CAMCI: Advancing the Use of Computerized Screening in Healthcare

Clinical Trial: NCT03512301

Secondary ID: NIH: 2SB1AG037357-04A1

DATE: Approved by IRB – September 13, 2018
Uploaded to clinicaltrials.gov - February 14, 2025

Experimental Protocol

CAMCI: Advancing the Use of Computerized Screening in Healthcare (Phase II Renewal)

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1.0 Objective and Specific Aims

The purpose of this NIH funded grant opportunity is to address the issues necessary to move cognitive screening technologies developed and validated by PST from successful research endeavors to clinical tools effective in common practice. The project includes the specific aims indicated below. Participation of human subjects occurs during Specific Aims 3-5 only.

Specific Aim #1. *Obtain confirmation of acceptable regulatory plan from the FDA*

Specific Aim #2. *Develop intellectual property strategy to capitalize on and maximize the value of IP*

Specific Aim #3. *Algorithm validation/Change metric development*

Specific Aim #4. *Data collection to increase minority representation*

Specific Aim #5. *Report validation*

2.0 Background and Significance

Many adults experience cognitive decline with aging. The causes of cognitive dysfunction in older adults range from the devastating effects of Alzheimer's disease (AD) to treatable causes of dysfunction and include the normal mild forgetfulness described by many older individuals. Recently, there has been a move to identify cognitive difficulties at the earliest stage, rather than waiting until difficulties progress to the level of dementia. Early detection is crucial, as even mild cognitive dysfunction can impair decision making and impact functional abilities. Early detection can provide an opportunity to identify potentially treatable causes of cognitive loss, and the opportunity to make future plans at a time when symptoms are mild and patients are able to make informed decisions. Identifying mild cognitive loss, regardless of etiology, will also help the family and physician determine whether the individual can safely manage complex activities, such as making financial decisions, handling complex medication regimens, or continuing to work and drive.

Identifying cognitive impairment becomes increasingly important as the US population ages and increasing numbers of older individuals live with cognitive dysfunction. Current trends in healthcare suggest that the majority of elderly individuals obtain their care solely from their family physician and will not be referred for specialist evaluation. Beginning in January 2011, in compliance with the Patient Protection and Affordable Care Act (PPACA, Sec 4103), the Centers for Medicare and Medicaid Services began covering the costs of an Annual Wellness Visit. As part of this visit, primary healthcare providers are instructed to detect cognitive dysfunction based on direct observation, objective testing, the patient's own reports, and/or information from family members, friends, and caregivers. Although published guidelines exist to aid the physician in this assessment, the availability of effective tools to accomplish this goal in the context of a busy office with abundant and competing priorities remains scarce.

The specific aims included in the current project are focused on activities required to successfully move CAMCI to commercialization by extending support for later stage research and development and product development, including regulatory strategy and intellectual property development, data collection to replicate key studies, product extension through increasing minority representation, and development of a measure of change.

3.0 Research Design and Methods

3.1 Description of Testing Tools

Neuropsychological Test Battery
The neuropsychological test battery includes the Montreal Cognitive Assessment (MoCA) and neuropsychological tests designed to detect deficits across multiple cognitive domains:

(1) WAIS-IV Digit Span Forward and Backward (Wechsler, 1987)
(2) WAIS-IV Digit Symbol (Wechsler, 1987)
(3) Hopkins Verbal Learning Test – Revised (HVLT-R;Brandt and Benedict,2001;Benedict, Schretlen, Groninger, & Brandt, 1998)
(4) Logical Memory; Wechsler Memory Scale IV (WMS-IV)
(5) Trail Making Test part A and part B (Reitan, 1958)
(6) Boston Naming Test 2nd edition (Kaplan et al., 2000)
(7) REY Figure copy and delayed recall (Meyers and Meyers, 1995)
(8) Semantic Fluency (animals) (Spreen and Strauss, 1997)
(9) Letter Fluency (number of letters starting with “F” “A” and “S” in 60 seconds each)

CAMCI Computerized Task Battery
CAMCI is a computerized screening tool for the assessment of cognitive status. CAMCI accurately assesses cognitive performance using standard neuropsychological tests of memory, attention, and executive ability modified for computer administration, and an innovative Virtual Environment task, testing domains such as incidental memory, not easily assessed using paper-pencil tests. Computer-administered tasks ensure standard administration and scoring, avoiding inter-site and inter-examiner variability. The CAMCI battery consists of tasks testing multiple aspects of cognitive function, and a series of self-report questions administered via tablet computer. Using touchscreen technology for response input, CAMCI takes approximately 15 minutes to complete.

