Street). The e-learning intervention will occur via a MoodleCE online learning platform.

**Duration of Subjects' Participation:** After enrollment, subjects will participate in a 3-month e-learning + in-clinic stroke rehabilitation program. Subjects will complete a follow up assessment ~60 days after the end of the 3-month program. Thus, subjects will be involved with this study for 5 months.

**Audio and Video Recording:**

- Audio Recording: Each subject will participate in 3 focus groups; one at baseline, immediately following the end of the 5-month intervention, and at the post-intervention follow up. The purpose of the focus groups will be to understand the participants' experiences with regards to the feasibility of the program and changes in his/her self-management skills. Each focus group will be audio recorded. The audio recording will be transcribed. The transcription will be analyzed using qualitative data analyses techniques to ascertain thematic data.
- Video Recording: Subjects will be video recorded during administration of two arm movement tests: the Fugl Meyer Assessment of the Upper Extremity and Wolf Motor Function Test. Trained assessment raters who are blind to testing time point will score the assessments from the video tapes. All videos will be stored on secured, password protected servers behind the MUSC firewall. The procedure for training raters and scoring from videos was developed in the PIs research laboratory and has been used in past and ongoing stroke rehabilitation research clinical trials. Of note- the only people having access to the videos are laboratory personnel who have been approved by the IRB to be part of this study, and who have completed all required IRB privacy and university training.

**Primary and Secondary outcome measures** are identified in the schedule of events table below.

| Measurement Construct | Assessment method | Baseline (E1) | Mid (E2) | Post (E3) | Follow up (E4) |
|---|---|---|---|---|---|
| **SA1: Primary Endpoint: Feasibility** | | | | | |
| Health Literacy | Short Assessment of Health Literacy | X | | X | |
| Tech Literacy | Technology Literacy self-evaluation | X | | X | |
| Participants' experiences | Qualitative (focus group) | X | | X | |
| **SA2: Secondary Outcomes: Initial efficacy in the following areas:** | | | | | |
| **SA2a. Effect on self-confidence and social-support** | | | | | |
| Self-Efficacy | PROMIS Self-Efficacy for Managing Daily Activities assessment | X | | X | X |
| Social Isolation | PROMIS Social Isolation assessment | X | | X | X |
| Emotional Support | PROMIS Emotional support assessment | X | | X | X |
| **SA2b. Effect on self-management skills** | | | | | |
| Self-Management Skills | Qualitative (focus group) | X | | X | X |
| **SA2c. Effect on arm movement abilities** | | | | | |
| Arm movement Impairment | Fugl-Meyer Assessment of the Upper Extremity (FMA-UE) | X | X | X | X |
| Arm motor function | Wolf Motor Function Test (WMFT) | X | X | X | X |
| Paretic arm use in the home | Wrist Worn Accelerometry | X | X | X | X |
| Difficulty using the paretic arm | Stroke Impact Scale – Hand subsection (SIS-H) | X | X | X | X |

**Procedures to lessen the probability or magnitude of risks:**

- Possible risk: Pain and/or Fatigue during stroke rehabilitation therapy.
    - Therapy sessions will be conducted by a licensed occupational therapist. Heart rate and blood pressure will be recorded before, during and after each session and the study therapist will closely monitor the subject for possible pain or fatigue. Subjects will complete pain and fatigue rating scales at the start, middle and end of each therapy session. If pain and/or fatigue ratings exceed minimal (e.g., greater than 4 on a 0-10 rating scale), the therapy session will be stopped, and the subject provided a rest period. If needed, the session will be rescheduled. In previous work we demonstrated that the functional tasks practiced in a session were at a difficulty level that matched or slightly exceeded the subjects' movement ability level,[59] therefore we do not expect that the patient will show movement compensations (movement compensations are known to cause pain and fatigue). To further assure that movement compensations do not emerge and cause pain or fatigue, aspects of each task such as object weight, speed of performance or surface heights will be manipulated by the therapist.

