Word Retrieval in the Wild: An Ecological Momentary Assessment Pilot Study in People with Post-Stroke Aphasia

This title should include, where possible, information on the participants, condition being evaluated, and intervention(s) studied.

Unique Protocol Identification Number:

National Clinical Trial (NCT) Identified Number: 05338216

Principal Investigator: Erin Meier

Sponsor: Tufts Clinical and Translational Science Institute (CTSI)

"Sponsor" indicates an institution, foundation, or individual who takes responsibility for and initiates a clinical investigation; often times this is the university with which the Principal Investigator is affiliated.

Grant Title: Tufts CTSI NIH Clinical and Translational Science Pilot Stuy Award

Grant Number: UL1 TR002544

Funded by: NCATS

Version Number: v.1.000

15 March 2022

All versions should have a version number and a date. Use an international date format (e.g.,YYYY-MM-DD [2017-12-21] or write out the month (e.g., 21 December 2017).
For the initial submission of a protocol to the IRB, indicate "Not applicable; this is the first version of the protocol." in the table below. For any subsequent amendment being submitted to the IRB, add details of the specific changes that are being implemented in the amendment. Please note that Section 10.4 is a high-level summary of all formal protocol versions/amendments.

Participants may voluntarily withdraw from the study at any time. If a participant withdraws, the study team will obtain the reason(s) for withdraw. If the study term observes several time periods of missed trials, they will address the issue with a participant during the weekly check-in. As feasibility is the cornerstone of this trial, the study team will not discontinue participants for reasons related to protocol adherence. As the exception, if a participant's medical status changes during the study, the study team

Table of Contents

Table of Contents - Please right-click and choose 'Update Field'.

STATEMENT OF COMPLIANCE

Provide a statement that the trial will be conducted in compliance with the protocol, International Council on Harmonisation Good Clinical Practice (ICH GCP) and applicable state, local and federal regulatory requirements. Each engaged institution must have a current Federal-Wide Assurance (FWA) issued by the Office for Human Research Protections (OHRP) and must provide this protocol and the associated informed consent documents and recruitment materials for review and approval by an appropriate Institutional Review Board (IRB) or Ethics Committee (EC) registered with OHRP. Any amendments to the protocol or consent materials must also be approved before implementation. Select one of the two statements below. If the study is an ***intramural*** *NIH study, use the second statement below:*

1. The trial will be carried out in accordance with International Council on Harmonisation Good Clinical Practice (ICH GCP) and the following:

    - United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, 21 CFR Part 312, and/or 21 CFR Part 812).

    National Institutes of Health (NIH)-funded investigators and clinical trial site staff who are responsible for the conduct, management, or oversight of NIH-funded clinical trials have completed Human Subjects Protection and ICH GCP Training.
    OR
2. The trial will be conducted in accordance with International Council on Harmonisation Good Clinical Practice (ICH GCP), applicable United States (US) Code of Federal Regulations (CFR), and the [specify NIH Institute or Center (IC) [Terms and Conditions of Award. The Principal Investigator will assure that no deviation from, or changes to the protocol will take place without prior agreement from the funding agency and documented approval from the Institutional Review Board (IRB), and the Investigational New Drug (IND) or Investigational Device Exemption (IDE) sponsor, if applicable, except where necessary to eliminate an immediate hazard(s) to the trial participants. All personnel involved in the conduct of this study have completed Human Subjects Protection and ICH GCP Training.
    For either option above, the following paragraph would be included:
    The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the IRB for review and approval. Approval of both the protocol and the consent form(s) must be obtained before any participant is consented. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. All changes to the consent form(s) will be IRB approved; a determination will be made regarding whether a new consent needs to be obtained from participants who provided consent, using a previously approved consent form.

INVESTIGATOR'S SIGNATURE

Principal Investigator or Clinical Site Investigator:

Signed:	Erin L. Meier	Date:	3/18/2022
Name*:	Erin Meier		
Title*:	Assistant Professor of Communication Sciences and Disorders		

Investigator Contact Information:

Affiliation*:	Northeastern University
Address:	360 Huntington Avenue, FR228C; Boston, MA 02115
Telephone:	617-373-7438
Email:	e.meier@northeastern.edu

For multi-site studies, the protocol should be signed by the clinical site investigator who is responsible for the day to day study implementation at his/her specific clinical site:

Signed:		Date:	
Name:			
Title:			
Affiliation:			

1 PROTOCOL SUMMARY

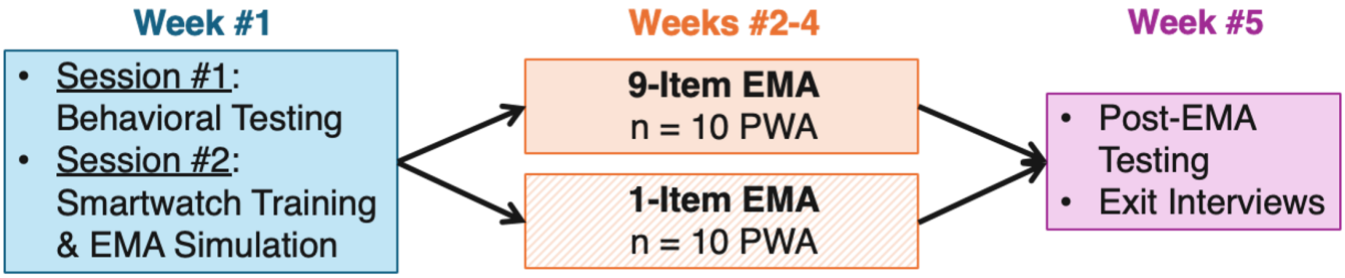
1.1 SYNOPSIS

Title:	Word Retrieval in the Wild: An Ecological Momentary Assessment Pilot Study in People with Post-Stroke Aphasia
Grant Number:	UL1 TR002544
Study Description:	People with post-stroke aphasia (PWA) suffer from anomia, a condition where they know what they want to say but cannot retrieve the words. For PWA, word retrieval changes moment-to-moment, leading to diminished motivation to participate in conversations and disengagement from social interactions. In the real world, anomia variability and severity are compounded by contextual factors of communication exchanges (noise, dual-tasking). Ecological momentary assessment (EMA) involves in-situ measurement of a behavior over time during everyday life. EMA has promise for capturing real-world anomia, yet EMA methods have not been tested in PWA. To target in-situ anomia, PWA will complete 36 picture-naming trials/day for three weeks, delivered either as a single trial 36 times per day (1-item EMA condition) or in four sets of nine trials/set per day (9-item EMA condition). Prior to completing community/home-based EMAs, participants will undergo standardized testing and smart device training. During the EMA period, participants will complete a brief survey about their EMA experiences at the end of each week. Following completion of the EMA protocol, participants will complete one final assessment and exit interview session.
Objectives*:	Primary Objective: To evaluate the feasibility of ecological momentary assessment (EMA) of naming abilities in people with post-stroke aphasia Secondary Objectives: Determine relationships between feasibility metrics and personal factors
Endpoints*:	Primary Endpoint: Compliance and completion over a 3-week EMA protocol Secondary Endpoints: Perceived burden of completing EMAs during the 3-week protocol
Study Population:	Individuals with post-stroke aphasia
Phase* or Stage:	Chronic stroke (at least 6 months after stroke onset)