Reading Assessment
The WRAT5 Word Reading subtest is a norm-referenced test that measures the basic academic skills of word reading. Word Reading measures letter and word decoding through letter identification and word recognition.

3.2 Protocol 1 (Specific Aim 3)
The purpose of this protocol is to validate the CAMCI scoring algorithm on an independent sample of older individuals. Approximately 420 Adult male and female participants 60-95 years of age will be enrolled into this portion of the research study. Prior to enrollment, participants will be screened to determine eligibility for the study.

Baseline
After obtaining informed consent, participants will be asked to complete the MoCA, the CAMCI battery of tasks, a complete paper-pencil neuropsychological test battery, a survey requesting feedback from the participant concerning their experience with the CAMCI application, and a brief reading assessment. The paper-pencil tests will be used by three neuropsychologists (see Appendix A) to adjudicate the participants. The baseline test session will take approximately 2.5 hours to complete, and participants will be paid $100 for completion of this portion of the study.

If an equivalent and valid neuropsychological task battery assessment (as determined by the project-certified examiner) is available at the time of enrollment in the study, the neuropsychological task battery will not be re-administered, and the protocol will be shortened to administer all remaining elements. In this case, total test session time is estimated to be approximately 60 minutes, and participants will be paid $50 for completion of the shortened protocol.

Follow-Ups
Participants will be asked to return for two follow-up test sessions at set intervals in relation to their baseline test session (either 6 months and 12 months, or 12 months and 24 months). During the follow-up test sessions, participants will be asked to complete the MoCA, the CAMCI battery of tasks, and a complete paper-pencil neuropsychological test battery (the survey and reading assessment will not be repeated). Each follow-up test session will take approximately 2 hours to complete, and participants will be paid $75 for each follow-up test session completed. Total compensation for each participant may be up to $250 for completion of the baseline and 2 follow-up test sessions.

If a participant is unable to complete a test session, or if the experimenter must discontinue a test session before completion, the participant will be paid $25.

3.3 Protocol 2 (Specific Aim 4)
The purpose of this protocol is to verify applicability of the scoring algorithm for older individuals to additional populations. Therefore, the focus will be to recruit a sample of African American (n=225) and Hispanic (n=175) subjects (of any race). Adult male and female African American and/or Hispanic participants 60 years of age or older will be enrolled into this portion of the research study. Prior to enrollment, participants will be screened to determine eligibility for the study.

Baseline only
After obtaining informed consent, participants will be asked to complete the MoCA, the CAMCI battery of tasks, a complete paper-pencil neuropsychological test battery, a survey requesting feedback from the participant concerning their experience with the CAMCI application, and a brief reading assessment. The paper-pencil tests will be used by three neuropsychologists (see Appendix A) to adjudicate the participants. The baseline test session will take approximately 2.5 hours to complete, and participants will be paid $100 for completion of this portion of the study.

If an equivalent and valid neuropsychological task battery assessment (as determined by the examiner) is available at the time of enrollment in the study, the neuropsychological task battery will not be re-administered, and the protocol will be shortened to administer all remaining elements. In this case, total test session time is estimated to be approximately 60 minutes, and participants will be paid $50 for completion of the shortened protocol.

If a participant is unable to complete a test session, or if the experimenter must discontinue a test session before completion, the participant will be paid $25.

3.4 Protocol 3 (Specific Aim 5)
The purpose of this protocol is to validate the readability and usefulness of the CAMCI report with a sample of potential users of the product. We will recruit and test healthcare professionals (N=60) who would be responsible for interpretation of the CAMCI report and decisions concerning patient care (e.g., physicians, physician's assistants, neuropsychologists).

After consent, participants will be presented with a series of case studies including information expected to be available during an assessment of cognitive status (e.g., MoCA, list of medications, patient report, etc.) as well as the results of CAMCI testing, and will be asked to respond to a series of questions related to 1) thoroughness of the information provided, 2) usefulness of information, and 3) recommended course

of action based on the CAMCI report, and 4) their likelihood to use the tool. In addition, the readability of the CAMCI report will be evaluated by requesting the participant to supply information available on the report. Report validation will occur in two phases during Year 1 (N=30) and Year 3 (N=30) in conjunction with the efforts to validate the scoring algorithm and develop the change metric. Each test session will take approximately 60 minutes to complete, and participants will be paid $100 for completion of this portion of the study.

