

Coversheet

Study Title: Cognitive Rehabilitation in Post-COVID-19 Syndrome: A feasibility trial

Institution: University of Missouri

NCT Number: NCT06136871

IRB Number: 2096158

Consent Approval Date: May 1, 2023

Protocol and Statistical Analysis Plan approval date: February 11, 2025

Written Consent to Participate in a Research Study

Project Title: Cognitive strategy training in Post-COVID-19 Syndrome: A feasibility trial

Principal Investigator Name: Anna E. Boone, PhD, MSOT, OTR/L

IRB Assigned Project Number: 2096158

Funding Information: National Institutes of Health, National Center for Medical Research and Rehabilitation

Key Information About the Study

You are being asked to participate in a research study. The purpose of the research study is to evaluate how well a telehealth cognitive intervention works to improve activity performance, cognition (i.e., thinking abilities), and quality of life in individuals with post-COVID syndrome who are experiencing cognitive impairment that affects everyday life activities. You are being asked to take part in 10 virtual sessions. You are also being asked to complete a series of tests before and after the intervention. \

Possible benefits include performing everyday life activities better and/or experiencing fewer cognitive symptoms. Some possible risks may include: (1) a breach (i.e., break) of confidentiality where identifiable health information related to the participants is accidentally made available to individuals outside of the research team; (2) emotional distress while talking about changes in your abilities due to post-COVID syndrome; or (3) physical injury. Participants will be encouraged to perform their activity-related goals at home. Some of these goals involve physical activity, (e.g., cooking), in which the participant could sustain a physical injury such as a cut on the hand. These activities will all be common everyday life activities that the participant is already doing at home.

Please read this form carefully and take your time. Let us know if you have any questions before participating. The research team can explain words or information that you do not understand. Research is voluntary and you can choose not to participate. If you do not want to participate or choose to start then stop later, there will be no penalty or loss of benefits to which you are otherwise entitled.

Purpose of the Research

You are being asked to participate in this study because you are (1) between the ages of 18-60 years, (2) are experiencing persistent symptoms associated with COVID-19, (3) are experiencing cognitive symptoms that impact your ability to perform everyday activities, (4) have no neurological/psychiatric diagnoses, and (5) are able to read, write, and speak English. The purpose of the research study is to evaluate how well a telehealth cognitive intervention works to improve activity performance, cognition (i.e., thinking abilities), and quality of life in individuals with post-COVID syndrome who are experiencing cognitive impairment that affects everyday life activities.

What will happen during the study?

You are being asked to complete the following activities:

- **Pre-intervention tests** for approximately 2.5 hours that will consist of questionnaires, interviews, and thinking tests.
- **10, 45-minute telehealth intervention sessions.** These will either consist of the cognitive intervention or weekly contact with the study team. You will be randomized to one of two study groups: a treatment group or a control group. Within the cognitive intervention, we will work together to identify problems and possible solutions to the everyday life activity problems you are having over 10, 45-minute intervention sessions. The weekly contact with the study team will involve discussion about things you may have done in the past week that could have impacted your post-COVID syndrome symptoms and will last approximately 20 minutes. Each intervention session will be videorecorded.
- **Post-intervention tests:** for approximately 2 hours that will consist of questionnaires, interviews, and thinking tests.

Your participation is expected to last a total of 12 weeks.

There will be about 65 subjects participating in this study.

What are the expected benefits of the study?

You may or may not benefit as a result of your participation in the study. Information learned from the study may help other people in the future. You may potentially experience improvement in your ability to perform everyday life activities better and/or experience fewer cognitive symptoms.

What are the possible risks of participating in this study?

There are minimal risks expected when taking part in this study. There are some that we know about and some may not know about yet. Some possible risks include (1) a breach (i.e., break) of confidentiality where identifiable health information related to the participants is accidentally made available to individuals outside of the research team; (2) emotional distress while discussing potentially sensitive topics such as changes in one's abilities due to post-COVID syndrome or suicidal thoughts; or (3) physical injury.