Description of Sites/Facilities Enrolling Participants:	Participants will be recruited through The Aphasia Network (TAN) Lab at Northeastern University.
Description of Study Intervention/Experimental Manipulation:	Following consent and prior to completing community/home-based EMAs, participants will undergo standardized testing and smart device training. PWA will be pseudorandomly assigned to either the 1-item or 9-item EMA condition, counterbalanced for aphasia severity. Next, PWA will complete the three-week community/home-based EMA protocol. Each day, PWA will be scheduled to attempt naming aloud 36 pictures that appear on the smartwatch, either delivered either as a single trial 36 times per day (1-item EMA condition) or in four sets of nine trials/set per day (9-item EMA condition). During the EMA period, participants will complete a brief survey about their EMA experiences at the end of each week. Following completion of the EMA protocol, participants will complete one final assessment and exit interview session.
Study Duration*:	1 year
Participant Duration:	5-6 weeks

1.2 SCHEMA

Figure 1. Study Design



1.3 SCHEDULE OF ACTIVITIES

Study Phase	Activities

Pre-EMA Testing	Testing: (1) Quick Aphasia Battery (QAB) to measure overall aphasia severity, (2) the Pattern Comparison Processing Speed Test and Flanker Inhibitory Control and Attention Test from the NIH Cognition Toolbox to measure non-linguistic visual attention and executive functions, respectively, (3) brief, standardized picture description and story elicitation tasks to index anomia in discourse, and (4) an overt object naming test to index word retrieval via a standard SLP assessment format (i.e., single administration in a quiet 1:1 interaction). The naming test will include normed real photos17 of the 260 items from the Snodgrass and Vanderwart stimuli set. PWA will also participate in an intake interview and complete a questionnaire about their comfort with technology, adapted for aphasia (simple language, short phrases). Smart device training including: (1) Smartwatch Orientation: PWA will be oriented to the smartwatch (interface, charging, etc.) through simple verbal and written instructions and visual demonstrations. (2) EMA Task Training: PWA will be instructed on the specific EMA naming task, including instructions on how to tap on the screen and the optimal approach for providing verbal responses (i.e., mouth close to the watch). Then, PWA will complete an 18-item traditional EMA-style naming task probe (i.e., several trials back-to-back on the smartwatch) in a quiet room in The Aphasia Network (TAN) Lab at Northeastern University. During this probe, SLP graduate student research assistants (RAs) will provide cueing and feedback so that PWA successfully learn how to operate the smartwatch and respond to prompts. (3) EMA Protocol Simulation: PWA will complete a “real-world” EMA task probe in a distracting environment (i.e., coffee shop or university bookstore on Northeastern’s campus). For this final activity, over a 45-minute period, 18 smartwatch prompts will be given, either randomly interspersed with one naming trial per prompt (for PWA in the 1-item condition) or split into two sets of 9 trials per prompt (for PWA in the 9-item EMA condition). This final activity will mirror the three-week EMA protocol.
EMA Protocol	For three weeks, PWA will name aloud pictures that appear on the smartwatch as they go about their daily activities. At the end of each week, PWA will complete a virtual check-in with the study team at which time they will also complete a brief (16-item) Qualtrics survey about their EMA experiences that week.

Post-EMA Protocol Testing and Exit Interview	In a final session, PWA will complete the overt object naming test in standard SLP format once more. Finally, they will participate in an exit interview about the study.

2 INTRODUCTION

2.1 STUDY RATIONALE

Ecological momentary assessment (EMA) holds promise for providing objective insight into the everyday experiences of patients with a variety of clinical conditions. To date, there is little EMA research that includes stroke survivors with aphasia. Thus, the primary rationale for this study is to evaluate and demonstrate the feasibility of a novel smartwatch-delivered, audio-based EMA of naming protocol in individuals with chronic aphasia. This project is an important first step towards testing the clinical utility of EMA for better understanding everyday communication difficulties and other challenges that PWA face in daily life.

2.2 BACKGROUND

Impaired word retrieval—also known as anomia—is one of the most debilitating symptoms stroke survivors with aphasia, a communication disorder characterized by impaired language, face in their daily lives. Like “tip-of- the-tongue” states experienced by neurotypical individuals, anomic moments in people with aphasia (PWA) occur when an individual knows what they want to say but cannot retrieve the word. Unlike “tip-of-the-tongue,” anomia in PWA pervades communication exchanges and is characterized by inconsistent ability to retrieve a given word across attempts. The severity and unpredictability of anomia lead many PWA to disengage from conversation and social situations, which can severely impact their participation and quality of life. In daily life, anomia can be further compounded by real-world communication contexts such as attempting to communicate in distracting settings (e.g., with background noise and/or other people in the vicinity) or when completing other tasks. In clinical practice, speech-language pathologists (SLPs) typically assess anomia by administering a standardized test once to a patient in a quiet room. This approach captures neither the variability typical of post-stroke anomia nor the realities of real-world communication. In contrast, ecological momentary assessment (EMA) is a method often used in health research to measure physical, mental, or cognitive states in a person’s daily life over several days, weeks or even months. Traditional EMA involves a device prompting a participant to answer a set of questions a few times a day, whereas micro-interaction-based EMA (µEMA) uses single-question, “at-a-glance” prompts that are interspersed over time rather than grouped into sets. Our pilot studies demonstrate that µEMA has higher response rates and lower perceived burden than traditional EMA in neurotypical individuals despite its higher interruption rate. Thus, we propose that EMA—particularly µEMA—is a viable approach to capture real-world anomia in PWAs’ daily lives. Yet, despite the increasing use of technology-based assessments and therapy platforms for PWA, neither EMA nor µEMA methods have been utilized in aphasia.