- Possible risk: Embarrassment during the online learning course
    - Subjects enrolled in this study will participate in an online learning course. Other stroke survivors will also be enrolled at the same time. Learning activities will include peer-to-peer asynchronous discussions via the forums, and synchronous discussions via the WebEx Collaborate virtual classroom. It is possible that a subject may feel embarrassed during these discussions. To lessen the probability of embarrassment, subjects will be given the option of choosing a username. If desired, the username can be one that does not reveal the subjects' name. In this way, he/she can remain anonymous during discussion posts. Also, the "guidelines and expectations" for the course (a document posted and reviewed during the first week) will clearly specify that a subject has a choice whether to reveal personal details during peer-to-peer discussions during virtual classroom sessions. This expectation will be repeated before each virtual classroom session.

- Possible risk: Loss of privacy due to the focus groups. A focus group is a discussion group and therefore it is possible that a stroke survivor may reveal information about him/herself during the discussion. This information may cause embarrassment. It is also possible that a focus group member inadvertently shares information outside the focus group. The focus group leader will remind members of this possible risk, that participation is voluntary, and to respect each other's privacy.

**Source Records:** All data about subjects will be collected from the subjects themselves. No other medical records will be accessed in this study.

**Data Collection Procedures:** Subjects will be assessed by trained evaluators who will be members of the study team. The following constructs will be measured by the following methods:

- Short Assessment of Health Literacy is an 18-item test designed to assess an adult's ability to read and understand common medical terms. It will be administered by the

study therapist in a standardized manner. Subjects' receive 1 point for each correct item. A score below 14/18 indicates poor health literacy.

- Technology Literacy self-evaluation is a 23-item questionnaire in which the subject answers true/false to questions about his/her readiness to participate in an online course. Any items in which the subject answers "false" will be reviewed with the subject by the study team in efforts to remedy the lack of technological confidence or literacy.

- Participants' Experiences and Participants' Self-Management Skills: Participants' viewpoints on the course will be assessed qualitatively using focus groups. A focus group guide will structure these sessions. The focus groups will be led by the co-I, Dr. Michelle Nichols who is an experience focus group leader and has the necessary expertise for qualitative data analyses.

- Self-Efficacy will be assessed using the NIH PROMIS Self-Efficacy for Managing Daily Activities assessment. This is an 8-item assessment where a participant reports his/her level of confidence in doing 8 daily activities such as performing household chores, lift/carry groceries and shop/run errands.

- Social Isolation will be assessed using the NIH PROMIS Social Isolation assessment. This is an 8-item patient self-report assessment indicating patients' frequency (never, rarely, sometimes, usually, always) having feelings such as being left out, detached, isolated etc.

- Emotional Support will be assessed using the NIH PROMIS Emotional Support assessment. This 8-item assessment records patient's self-reported view of the frequency (never, rarely, sometimes, usually, always) with which he/she has emotional support from others in areas such as listening, someone to confide it, someone who understands one's problems etc.

- Arm movement impairment will be measured with the Fug-Meyer Assessment of the Upper Extremity, a 30-item assessment that indicates how well a stroke survivor is able to move his/her paretic arm into/out of various postures. Each assessment item is scored on a 3 point ordinal scale (0=unable, 1=partial ability, 2=near normal ability), and the item ratings are totaled and reported out of 60 points so that higher scores indicate less impairment (i.e., more ability).

- Arm motor function will be measured with the Wolf Motor Function Test (WMFT), a 15-item assessment indicating the speed at which a stroke survivor can move the paretic arm to complete functional tasks such as stacking checkers or picking up a soda can. Each assessment item is timed, and the average time per item is reported in seconds so that lower scores indicate greater functional ability.

- Paretic arm use in the home will be measured with wrist worn accelerometers. Subjects will be issued 2 accelerometers which are worn on each wrist for 48 hrs. They are the size of an Apple Watch. Subjects will either bring the devices back to the research center at their next visit or mail them back in mailers that we will provide (we pay postage). 3-D acceleration data will be downloaded and used to calculate variables that indicate the acceleration of the paretic arm relative to the non-paretic arm. A neurologically healthy

individual will have values close to 1 to indicate bimanual arm use, smaller numbers indicate less use of the paretic arm, i.e., over-reliance on the non-paretic arm.