To help lower these possible risks, we will keep your information in a password protected file on a secure network that has restricted access. All data obtained by the study team will be for research purposes only and will be de-identified prior to data entry into our secure electronic database. Additionally, only select members of the research team will have access to videorecordings; these recordings will also be stored on a password protected, secure electronic platform on Mizzou Servers. Any hard copy data will be locked in filing cabinets in the private offices of the PI. All electronic data will be maintained on one web-based, secure, centralized database. The database will use the REDCap® platform and can only be accessed through two

password protected portals. All data entered into the REDCap® database will be stored on University of Missouri secure servers and will have access restricted to only members of the research team. In the rare event participants experience emotional distress when answering questions during assessments, they will be reminded that they can choose not to answer any questions that may make them uncomfortable and that participation is completely voluntary. Additionally, researchers have a list of available mental health resources that can be provided.

We will tell you about any new important information we learn that may affect your decision to continue to participate in this study.

What other choices do I have if I don't want to be in this study?

You are not required to be in this study. You can simply choose not to participate. You can look for other research projects you may be interested in instead of this study.

Will I receive compensation for taking part in this study?

You will be compensated (i.e., paid) for taking part in this study. For your time and effort, you will receive \$60 via check payment within one month of your pre-tests and post-tests for a total of \$120. Compensation is provided for completion of the pre-intervention tests and post-intervention tests; therefore, payment will be prorated if a participant withdraws from the study prior to the post-tests.

Are there any costs for participating in this study?

You should not expect any additional costs by participating in this study.

Other costs to you from being in this study may include childcare and/or time off work.

You should discuss any questions about costs with the researchers before agreeing to participate.

Will information about me be kept private?

The research team is committed to respecting your privacy and keeping your personal information confidential. We will make every effort to protect your information to the extent allowed by law. Your records will be given a code number and will not contain your name or other information that could identify you. The code number that connects your name to your information will be kept in a separate, secure location.

When the results of this research are shared, we will remove all identifying information so it will not be known who provided the information. Your information will be kept as secure as possible to prevent your identity from being disclosed.

What we collected from you as part of this research will not be used or shared for future research studies. It will only be used for purposes of this study.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by National Institutes of Health which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of child abuse and neglect or harm to self or others.

Where can I get more information about this clinical trial?

A description of this clinical trial will be available on www.clinicaltrials.gov, as required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

Who do I contact if I have questions or concerns?

If you have questions about this study or experience a research-related injury, you can contact the University of Missouri researcher at (573) 882-7023 or booneae@umsystem.edu. If you have questions about your rights as a research participant, please contact the University of Missouri Institutional Review Board (IRB) at 573-882-3181 or muresearchirb@missouri.edu. The IRB is a group of people who review research studies to make sure the rights and welfare of participants are protected.

If you want to talk privately about any concerns or issues related to your participation, you may contact the Research Participant Advocacy at 888-280-5002 (a free call) or email muresearchrpa@missouri.edu.

Do I get a copy of this consent?

You will receive a copy of this consent for your records.
We appreciate your consideration to participate in this study.

Consent Signatures

Subject's Signature	Date

SOCIAL/BEHAVIORAL/EDUCATIONAL RESEARCH PROTOCOL

UNIVERSITY OF MISSOURI

Project Title: Cognitive strategy training in Post-COVID-19 Syndrome: A feasibility trial

IRB Number: 2096158

Version Number: 5

Version Date: February 11, 2025

Principal Investigator: Anna E. Boone, PhD

Funding Source: National Institute of Child Health and Human Development

I. Research Objectives/Background

1. The goal of this proposed project is to evaluate the feasibility and preliminary effect of metacognitive strategy training delivered via telehealth methods to improve activity performance, cognition, and quality of life in individuals experiencing cognitive impairments that limit everyday activities in post-COVID-19 syndrome (PCS).
2. The precise prevalence and etiology of PCS will become better understood with time, but the reality of ongoing symptoms requires immediate intervention to diminish the effect of COVID-19 on daily lives. One of the most common PCS symptoms is cognitive impairment, or “brain fog.” Cognitive impairment in PCS typically manifests in executive functioning difficulties that impact complex or novel task performance. PCS cognitive symptoms require the rehabilitation community to investigate ways to: (1) reduce the functional impact of the symptoms on daily life and (2) support individuals with PCS to establish new habits to improve and maintain health. While the cognitive impairment associated with PCS has not been well evaluated, it is reminiscent of cognitive symptoms seen in other conditions (e.g., mild stroke, cancer-related cognitive impairment, mild traumatic brain injury). The most efficient course of action to address this unmet need is to explore established interventions used with neurologically impaired populations with persons with PCS. Metacognitive strategy training (MCST) approaches are an evidence-based practice standard for improving capacity to self-manage chronic cognitive symptoms and reduce their functional impact on everyday life activities.