2.3 RISK/BENEFIT ASSESSMENT

2.3.1 KNOWN POTENTIAL RISKS

There are no known risks of ecological momentary assessment (EMA).

2.3.2 KNOWN POTENTIAL BENEFITS

There are no direct benefits as EMA is an assessment, not treatment method. Some participants may find completing the protocol engaging.

2.3.3 ASSESSMENT OF POTENTIAL RISKS AND BENEFITS

The risks do not outweigh any potential benefits.

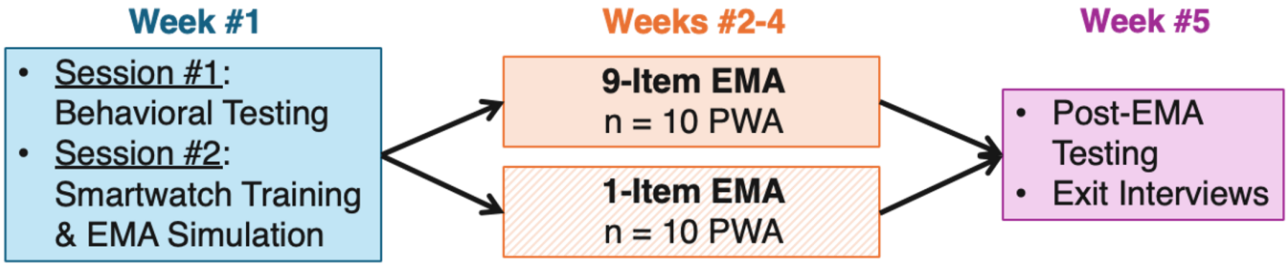
3 OBJECTIVES AND ENDPOINTS

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS	PUTATIVE MECHANISMS OF ACTION
Primary			
Assess EMA compliance in PWA Assess EMA completion in PWA	Compliance will be calculated by dividing the number of answered prompts by the number of *scheduled* prompts Completion will be calculated by dividing the number of answered prompts by the number of *delivered* prompts	This metric is often used in describing feasibility of EMA protocols. Compliance reflects protocol adherence excluding trials missed due to the watch being off/uncharged or a problem with the trial flow.	N/A - not an intervention
Secondary			
Assess speech intelligibility of EMAs	Recorded responses will be tagged as fully intelligible (1) or partially or completely unintelligible (0)	Speech EMA requires intelligible responses to be clinically useful	N/A - not an intervention
Assess perceived burden from EMAs in PWA	Perceived burden will be calculated by averaging Likert ratings from the Qualtrics survey questions regarding perceived burden	Gathering information about participants experiences with a novel protocol is important for establishing its clinical utility	N/A - not an intervention
Tertiary/Exploratory			
Determine relationships between EMA feasibility metrics and personal factors	N/A	No explicit endpoint are applicable for this objective	N/A - not an intervention

4 STUDY DESIGN

4.1 OVERALL DESIGN

Figure 1. Study Design



4.2 SCIENTIFIC RATIONALE FOR STUDY DESIGN

The study design will allow the research team to address the primary objectives of assessing protocol feasibility in multiple ways (compliance, completion, and perceived burden) as well as the secondary objective of exploring personal factors (age, cognitive abilities) that relate to feasibility metrics.

4.3 JUSTIFICATION FOR INTERVENTION

N/A - This study does not involve an intervention.

4.4 END-OF-STUDY DEFINITION

The end-of-study will be at the end of the funding period (i.e., 1 year). This study is a small-scale, observational feasibility trial in which no impact on clinical outcomes is expected.

5 STUDY POPULATION

5.1 INCLUSION CRITERIA

Inclusion criteria include: (1) current/pre-stroke English proficiency, (2) normal/corrected-to-normal vision and hearing, (3) medical stability, (4) history of left hemisphere stroke at least six months prior to enrollment, and (5) presence of aphasia as determined by consideration of scores on language assessments (e.g., Quick Aphasia Battery, discourse tasks) and the study team's clinical judgment.

5.2 EXCLUSION CRITERIA

The exclusion criterion will be a history of neurological disease affecting the brain besides stroke.

5.3 LIFESTYLE CONSIDERATIONS

PWA with severe aphasia who do not have a care partner to assist with study logistics (e.g., charging smartwatches, scheduling appointments) may have more difficulty participating, but they will not be precluded from participating. PWA who have severe hemiplegia or hemiparesis may also have more difficulty participating, but accommodations (e.g., use of stretch wristbands to ease donning the watch) will be employed.

5.4 SCREEN FAILURES

Participants who do not test as aphasic on standardized testing or who do not endorse language challenges consistent with aphasia will be ineligible to participate.

5.5 STRATEGIES FOR RECRUITMENT AND RETENTION

Dr. Meier has a strong foothold in the Boston aphasia research community due to her time at Boston University as a PhD student and has several existing and developing collaborations at area institutions that will offer ample opportunities for recruitment for this study. Although the final sample for this pilot study is small, a multipronged approach will be implemented to ensure recruitment goals are met.

Specifically, recruitment at the following sites and via the following methods will be launched in parallel at the beginning of the project and will continue until the project's end and/or until recruitment goals are achieved:

Northeastern University Speech, Language, and Hearing Center (SLHC): The Northeastern University SLHC provides clinical SLP and audiology services to individuals across the lifespan with communication disorders. Led by Professor Elizabeth Martin, the Aphasia Workshop is a new program offered through the SLHC in which PWA complete a one-time assessment of speech and language skills. Each academic semester, up to five PWA participate in this program. Prof. Martin has agreed to share study flyers with new participants each semester and to email previous Aphasia Workshop attendees. Prof. Martin is also the coordinator of adult SLP practicum placements for graduate students in the Communication Sciences and Disorders Department at Northeastern and has contacts with several SLPs working in the greater Boston area. Prof. Martin has agreed to email area SLPs with information about TAN Lab and the proposed study.

Boston University (BU) Aphasia Research Laboratory: Directed by Dr. Swathi Kiran, the BU Aphasia Research Lab maintains a database of nearly 300 PWA. Dr. Kiran has agreed to share study flyers with the many PWA currently active in her research lab and allow TAN Lab study team members to speak directly to interested PWA following their sessions at the BU Aphasia Research Lab. The BU Aphasia Lab manager will also follow up with PWA who agreed to be contacted for future research opportunities and will provide interested PWA the contact information for TAN Lab.