- Difficulty using the paretic arm during daily activities will be assessed with the Stroke Impact Scale – Hand subtest. This is a 5-item assessment in which the patient reports the amount of difficulty using the paretic hand along an ordinal scale (0=no difficulty, 5=great difficulty).

## 11.0 Specimen Collection and Banking (if applicable)

N/A. No specimens will be collected or banked.

## 12.0 Data Management

**Data Analysis**: Feasibility will be described. Early indication of efficacy will be described by plotting repeated measures of the secondary outcomes at each assessment timepoint to indicate the longitudinal impact of the interventions on paretic arm impairment and function.

**Sample Size:** The primary outcome measure is **feasibility**. One aspect of feasibility will be subjects' "engagement" in the program which will be defined as a point estimate[35] by creating a nominal variable to describe subjects' engagement level: "Engaged" defined as completing ≥80% of the in-clinic/online activities, "Less Engaged" as completing <80% of the activities. This project is a step towards a full roll out of this program in which estimating engagement is critical for both future sample size estimates and understanding/planning for the possible pitfalls of a subsequent implementation trial. We anticipate that 5% or fewer will demonstrate non-engagement based on previous low attrition rates in our RCTs. A point estimate calculation yielded **N=12** to give us 95% confidence that ~90% of a sample should be "engaged" in the TEAACH course if the true rate of engagement is 3%.

**Data Security and Confidentiality:** The IRB-approved study team will be the only people with access to PHI. All hard-copy PHI (e.g., signed ICFs) will be stored in a locked cabinet in a locked office in the PIs research laboratory office space on the 2nd floor of CHP-C. All e-copy PHI (e.g., enrollment logs) will be stored on the MUSC network in the PI's dedicated network space which is behind the MUSC firewall with MUSC approved security. All files will be password protected and accessible only to the study team with the correct passwords. All subjects will be assigned a study specific code that will not relate to any of his/her PHI. This code will be used on all CRFs. No PHI will appear on CRFs. The link between PHI and the subject ID code will be separated from data during storage and data use.

**Quality Control of Collected Data:** One study team member will be assigned the task of routinely reviewing data entry to assure its completeness. In addition, all data will be entered into a study specific Redcap dataset which will be designed to provide alerts if the data are missing or entered incorrectly.

No data will leave MUSC.

## 13.0 Provisions to Monitor the Data to Ensure the Safety of Subjects (if applicable)

**Overall framework for monitoring:** Participant safety will be monitored by the research therapist and PI who are licensed, registered occupational therapists as well as the study co-I who is an experience stroke rehabilitation nurse. The risks of this study include subject fatigue. Pain, embarrassment, and loss of privacy.

**Frequency of monitoring:** Therapy sessions will be conducted by a licensed occupational therapist. Heart rate and blood pressure will be recorded before, during and after each session and the study therapist will closely monitor the subject for possible pain or fatigue by having subjects complete a self-reported summary of pain and fatigue using a Borg rating scale. In previous work we demonstrated that the functional tasks practiced in a session were at a difficulty level that matched or slightly exceeded the subjects' movement ability level, therefore we do not expect that the patient will show movement compensations. To further assure that movement compensations do not emerge and cause pain or injury, aspects of each task such as object weight, speed of performance or surface heights will be manipulated by the therapist.

**Process for reporting adverse events:** The PI, Co-I, research therapist and/or project coordinator will be responsible for reporting adverse events as per the policies and procedures of the MUSC Institutional Review Board.

**Trial monitoring:** the PI and co-I will be responsible for trial monitoring and assure that the trial is conducted according to the approved protocol. Because this trial is low risk, i.e., no greater risk than a traditional outpatient occupational therapy rehabilitation program, the PI and co-PI are appropriate monitors. The study team will meet at a minimum each week to identify and address any safety issues but can meet immediately if an urgent issue arises. In addition, the building in which this study will take place has offices for several of the MUSC COBRE in Stroke Recovery investigators who are experienced stroke MDs. As needed, an MD can immediately be consulted.