Cognitive Orientation to daily Occupational Performance (CO-OP), a specific MCST protocol, uses a structured approach to goal-setting and problem-solving to compensate for executive functioning deficits and improve client autonomy.^{1,2} CO-OP is a recognized practice standard and has demonstrated positive effects for improving function in a number of populations including mild stroke, cancer-related cognitive impairment, and traumatic brain injury.^{1,3-6} The goal of CO-OP is to help participants develop and enhance control over cognitive functions and remove cognitive, emotional, and behavioral obstacles inhibiting performance. The CO-OP approach is an MCST intervention in which participants are taught a general cognitive strategy that can be applied in known and novel contexts to devise task specific strategies for engaging in an activity. Existing evidence with other populations suggests that CO-OP has more of a positive effect on improving activity performance and cognition than remediation/retraining-based approaches.¹ These effects have been demonstrated in

individuals with mild cognitive impairment that mirrors that found in PCS. The overall research hypothesis is that CO-OP can feasibly be administered remotely and will improve activity performance, subjective and objective cognitive function, and quality of life in individuals with PCS.

II. Recruitment Process

1. All participants will have had a COVID-19 diagnosis and will have experienced ongoing symptoms for a minimum of 6 weeks. These ongoing symptoms will include self-reported cognitive impairment that is impacting ability to participate in daily life activities. All patients seen at MU Healthcare for a COVID-19 diagnosis will be available for recruitment for this study through the MU School of Medicine Show Me Portal. A recruitment flyer will be used to recruit individuals from the community. We will also share the recruitment flyer virtually on Facebook support group pages and via email blast with the help of the Washington University Research Participant Registry (RPR) and MUInfo. We will also advertise the study on researchmatch.org and the MU RII website using IRB-approved language and our recruitment flyer.
2. The MU School of Medicine Show Me Portal and MU's data request system will identify potential participants based on the following inclusion/exclusion criteria of this study (see complete list below): (1) age, (2) COVID-19 diagnosis. Contact information for potential participants will be forwarded to the research team for this study. Potential participants will be contacted over the phone by a research coordinator to determine interest in this study. A maximum of three calls will be made in attempt to reach participants. If a participant does not answer, a voicemail will be left. Interested potential participants will complete a 10-minute prescreening survey via phone to further establish eligibility. After completion of the prescreening survey, the research coordinator will arrange a time to obtain electronic written informed consent and to complete the screening/baseline assessment remotely via Zoom teleconferencing platform.

III. Consent Process

1. Potential participants who are scheduled for a baseline assessment will be e-mailed a copy of the consent form prior to the baseline testing session to allow sufficient time for review. On the first session via videoconferencing the research coordinator or research assistant will explain the informed consent process to the potential participant. The specific details on the informed consent form will be reviewed. In particular, the person will be told the procedures they will participate in, the potential risks and benefits of participation, and their right to refuse participation at any time without any effect on subsequent health care. The person then will be given another opportunity to read the consent form. After reading it, the study team member will answer any specific questions, highlight the important details of the study again, and remind the person of their rights as a participant. The person will then be asked to electronically sign the consent form if they would like to participate. A copy of the form will be electronically given to the person via email for their records. The electronic consent form will be filed on a secure server and will only be accessible by a few members of the research team.

IV. Inclusion/Exclusion Criteria

Inclusion Criteria:

- 18-60 years of age
- self-reported cognitive symptoms persisting for at least 6 weeks following COVID-19 infection (Cognitive Failures Questionnaire (CFQ) score >43)
- self-identified activity performance goals per the Canadian Occupational Performance Measure (COPM)
- documented prior diagnosis of COVID-19
- read, write, and speak English fluently; and
- ability to provide valid informed electronic consent.

Exclusion Criteria:

- diagnosis of severe neurological or psychiatric condition(s)
- dementia symptoms as indicated by a score of <23 on the Montreal Cognitive Assessment (MoCA)
- untreated sleep apnea (≥ 5 on the STOP-Bang)
- prior cancer treatment
- severe depressive symptoms (>21 on Patient Health Questionnaire-9)

The screening methods identified in parentheses next to appropriate inclusion/exclusion criteria will be used to verify appropriate selection of study participants.