Other Recruitment Methods: We will recruit stroke survivors via flyers placed at local hospitals, senior centers, and clinics that serve individuals with neurogenic disorders. We will also develop and implement a pipeline for recruiting stroke survivors through Tufts Medical Center that will be initiated following a meeting with the Tufts Recruitment and Retention Team. Finally, we will present at the Boston University Aphasia Community Group in April 2022 (established via personal communication between Dr. Meier and Dr. Elizabeth Hoover, the clinical director of the BU Aphasia Resource Center). The Aphasia Community Group is held one Saturday per month and regularly welcomes up to 100 PWA and their family/friends.

When possible, TAN Lab study team members will take advantage of "the clinical moment" that occurs with face-to-face interactions with patients at community engagement events and via one-on-one clinical research encounters. The goal of these interactions will not solely be to inform potential participants of the present study but to engage PWA in the research process, convey the larger goals of TAN Lab, and describe our work towards maximizing outcomes for PWA. Dr. Meier and TAN Lab SLP graduate student RAs will utilize their clinical aphasia expertise and collaborate with the Tufts CTSI Recruitment and Retention Team to develop effective externally facing materials for engaging potential participants. Written recruitment materials and in-person communications will incorporate aphasia-friendly language (simple language, short phrases) and multimodal auditory-visual strategies to aid comprehension for PWA with severe language deficits. Working with the Tufts CTSI Recruitment and

Retention Team, we will also develop and implement strategies to ensure recruitment of participants of color. One strategy will be to maximize engagement with Hispanic/Latinx and Asian PWA involved in an active clinical trial conducted by the BU Aphasia Research Lab on bilingual aphasia recovery. Given our multipronged approach, the large pool of potential participants, and expected high interest in the study, we anticipate having a waitlist of potential participants. Thus, a second approach will be to prioritize participation of PWA of color on the waitlist to ensure their necessary inclusion in this study. All efforts will be made to maximize retention of enrolled participants. We will do so by: (1) careful screening of potential participants in which we explain in detail the procedures (e.g., protocols, time commitment) and provide time and opportunity for addressing the questions/concerns of participants and/or care providers, (2) providing flexible scheduling options and assistance with arranging transportation as needed, and (3) weekly contacts in weeks 2-4 during the EMA/µEMA protocols with PWA and/or their care providers.

6 STUDY INTERVENTION(S) OR EXPERIMENTAL MANIPULATION(S)

6.1 STUDY INTERVENTION(S) OR EXPERIMENTAL MANIPULATION(S) ADMINISTRATION

6.1.1 STUDY INTERVENTION OR EXPERIMENTAL MANIPULATION DESCRIPTION

Participants will be pseudo-randomly assigned to either the 1-item EMA condition (n = 10) or 9-item EMA condition (n = 10). For every prompt, the smartwatch will vibrate to alert the participant to a prompt to complete either a single picture naming trial (in the 1-item condition) or a set of picture naming trials (in the 9-item EMA condition). Participants in both conditions will be scheduled to complete 36 overt picture naming trials per day for three weeks. The only difference between conditions will be the trial delivery schedule: PWA in the 1-item condition will complete a single naming trial at a time, 36 times per day whereas PWA in the 9-item EMA condition will receive four prompts per day to complete a set of nine picture naming trials per prompt. The twofold rationale for comparing 1-item and 9-item EMA conditions is that we will be able to ensure the results reflect the viability of either delivery schedule specifically and not just the novelty of smartwatch use, and this approach will provide preliminary data regarding which method works best for which PWA.

6.1.2 ADMINISTRATION AND/OR DOSING

In each condition, the smartwatch will vibrate to alert PWA to a single naming trial (1-item condition) or naming trial set (9-item EMA condition). After the vibration alert, PWA will see a screen that says “Ready to name a picture?” (1-item condition) or “Ready to name some pictures?” (9-item EMA condition). If the participant taps YES, a picture will appear, and the device will begin recording audio. PWA will have up to five seconds to provide an oral response, after which a “Thanks!” screen will appear. The five-second response window was selected based on research showing that PWA correctly name pictures within 3.5 seconds, on average, with longer response latencies for incorrect responses. If a participant fails to respond to a vibration prompt or pushes the NO button to the “Ready?” screen, they will be re-prompted five minutes later via one more vibration alert. During the three-week EMA protocol, each participant will attempt to name 108 unique objects derived from the 260-item Snodgrass and Vanderwart photoset. The subset of pictures presented to each participant will be based on their naming evaluation (during week 1, session 1). When possible, half of the pictures will be items the PWA named correctly during the evaluation, and the other half will be incorrectly named pictures. This approach will allow us to gauge naming variability over time of items PWA are able versus unable to name during traditional SLP assessment, providing an important window into anomia. To mitigate practice effects, the individual pictures (1-item condition) or picture sets (9-item EMA condition) will be presented randomly without replacement until all 108 pictures have been presented, and then the picture cycle will restart. In both conditions, 36 naming trials will be scheduled per day, resulting in a total of 756 scheduled trials for each participant across the experiment. In the 1-item EMA condition, single-naming trial prompts will appear at random intervals from 10am to 8pm. In the 9-item EMA condition, PWA will receive four prompts per day to complete a set of nine picture naming trials per prompt; one prompt will be scheduled in every 2.5-hour block between 10am and 8pm.

6.2 FIDELITY

6.2.1 INTERVENTIONIST TRAINING AND TRACKING

N/A - There is no intervention as part of this trial. Data used to calculate compliance, completion, and perceived burden will be automatically digitally recorded. Speech intelligibility ratings will be completed for all samples by one rater, and 20% of samples will be assessed by a second rater.

6.3 MEASURES TO MINIMIZE BIAS: RANDOMIZATION AND BLINDING

PWA will be pseudo-randomly assigned to either the 1-item or 9-item EMA condition. This quasi-randomization will be done to ensure the conditions are balanced for overall aphasia severity. No blinding will be performed.

6.4 STUDY INTERVENTION/EXPERIMENTAL MANIPULATION ADHERENCE

N/A - This study does not involve intervention.

6.5 CONCOMITANT THERAPY

6.5.1 RESCUE THERAPY

Participants are allowed to continue any therapy (including speech-language therapy) that they are receiving at the time of the study. Because this trial involves no intervention, concomitant therapy will not impact the trial results. The study team will not dispense rescue therapy.

7 STUDY INTERVENTION/EXPERIMENTAL MANIPULATION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1 DISCONTINUATION OF STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

If the study term observes several time periods of missed trials, they will address the issue with a participant during the weekly check-in. As feasibility is the cornerstone of this trial, the study team will not discontinue participants for reasons related to protocol adherence.