## 14.0 Withdrawal of Subjects (if applicable)

**Subject Voluntary Withdrawal:** As participation in this study is voluntary, the subject has the right to withdraw from the study at any time for any reason without prejudice to his/her future stroke rehabilitation care. For the subject who withdraws consent, the date and reason for withdrawal will be documented. Subject data will be included in the analyses up to the date of withdrawal and no further data will be collected.

**Subject removal from the study:** The PI may stop study therapy if there is a safety concern (e.g., excessive pain/fatigue, hospitalization), if the subject fails to attend evaluation sessions or adhere to study procedures. Subject data will be included in the analyses up to the date of withdrawal and no further data will be collected.

## 15.0 Risks to Subjects

The risks to the subjects are related to the therapy intervention are no greater than an outpatient stroke rehabilitation program. These risks include fatigue and pain.

- **Fatigue:** Although most of the upper extremity rehabilitation activities will occur while the subject is seated, it is possible that subjects become fatigued as a result of participating the therapy intervention. In our past studies (including an RCT with n=103 stroke survivors) using the same or similar therapy protocol, subjects routinely reported fatigue during and immediately following the therapy session. However, the level of fatigue was rated as an average of 3-5/10 on a self-report Likert scale. This was considered low to moderate fatigue, and in no case limited subjects' ability to carry on with their day. If subjects in the present study report fatigue during therapy,
- **Pain**: In our past stroke rehabilitation RCT (n=103) ~60% of subjects reported some level of pain in the paretic arm. In 10% of those cases (n=11), the pain was severe enough that the therapist recommended that the see a primary care physician. In most of cases, the therapist adjusted the intensity of therapy to reduce pain level (e.g., reduced the height of the tasks practiced, provided assistance).
- **Loss of confidentiality due to e-learning course participation:** it is possible that participating in the online course will cause subjects to lose confidentiality because others in the course will know their name. To mitigate this risk, we will offer subjects opportunity to choose their own username when logging into the course. This will enable them to remain anonymous.
- **Embarrassment:** It is also possible that subjects will be embarrassed by the e-learning course because lessons or assignments may showcase a weak area (e.g., something the subject has difficulty doing). Subjects will be informed that they can "opt out" of any assignment or discussion as they wish. Also, subjects will be shown how to delete a post in the e-learning course forum and discussion boards in case they have second thoughts about something they wrote.
- **Loss of privacy due to focus group discussions.** It is possible that a focus group member may share information about another focus group member outside of the group. The study team will remind focus group members that participation is voluntary and to respect each other's privacy.
- **Loss of confidentiality due to breach of data**: Dr. Woodbury's team will take appropriate steps to protect subject data. However, there is a slight risk that information could be revealed inappropriately or accidentally. All hard-copy information with the subject's name on it will be stored in a locked cabinet in a locked office in a secure building at the MUSC (77 President Street, Charleston, SC). All electronic information will be stored in a secured database on the firewall protected MUSC network. No PHI will be transmitted outside of MUSC, stored on portable electronic devices, shared or sold at any time. All the data from the test results will be de-identified before it is stored in a research database

## 16.0 Potential Benefits to Subjects or Others

We expect that subjects will improve their own skills for managing their stroke. For example, we anticipate that subjects will know more about stroke, stroke recovery, and develop skills that promote increased use of the paretic arm in the home and community environments. However, it is possible that subjects do not have any direct benefit.

Although the subjects may not benefit individually, we will understand more about the feasibility of providing online education to this patient population.

## 17.0 Sharing of Results with Subjects

The study will be registered as a clinical trial at clinicaltrials.gov. All data will be shared as per clinicaltrials.gov requirements. In addition, each subject can request a copy of his/her own data at any time during the study.

## 18.0 Drugs or Devices (if applicable)

N/A. There are no drugs or devices studied.

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