V. Number of Participants

1. We will enroll approximately 65 (final sample of 52 human participants) for this single-blind, parallel, randomized clinical trial.
2. The purpose of this R21 is to obtain estimates of effect and precision of response so that a more formal sample size calculation can accompany our future NIH R01 application. A total sample size of 65 will allow for 52 participants required for this study after 25% attrition. While we will not complete hypothesis testing, we used the following assumptions of hypothesis testing to estimate our sample: (1) power of 0.80; (2) a 2-tailed alpha of .05; and (3) an estimated attrition rate of 25%. The primary outcome of the intervention is activity performance, therefore, the Canadian Occupational Performance Measure (COPM) was used to drive the power analysis. A sample size of 65 will allow for detection of a large between groups effect (Cohen's $d = 0.8$ or greater) which is a conservative estimate based upon our prior work that has demonstrated large effects on the COPM in stroke ($d=1.6$) and cancer-related cognitive impairment ($r=0.88$). Additionally, this sample size is sufficient to permit detection of the minimally clinically important difference (MCID) of the COPM (i.e., 2 points) with standard deviations obtained from our team's prior work. Based on these assumptions, a minimum sample of 65 participants would need to be enrolled.

VI. Study Procedures/Study Design

1. This is a single-blind, parallel, exploratory, randomized controlled trial to further evaluate the feasibility and the effect of remote delivery of CO-OP on cognitive impairment limiting activity performance in PCS. Individuals from the community and MU HealthCare will be recruited. Those meeting initial screening criteria will undergo further screening and eligible participants will complete baseline assessment remotely. After baseline assessment, participants will be randomized to one of two groups: (1) a 10-session CO-OP intervention; or (2) an inactive control group. Block randomization will be used to ensure equal distribution between groups. The study statistician will create and oversee the randomization sequence. Each CO-OP session will last 45 minutes and participants will complete one session per week over the course of 10 weeks. Participants will complete the same assessment battery that was completed at baseline at post-intervention remotely.
 - a. Cognitive Orientation to daily Occupational Performance (CO-OP). CO-OP is a metacognitive strategy training intervention that will be used in this study. First, five functional, everyday life goals are identified collaboratively by the participant and interventionist. In the second meeting, when CO-OP actually begins, we introduce the approach to the participant and teach the global cognitive strategy (i.e., GOAL-PLAN-DO-CHECK). In all subsequent sessions, this strategy is used as the main problem-solving framework to facilitate skill acquisition. The participant identifies a GOAL, and then is guided by the therapist to discover a PLAN to potentially achieve the goal. The participant is then asked to DO the plan (if feasible during the therapy session otherwise asked to complete at home prior to the next intervention session), and subsequently to CHECK to see if the plan worked, i.e. the goal was achieved. This process is repeated until satisfactory performance is met for each established goal.
 - b. Inactive Control Group: An inactive control group will be used to control for maturation and testing effects. Weekly contact will be made via teleconferencing to (1) maintain study engagement, (2) introduce weekly social contact with researchers, mimicking some of the potential incidental effects of the experimental group, and (3) ascertain what, if any, additional steps participants have taken to reduce PCS symptoms. The content of each of these meetings will be tracked in intervention notes. These weekly contacts have no established time threshold that must be met but are expected to last no longer than 20 minutes. Each contact will be recorded for fidelity monitoring to ensure all active ingredients of the CO-OP intervention are avoided.
2. The study duration is approximately 12 weeks. This includes about 2.5 hours of pre-intervention assessments (Table 1), 10, 45- minute intervention sessions, and about 2 hours of post-intervention assessments.
3. All study procedures are for research purposes only.
- 4.

Table 1. Study Measures

Assessment	Construct	Score Evaluated	Administration Time	Specific Aim
Screening Measures				