7.2 PARTICIPANT DISCONTINUATION/WITHDRAWAL FROM THE STUDY

Participants are free to withdraw from participation in the study at any time upon request. If a participant withdraws, the study team will obtain the reason(s) for withdraw. An investigator may discontinue a participant from the study for the following reasons: (1) Lost-to-follow up; unable to contact subject (see Section 7.3, Lost to Follow-Up), and (2) any event or medical condition or situation occurs such that continued collection of study data would not be in the best interest of the participant or might require an additional EMA period that would confound the interpretation of the study.

7.3 LOST TO FOLLOW-UP

A participant will be considered lost to follow-up if they fail to return for three scheduled check-ins or sessions and study staff are unable to contact the participant after at least 3 attempts. The following actions will be taken if a participant fails to return to the lab for a required study visit:

- The site will attempt to contact the participant, reschedule the missed visit or check-in, counsel the participant on the importance of maintaining the assigned visit schedule, and ascertain if the participant wishes to and/or should continue in the study
- Before a participant is deemed lost to follow-up, the investigator or designee will make every effort to regain contact with the participant (where possible, 3 telephone calls and/or emails). These contact attempts will be documented in the participant's study file.
- Should the participant continue to be unreachable, they will be considered to have withdrawn from the study with a primary reason of lost to follow-up.

8 STUDY ASSESSMENTS AND PROCEDURES

8.1 ENDPOINT AND OTHER NON-SAFETY ASSESSMENTS

Endpoint Assessments: Feasibility will be classified in three ways: (1) PWAs' adherence to the smartwatch µEMA or EMA protocol via compliance and completion, (2) PWAs' perceived burden of completing the EMA protocol, and (3) speech intelligibility of recorded naming attempts. Currently, PWAs' capacity for adhering to a smartwatch EMA protocol via button press responses or verbal responses is unknown. As such, compliance will be based on the number of YES button responses to the "Ready?" screen whereas completion will be based on naming attempts. Specifically, similar to Intille et al. (2016), compliance will be determined by the number of YES responses over scheduled trials, including trials missed due to the watch being off/uncharged. Completion will be calculated as trials with captured audio (reflecting attempted naming) over delivered trials, excluding trials missed to the watch being off/uncharged. Perceived burden will be measured via responses to the weekly surveys during weeks 2-4. Finally, speech intelligibility will be measured by a categorical rating of responses captured in each audio clip (i.e., completely intelligible, partially intelligible, or completely unintelligible).

Other Non-Safety Assessments: Before the EMA period, PWA will be administered the following testing battery. The Quick Aphasia Battery (QAB) will be used as our eligibility assessment and to measure overall aphasia severity. The Pattern Comparison Processing Speed Test and Flanker Inhibitory Control and Attention Test from the NIH Cognition Toolbox will be used to measure non-linguistic visual attention and executive functions, respectively. We will use brief, standardized picture description and story elicitation tasks from the AphasiaBank protocol to index anomia in discourse. Participants will complete an overt object naming test twice before EMA and once after EMA so that the research team can evaluate word retrieval via the standard SLP assessment format (i.e., single administration in a quiet 1:1 interaction). This picture naming probe will include normed real photos of the 260 items from the Snodgrass and Vanderwart stimuli set. Before EMA, PWA will also participate in an intake interview and complete a questionnaire about their comfort with technology, adapted for aphasia (simple language, short phrases).

8.2 SAFETY ASSESSMENTS

No safety assessment were administered.

8.3 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

8.3.1 DEFINITION OF ADVERSE EVENTS

An adverse event is defined as any untoward medical occurrence associated with the use of the EMA system.

8.3.2 DEFINITION OF SERIOUS ADVERSE EVENTS

A serious adverse event is defined as any untoward medical occurrence in a clinical trial participant that meets at least one of the following criteria: death, life-threatening injury, results in hospitalization and/or permanent injury.

8.3.3 CLASSIFICATION OF AN ADVERSE EVENT

Please see below.

8.3.3.1 SEVERITY OF EVENT

For adverse events (AEs) not included in the protocol defined grading system, the following guidelines will be used to describe severity.
(1) Mild: Events require minimal or no treatment and do not interfere with the participants' daily activities.
(2) Moderate: Events result in a low level of inconvenience or concern with the EMA measures. Moderate events may cause some interference with functioning.
(3) Severe: Events interrupt a participant's usual daily activity and may require treatment. Severe events are potentially life-threatening or incapacitating.

8.3.3.2 RELATIONSHIP TO STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

All adverse events (AEs) will have their relationship to study procedures, including EMAs, assessed by an appropriately-trained lab member based on temporal relationship and their judgment. The degree of certainty about causality will be graded using the categories below.
- Related: The AE is known to occur with the study procedures, there is a reasonable possibility that the study procedures caused the AE, or there is a temporal relationship between the study procedures and the event. Reasonable possibility means that there is evidence to suggest a causal relationship between the study procedures and the AE.
-Not Related: There is not a reasonable possibility that the study procedures caused the event, there is no temporal relationship between the study procedures and event onset, or an alternate etiology has been established.

8.3.3.3 EXPECTEDNESS

A trained lab member with appropriate expertise in will be responsible for determining whether an adverse event (AE) is expected or unexpected. An AE will be considered unexpected if the nature,

severity, or frequency of the event is not consistent with the risk information previously described for the study procedures.

8.3.4 TIME PERIOD AND FREQUENCY FOR EVENT ASSESSMENT AND FOLLOW-UP

The occurrence of an adverse event (AE) or serious adverse event (SAE) may come to the attention of study personnel during study visits and interviews of a study participant. All AEs, not otherwise precluded per the protocol, will be captured on the appropriate case report form (CRF). Information to be collected includes event description, time of onset, study team member's assessment of severity, relationship to study procedures (assessed only by those with the training and authority to make a diagnosis), and time of resolution/stabilization of the event. All AEs occurring while on study will be documented appropriately regardless of relationship. All AEs will be followed to adequate resolution.

Any medical or psychiatric condition that is present at the time that the participant is screened will be considered as baseline and not reported as an AE. However, if the study participant's condition deteriorates at any time during the study, it will be recorded as an AE. Changes in the severity of an AE will be documented to allow an assessment of the duration of the event at each level of severity to be performed. Documentation of onset and duration of each episode will be maintained for AEs characterized as intermittent.

PI Meier will record events with start dates occurring any time after informed consent is obtained until 7 (for non-serious AEs) or 30 days (for SAEs) after the last day of study participation.At each study visit, the investigator will inquire about the occurrence of AE/SAEs since the last visit. Events will be followed for outcome information until resolution or stabilization.

8.3.5 ADVERSE EVENT REPORTING

In consultation with the PI, a trained member of the study team will be responsible for conducting an evaluation of a serious adverse event and will report the results of such evaluation to the Tufts CTSI program director, NCATS, and the reviewing Institutional Review Board (IRB) as soon as possible, but in no event later than 7 working days after the investigator first learns of the event.

8.3.6 SERIOUS ADVERSE EVENT REPORTING

PI Meier will record events with start dates occurring any time after informed consent is obtained until 7 (for non-serious AEs) or 30 days (for SAEs) after the last day of study participation.At each study visit, the investigator will inquire about the occurrence of AE/SAEs since the last visit. Events will be followed for outcome information until resolution or stabilization.

8.3.7 REPORTING EVENTS TO PARTICIPANTS

Participants will be informed of any significant adverse events (AEs) or serious adverse events (SAEs) that may impact their safety or participation in the study. If an AE occurs, study staff will assess the

severity, provide appropriate medical guidance, and, if necessary, refer the participant for further medical care. Serious adverse events will be reported to the study's principal investigator, institutional review board (IRB), and relevant regulatory authorities in accordance with established guidelines. Participants will be notified of any changes to study procedures or risks based on reported events. Contact information for reporting concerns or symptoms is provided in the informed consent document.

8.3.8 EVENTS OF SPECIAL INTEREST

N/A

8.3.9 REPORTING OF PREGNANCY

N/A

8.4 UNANTICIPATED PROBLEMS

8.4.1 DEFINITION OF UNANTICIPATED PROBLEMS

This protocol uses the definition of Unanticipated Problems as defined by the Office for Human Research Protections (OHRP). OHRP considers unanticipated problems involving risks to participants or others to include, in general, any incident, experience, or outcome that meets all of the following criteria:

- Unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, such as the Institutional Review Board (IRB)-approved research protocol and informed consent document; and (b) the characteristics of the participant population being studied;
- Related or possibly related to participation in the research ("possibly related" means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

8.4.2 UNANTICIPATED PROBLEMS REPORTING

The investigator will report unanticipated problems (UPs) to the reviewing Institutional Review Board (IRB) and to the principal investigators (PIs). The UP report will include the following information:

- Protocol identifying information: protocol title and number, PI's name, and the IRB project number
- A detailed description of the event, incident, experience, or outcome

- An explanation of the basis for determining that the event, incident, experience, or outcome represents an UP

- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the UP.

To satisfy the requirement for prompt reporting, UPs will be reported using the following timeline: UPs that are serious adverse events (SAEs) will be reported to the IRB and to the DCC/study sponsor/funding agency within [insert timeline in accordance with policy] of the investigator becoming aware of the event. Any other UP will be reported to the IRB and to the study sponsor within 10 days of the investigator becoming aware of the problem. All UPs will be reported to appropriate institutional officials (as required by an institution's written reporting procedures), the supporting agency head (or designee), and the Office for Human Research Protections (OHRP) within 30 days of the IRB's receipt of the report of the problem from the investigator.

8.4.3 REPORTING UNANTICIPATED PROBLEMS TO PARTICIPANTS

If participant notification is required, the research team will develop a clear, participant-friendly communication that provides a description of the issue, outlines any potential risks, and explains how it may impact participants. The communication will avoid unnecessary alarm while ensuring transparency. Additionally, participants will be informed of any changes to study procedures or additional precautions being implemented to ensure their safety. The notification will also include contact information for participants to reach the study team if they have questions or concerns. Before distribution, the IRB will review and approve the communication to ensure clarity, accuracy, and compliance with ethical guidelines. Participants will be informed through the most appropriate method based on the urgency and nature of the issue. Urgent matters affecting participant safety will be communicated via phone calls to ensure immediate awareness and response. Non-urgent updates, including general study-related changes, will be conveyed through email or mailed letters. In cases where participants are scheduled for in-person study visits, the research team may provide information and discuss concerns during these visits. Regardless of the method used, all communications will be documented in study records to ensure accountability and compliance with study protocols.

9 STATISTICAL CONSIDERATIONS

9.1 STATISTICAL HYPOTHESES

- Primary Efficacy Endpoint(s): Compliance and completion will be significantly higher for participants who complete the 1-item EMA condition versus participants who complete the 9-item EMA condition.
- Secondary Efficacy Endpoint(s): Speech intelligibility will be over 80% across trials. Perceived burden will not significantly differ between participants who complete the 1-item versus 9-item EMA conditions.

9.2 SAMPLE SIZE DETERMINATION

For the Aim #1 logistic mixed effects models, two groups of 10 PWA per group will achieve 80% power to detect an odds ratio of 1.20 in a design of 756 repeated measures with a AR(1) covariance structure and when the correlation between observations of the same subject is 0.600 and alpha is 0.05. If the proportion of completed trials for the EMA group is 0.500, a statistically significant result will occur if the µEMA group proportion is 0.545 or greater. In Intille et al.4, the mean difference in proportions between the µEMA and EMA conditions was >0.20 for compliance and completion, which is much higher than the needed 0.045 difference. This suggests we will have ample power to detect significant differences between the two conditions.

9.3 POPULATIONS FOR ANALYSES

Participants with post-stroke aphasia

9.4 STATISTICAL ANALYSES

9.4.1 GENERAL APPROACH

Please see specific information below.

9.4.2 ANALYSIS OF THE PRIMARY ENDPOINT(S)

We will code each trial in the EMA time series to index compliance, completion, and speech intelligibility. Every scheduled trial (n = 756 total trials) will be coded as 0 for a nonresponse/ NO button

response or 1 for a YES button response, reflecting compliance. Every delivered trial with a naming attempt captured on audio (n trials will vary by person) will be coded as 0 for incomplete or 1 for complete, reflecting completion. For each of these measures, we will run a logistic mixed effects model with one of the feasibility measures (i.e., compliance, completion) as the dependent variable, condition (1-item vs. 9-item) as the independent variable, and random effects of participant and trial.