STOP-bang	Sleep apnea symptoms	Total score	T1	1,2
Patient Health Questionnaire-9	Depressive symptoms	Total score	T1	1,2
Montreal Cognitive Assessment (MoCA)	Cognition	Total score	T1	1,2
Cognitive Failures Questionnaire (CFQ)	Cognitive abilities in everyday life	Total score	T1,T2	1,2
Primary Outcome Measures				
Feasibility measures	Recruitment rate, retention rate	N/A	T2	1
Acceptability of Intervention Measure (AIM)	Intervention acceptability	Total score	T2	1
Intervention Appropriateness Measure (IAM)	Intervention appropriateness	Total score	T2	1
Feasibility of Intervention Measure (FIM)	Intervention feasibility	Total score	T2	1
Telehealth Usability Questionnaire (TUQ)	Usability of telehealth platform	Total score	T2	1
Canadian Occupational Performance Measure (COPM)	Subjective activity performance	Average score across goals	Week 2,4,6 and 8 and T1, T2	2
Secondary Outcomes*				
PROMIS Cognitive Function	Subjective cognition	T-score	T1, T2	2
Delis-Kaplan Executive Function System (DKEFS) Color-Word Interference	Goal maintenance, inhibition, cognitive flexibility	Total score	T1, T2	2
WHO-QoL 100	Quality of life	Domain scores	T1, T2	2
Cambridge Neuropsychological Test Automated Battery (CANTAB) Rapid Visual Information Processing Subtest	Sustained attention	Total score	T1, T2	2
CANTAB Spatial Working Memory Subtest	Working memory and strategy	Total score	T1, T2	2
CANTAB Stockings of Cambridge Subtest	Planning and executive function	Total score	T1, T2	2
CANTAB Delayed Matching to Sample Subtest	Short-term visual recognition memory and attention	Total score	T1, T2	2
CANTAB Paired Associates Learning Subtest	Visual episodic memory	Total score	T1, T2	2
Additional Data Collected				

Medical record data	Medical history information	N/A	T1	N/A
Demographic data	Description of population	Age, race, gender, education level	T1	1,2
Therapy logs	Description of intervention provided	N/A	Continuously monitored	1, 2
21-Item Word List Performance Validity Test (PVT)	Exaggeration or feigning of memory impairment	Total score	T1	1, 2

VII. Potential Risks

1. There are minimal risks expected when taking part in this study. There are some that we know about and some may not know about yet. Some possible risks include (1) a breach of confidentiality where identifiable health information related to the participants is inadvertently made available to individuals beyond the research team; (2) psychological distress while discussing changes in your abilities due to PCS; or (3) physical injury. Should a participant indicate mental health concerns by (1) an affirmative answer on the Patient Health Questionnaire item "Thoughts that you would be better off dead, or of hurting yourself in some way," or a score of >21 on the PHQ-9, a document with mental health resources will be provided and the participant will be asked to contact either a trusted personal contact or a mental health emergency hotline while still in the Zoom meeting with the assessor.
2. To help lower these possible risks, we will keep participant information in a password protected file on a secure network that has restricted access. All data will be obtained by the study team will be for research purposes only and will be de-identified prior to data entry into our secure electronic database. Any hard copy data will be locked in filing cabinets in the private offices of the PI. All electronic data will be maintained on one web-based, secure, centralized database. The database will use the REDCap® platform and can only be accessed through two password protected portals. All data entered into the REDCap® database will be stored on University of Missouri secure servers and will have access restricted to only members of the research team. In the rare event participants experience psychological distress when answering questions during assessments, they will be reminded that they can decline to answer any questions that may make them uncomfortable and that participation is completely voluntary.
3. The table below provides information on how AEs will be reported in this study (see Table 1). The plan for reporting has been determined based on the severity of the AE and the study attribution of the AE per the definitions and categories previously discussed.

The reporting timeframe meets or exceeds the reporting requirements of the University of Missouri IRB. All AEs will be reported to by the University of Missouri IRB. IRB will review these as they are reported and also annually when the protocol is renewed. All severe adverse events below will also be reported to the sponsoring IC Program Officer within the timeframe listed. The University of Missouri IRB maintains a log of all reported AEs, including all details related to the AE, actions taken, and outcomes, over the course of the study that will be used by the study team for tracking purposes.

Table 1: AE Reporting Plan

Study Attribution	Time for Reporting by type of AE		
	Mild	Moderate	Severe
Unrelated	Not required	Not required	5 days
Definitely Related	5 days	5 days	24 hours
Probably Related	5 days	5 days	24 hours
Possibly Related	5 days	5 days	24 hours

VIII. Anticipated Benefits

1. Participants may or may not directly benefit as a result of participation in the study. Information learned from the study may likely help other people in the future. Participants may potentially experience improvement in their ability to perform everyday life activities better and/or experience less cognitive impairment.