9.4.3 ANALYSIS OF THE SECONDARY ENDPOINT(S)

Every audio clip (n trials will vary by person, depending on the number of naming attempts) will be coded as 0 for completely or partially unintelligible and 1 for completely intelligible, reflecting speech intelligibility. We will run a logistic mixed effects model with intelligibility as the dependent variable, condition (1-item vs. 9-item) as the independent variable, and random effects of participant and trial. For perceived burden, we will collect responses on three questions/survey for three weeks. Given the small amount of data, survey responses will be plotted to visualize trends in increasing/decreasing burden rather than compared statistically. We will statistically compared averaged burden ratings between participants in the 1-item vs. 9-item condition using t-tests or Wilcoxon rank sum tests (depending on the distribution of the data).

9.4.4 SAFETY ANALYSES

N/A

9.4.5 BASELINE DESCRIPTIVE STATISTICS

Descriptive statistics will include demographics (age, sex, race, ethnicity, and handedness) as well as baseline behavioral testing results, including overall aphasia severity (per the Quick Aphasia Battery), non-linguistic cognitive skills (per the NIH-Toolbox tasks), confrontation naming ability (per the Boston Naming Test and the Snodgrass & Vanderwart probe), and comfort with technology survey data.

9.4.6 PLANNED INTERIM ANALYSES

N/A

9.4.7 SUB-GROUP ANALYSES

No sub-group analyses based on demographics will be performed based on the small sample size for this feasibility study. Instead we will conduct exploratory analyses (see 9.4.9) regarding relationships between personal factors and EMA feasibility metrics.

9.4.8 TABULATION OF INDIVIDUAL PARTICIPANT DATA

Individual participant data will be listed by measure.

9.4.9 EXPLORATORY ANALYSES

We will conduct a series of partial correlations between patient-specific factors and feasibility measures (compliance, completion, speech intelligibility, and perceived burden), controlling for study condition. Patient-specific factors will include age, aphasia severity (derived from the QAB), non-linguistic cognitive skills (averaged performance on the two NIH Toolbox tasks), and a summary score derived from the

comfort with technology survey. Here, compliance will be the proportion of YES button responses divided by total scheduled trials (YESbutton/756) for each participant. Completion will be the proportion of naming attempts divided by total delivered trials (n naming attempts/n trials delivered). Speech intelligibility will be the proportion of completely intelligible responses divided by the total number of naming attempts (n completely intelligible trials/n naming attempts). Perceived burden will be calculated as the sum of all burden question Likert responses. Multiple comparison correction will be done at a false discovery rate of $p < 0.05$.

10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

10.1.1 INFORMED CONSENT PROCESS

Please see below

10.1.1.1 CONSENT/ASSENT AND OTHER INFORMATIONAL DOCUMENTS PROVIDED TO PARTICIPANTS

Consent forms describing in detail the study intervention, study procedures, and risks are given to the participant and written documentation of informed consent is required prior to starting intervention/administering study intervention.

10.1.1.2 CONSENT PROCEDURES AND DOCUMENTATION

Interested potential participants or family members/caregivers of PWA who contact The Aphasia Network (TAN) Lab will be contacted by PI Meier or a trained research assistant via phone or email, and an initial meeting will be scheduled in person at TAN Lab or in the comfort of the participant's home. During the initial meeting, study personnel will provide details about the study, answer questions, and complete a brief demographic and medical history intake. If the potential participant is interested in enrolling in the study, lab personnel (PI Meier or a trained TAN Lab research assistant) will explain study procedures and answer participant and caregiver questions. During the informed consent process, potential participants will be shown the EMA equipment (either through photographs or the physical apparatus). Additional measures will be taken to obtain informed consent from individuals with impairment language comprehension due to stroke. Individuals with post-stroke aphasia may have difficulty understanding spoken and/or written language due to their aphasia. To ensure these participants understand study protocols, lab personnel (PI Meier or a TAN Lab research assistant trained to communicate with people with aphasia) will supplement the standard consent form text with simpler spoken and/or written language and provide pictures or videos (of e.g., the smart watch) as needed. Supplemental spoken and/or written language will include key words/phrases from the provided materials but reframed or highlighted to maximize the understanding of study procedures by participants with aphasia. At the end of this process for both the longitudinal study and focus group, potential participants with aphasia will be asked a series of simple questions regarding basic study/group procedures to check their comprehension. If a participant fails the comprehension check (i.e., answers any question incorrectly), information pertaining to the incorrectly answered item(s) will be reviewed and another comprehension check will be done. For individuals with aphasia who are not capable of providing consent, informed written consent will be obtained from a legally authorized representative (e.g., family member, caregiver). Verbal or nonverbal assent will be obtained and reaffirmed throughout the study procedures. If participants exhibit discomfort, fatigue, or verbal or nonverbal signs of distress, breaks will be provided, and study procedures will be terminated early if

necessary. Potential participants will be allowed as much time as they require to consider study protocols and decide whether they wish to participate in the study. Then, informed written consent will be obtained.

10.1.2 STUDY DISCONTINUATION AND CLOSURE

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to study participants and funding agency. If the study is prematurely terminated or suspended, the Principal Investigator (PI) will promptly inform study participants, the IRB, and sponsor and will provide the reason(s) for the termination or suspension. Study participants will be contacted, as applicable, and be informed of changes to study visit schedule. Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants
- Insufficient compliance of study staff to the protocol (i.e., significant protocol violations)
- Data that are not sufficiently complete and/or evaluable
- Determination that the primary endpoint has been met

The study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the funding agency, sponsor, and IRB.

10.1.3 CONFIDENTIALITY AND PRIVACY

Confidentiality will be maintained throughout all data collection and data management procedures. Each participant will be assigned a unique alphanumeric code that will be used on paper documents, electronic databases, other digital data, and in conversations between study team members. Hard copies of paper documents containing identifying information (e.g., case history forms) will be stored in a locked cabinet within The Aphasia Network (TAN) laboratory (PI Meier). EMA data that inherently contain some identifying information (e.g., naming attempts in audio files) will be stored on a password-protected server. Only co-PIs Meier and Intille and approved, trained research assistants and co-investigators will have access to participant data. Participants' demographic (e.g., age, sex, education) and diagnostic information will be used only to describe group characteristics of study participants. Identifying information will be removed before compiling summary data. If during any study sessions that are conducted in a participant's home, the researchers observe specific acts of abuse or harm, the study team will bring this to the attention of the Principal Investigator overseeing this research and the Northeastern University Institutional Review Board who may take appropriate next steps.

10.1.4 FUTURE USE OF STORED SPECIMENS AND DATA

Electronic data, including EMA data and audio samples, will be kept indefinitely for use in future studies in TAN Lab.