IX. Compensation

1. Participants will be compensated for taking part in this study. For time and effort, participants will receive \$60 via check payment within one month of pre-assessments and post-assessments for a total of \$120. Compensation is provided for completion of the pre-intervention assessment battery and post-intervention assessment battery; therefore, payment will be prorated if a participant withdraws from the study prior to the post-intervention assessment battery (e.g., they would only be compensated for the assessment time points that were actually completed).

X. Data Safety Monitoring Plan

Data Quality and Management

The research coordinator will oversee the review of all data collection forms on an ongoing basis for data completeness and accuracy, as well as protocol compliance. The table below is an overview of the schedule for data review (see Table 2). All data files completed during the specified time period will be reviewed. The study coordinator will assign a rater to review each file who was not the person who collected the data. The reviewer will complete an audit sheet to review the completeness and accuracy of each data file. Data verification will be completed on all outcome data by double data entry. All data will be entered into a separate electronic database. The research coordinator will cross-check the two data files and resolve any discrepancies. The results of the data verification will be reported on the audit form. All audit

forms will be reviewed by the PI and further training of blind raters will occur if consistent errors are noted. Any protocol violations will be reported to the University of Missouri IRB.

Intervention fidelity and protocol adherence will be reviewed by Drs. Boone, Kiselica, and Wolf. The CO-OP Academy has developed a CO-OP Fidelity Checklist that is used to monitor fidelity of the CO-OP intervention. This checklist will be completed by reviewing video recordings of intervention sessions and therapists must maintain an overall score of 80% to be compliant with the intervention. Any items missed on the checklist will be reviewed with the therapist during the next weekly meeting following the audit. Failure to maintain an 80% on any fidelity check will require individual instruction. For every participant, a minimum of two sessions are recorded: (1) one from sessions 2-5; and (2) one from sessions 6-9. Additional sessions may be recorded and reviewed, if therapists are consistently scoring at or below the 80% threshold.

Table 2: Schedule for Data Review

Data type	Frequency of review	Reviewer
Subject accrual (including compliance with protocol enrollment criteria)	Quarterly	Blind rater (confirmation by researcher coordinator and Dr.Boone, PI)
Status of all enrolled participants, as of date of reporting	Quarterly	Blind rater (confirmation by researcher coordinator and Dr. Boone, PI)
Outcome data accuracy (double-data entry)	Quarterly	Blind rater (confirmation by researcher coordinator and Dr. Boone, PI)
Adherence data regarding study visits and intervention	Quarterly	PI
Intervention fidelity	Quarterly	Dr. Wolf, Co-I (with CO-OP Academy)
AEs and rates	Quarterly	PI

Participant Accrual and Compliance

Per Table 2 above, review of the rate of participant accrual and compliance with inclusion/exclusion criteria will occur quarterly during the recruitment phase to ensure that: (1) a sufficient number of participants are being enrolled; (2) participants are meeting eligibility criteria; and (3) the targeted ethnic diversity goals outlined in the grant proposal are being met.

Stopping Rules

This study will be stopped prior to its completion if: (1) the intervention is associated with adverse effects that call into question the safety of the intervention; (2) difficulty in study

recruitment or retention will significantly impact the ability to evaluate the study endpoints;
(3) any new information becomes available during the trial that necessitates stopping the trial; or
(4) other situations occur that might warrant stopping the trial.

Safety Review Plan

Study progress and safety will be reviewed quarterly per above. Annual progress reports, including patient recruitment, retention/attrition, and AEs, will be provided to the University of Missouri IRB. The annual report will include a list and summary of AEs. In addition, the annual report will address (1) whether AE rates are consistent with pre-study assumptions; (2) reason for dropouts from the study; (3) whether all participants met entry criteria; (4) whether continuation of the study is justified on the basis that additional data are needed to accomplish the stated aims of the study; and (5) conditions whereby the study might be terminated prematurely. The annual report will be provided to the sponsoring IC. The IRB and other applicable recipients will review progress of this study on an annual basis.

XI. Multiple Sites

1. N/A

XII. References

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6. Wolf TJ, Polatajko H, Baum C, et al. Combined cognitive-strategy and task-specific training affects cognition and upper-extremity function in subacute stroke: an exploratory randomized controlled trial. *American Journal of Occupational Therapy*. 2016;70(2):7002290010p1-7002290010p10.