10.1.5 KEY ROLES AND STUDY GOVERNANCE

Principal Investigator	**Medical Monitor or Independent Safety Monitor**
Erin Meier	
Stephen Intille	

10.1.6 SAFETY OVERSIGHT

A Data and Safety Monitoring Board (DSMB) is not warranted and therefore will not be used in this trial.

10.1.7 CLINICAL MONITORING

N/A

10.1.8 QUALITY ASSURANCE AND QUALITY CONTROL

Quality control (QC) procedures will be implemented as follows:

- Informed consent - Study staff will review both the documentation of the consenting process as well as a percentage of the completed consent documents. This review will evaluate compliance with GCP, accuracy, and completeness. Feedback will be provided to the study team to ensure proper consenting procedures are followed.
- Source documents and the electronic data - Data will be initially captured on source documents (see Section 10.1.9, Data Handling and Record Keeping) and will ultimately be entered into the study database. To ensure accuracy site staff will compare a representative sample of source data against the database, targeting key data points in that review.
- Protocol Deviations - The study team will review protocol deviations on an ongoing basis and will implement corrective actions when the quantity or nature of deviations are deemed to be at a level of concern.

Should independent monitoring become necessary, the PI will provide direct access to all trial related sites, source data/documents, and reports for the purpose of monitoring and auditing by the sponsor/funding agency, and inspection by local and regulatory authorities.

10.1.9 DATA HANDLING AND RECORD KEEPING

10.1.9.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

Data on the phones will be stored in the protected application space of the device and pushed to the study team's server over the course of the EMA/µEMA protocol for each participant. During the study, data will be periodically uploaded to a secure research server, and periodically backed up from the server onto an external hard drive that is password protected. Only the researchers will have access to the data. Raw electronic data files will be stored on a secure, password-protected server. A REDCap (Research Electronic Data Capture) database will be maintained that will contain participant data, including identifying information. REDCap is a free, secure, web-based application hosted by Tufts Clinical and Translational Science (CTSI). CTSI has all the necessary physical and operational security in place to meet or exceed federal and state security and privacy regulations for data transmissions and storage using REDCap. De-identified audio samples and behavioral and lexical access data may be shared for use in research studies at other sites. De-identified audio samples and behavioral and lexical access data may be used in teaching and academic presentations with participant approval (please see the consent forms). Videos, photographs, and identifying information about participants will not be shared with other research sites nor in academic presentations unless the participant provides separate explicit permission. Hard copies of forms containing identifying information and signed consent documents will be kept for 7 years and stored in a locked filing cabinet in TAN Lab. After that time, identifying documents will be destroyed (i.e., shredded).

10.1.9.2 STUDY RECORDS RETENTION

Once the study is complete, all final data will be removed from the phone to ensure maximum safety of data storage. The smart watch devices will be wiped clean of any information at the end of the study when the participants turn them back in to the researchers.

10.1.10 PROTOCOL DEVIATIONS

This protocol defines a protocol deviation as any noncompliance with the clinical trial protocol, International Council on Harmonisation Good Clinical Practice (ICH GCP). The noncompliance may be either on the part of the participant, the investigator, or the study site staff. As a result of deviations, corrective actions will be developed by the site and implemented promptly. Protocol deviations will be handled in accordance with the following GCP guidelines:

- Section 4.5 Compliance with Protocol, subsections 4.5.1, 4.5.2, and 4.5.3
- Section 5.1 Quality Assurance and Quality Control, subsection 5.1.1
- Section 5.20 Noncompliance, subsections 5.20.1, and 5.20.2.

It will be the responsibility of the site investigator to use continuous vigilance to identify and report deviations within 30 working days of identification of the protocol deviation, or within 10 working days of the scheduled protocol-required activity. Protocol deviations must be sent to the reviewing IRB per

their policies. The site investigator is responsible for knowing and adhering to the reviewing IRB requirements.

10.1.11 PUBLICATION AND DATA SHARING POLICY

This study will comply with the NIH Data Sharing Policy and Policy on the Dissemination of NIH-Funded Clinical Trial Information and the Clinical Trials Registration and Results Information Submission rule. As such, this trial will be registered at ClinicalTrials.gov, and results information from this trial will be submitted to ClinicalTrials.gov. In addition, every attempt will be made to publish results in peer-reviewed journals. Data from this study may be requested from other researchers 5 years after the completion of the primary endpoint by contacting PI Meier.

10.1.12 CONFLICT OF INTEREST POLICY

Any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the design and conduct of this trial. The study leadership in conjunction with the NCATS has established policies and procedures for all study group members to disclose all conflicts of interest and will establish a mechanism for the management of all reported dualities of interest.

10.2 ADDITIONAL CONSIDERATIONS

N/A

10.3 ABBREVIATIONS AND SPECIAL TERMS

AE	Adverse Event
ANCOVA	Analysis of Covariance
CFR	Code of Federal Regulations
CLIA	Clinical Laboratory Improvement Amendments
CMP	Clinical Monitoring Plan
COC	Certificate of Confidentiality
CONSORT	Consolidated Standards of Reporting Trials
CRF	Case Report Form
DCC	Data Coordinating Center
DHHS	Department of Health and Human Services

DSMB	Data Safety Monitoring Board
DRE	Disease-Related Event
EC	Ethics Committee
EMA	Ecological Momentary Assessment
eCRF	Electronic Case Report Forms
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Amendments Act of 2007
FFR	Federal Financial Report
GCP	Good Clinical Practice
GLP	Good Laboratory Practices
GMP	Good Manufacturing Practices
GWAS	Genome-Wide Association Studies
HIPAA	Health Insurance Portability and Accountability Act
IB	Investigator's Brochure
ICH	International Council on Harmonisation
ICMJE	International Committee of Medical Journal Editors
IDE	Investigational Device Exemption
IND	Investigational New Drug Application
IRB	Institutional Review Board
ISM	Independent Safety Monitor
ITT	Intention-To-Treat
LSMEANS	Least-squares Means
MedDRA	Medical Dictionary for Regulatory Activities
MOP	Manual of Procedures
NCT	National Clinical Trial
NIH	National Institutes of Health
NIH IC	NIH Institute or Center
OHRP	Office for Human Research Protections
PI	Principal Investigator
QA	Quality Assurance
QC	Quality Control
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SMC	Safety Monitoring Committee
SOA	Schedule of Activities
SOC	System Organ Class
SOP	Standard Operating Procedure
UP	Unanticipated Problem
US	United States

10.4 PROTOCOL AMENDMENT HISTORY

Version	Date	Description of Change	Brief Rationale
N/A			

11 REFERENCES