4.0 Human Subjects

4.1 General Characteristics.
The age, racial, gender and ethnic characteristics of the proposed participant population are based on the needs of each specific aim involving human subjects.

Protocol 1 (Specific Aim 3)
The goals of Specific Aim 3 are to validate the existing CAMCI scoring algorithm, and to develop a scoring method through repeated assessments of the subjects used for that validation. Recruitment for this aim will reflect the demographic distribution within the United States (https://www.census.gov/quickfacts/fact/table/US/PST045216, Population estimates, July 1, 2016). The proposed participant population of adults ages 60+ is 77% White, 13% Black or African American, 6% Asian, 4% all other racial groups, 18% Hispanic (of any race), and 51% female

Protocol 2 (Specific Aim 4)
The goals of Specific Aim 4 are to verify applicability of the scoring algorithm to additional populations and increase minority representation. We will recruit a total of 400 African American subjects and Hispanic subjects of any races (225 African American subjects, and 175 Hispanic subjects of any race). All subjects will be adults ages 60-95. The specific focus of this effort includes 100% participation from ethnic/racial minorities, with 50% of each gender.

Protocol 3 (Specific Aim 5)
The goal of Specific Aim 5, to validate the CAMCI reporting feature, will involve the recruitment of healthcare professionals as potential users of the product. The most important qualification for recruitment in accomplishing this aim is professional position and expertise concerning cognitive assessment. We will seek to recruit professionals at a rate matching that of the population of healthcare professionals. Females account for more than 80 percent of workers in most U.S. health occupations (http://bhpr.hrsa.gov/healthworkforce/supplydemand/usworkforce/diversityushealthoccupations.pdf). Whites make up 77.6%, Blacks or African Americans represent 13.6%, Asians make up 6%, and individuals reporting multiple races or other race represent 2%. Hispanics comprise 15.5% of workers in most U.S. health occupations. Therefore, the proposed participant population for specific aim 5 is 78% White, 14% Black or African American, 6% Asian, 2% all other racial groups, 16% Hispanic, and 80% female.

4.2. Inclusion of Children in Research. This study deals with disorders of memory in adults associated with aging and other causes. Therefore, the study is not applicable to children.

4.3 General Inclusion criteria. Signed informed consent; adequate visual and auditory acuity to allow neuropsychological testing; able to read, write and understand study and test requirements; within the age range of 60+ (Protocols 1 and 2), professional position in a healthcare field (Protocol 3).

4.4 General Exclusion criteria. Any significant neurologic disease, such as multi-infarct dementia, Parkinson's disease, epilepsy, stroke, multiple sclerosis or head trauma; history of major depression or other major psychiatric disorder, such as, schizophrenia and bipolar disorder; history of consuming 5 or more alcoholic drinks per day on a regular basis; MoCA score <10.

4.5 Recruitment Procedures.

Protocols 1-2: Potential participants will be identified by a subject recruiter through response to advertisement or referral, and at a variety of community and clinical sources (e.g., PCP offices, local churches, community centers, clinics). The test is purely cognitive, so no medical records will be requested. The subject recruiter will describe the study to the participant and ask if they are interested in participating. If they express an interest, study staff will meet with the participant to discuss the study in detail and to obtain informed consent. Participants who fail to demonstrate an adequate understanding of the material reviewed during the informed consent process, or who score <10 on the MoCA will be excluded.

Protocol 3: Potential participants will be identified through professional connections, referral, and advertisement. The PI, co-investigators, consultants, and research staff on the project have links to a broad range of academic and clinical departments at Universities and community health care services in the local area and across the country at which we will solicit for professionals interested in participating in the study. In addition, we will research community and health organizations in and around the city of Pittsburgh (spanning a 10 county area) providing varying services to older adults (e.g., rehab facilities, outpatient clinics, physician offices, community centers), and will provide flyers, presentations, and/or additional information to these organizations, as requested, to raise interest in the project and to recruit participants.

4.6 Risk/Benefit Ratio. Some individuals may experience fatigue, frustration, or feel slightly distressed if they think they are not doing well on a test of intellectual ability. If the participant indicates any distress the test will be discontinued, or breaks will be provided, if requested. Other than payment for participation, there are no direct benefits to participants from participating in this study. Participants will be informed that the results of this study may help identify early signs of memory problems. If a previously unknown disorder is identified (i.e., MoCA <10), we will refer the participant to the appropriate health and community services and if consent is provided, the results of the MoCA will be provided to their healthcare provider of choice. Results will not be provided directly to an individual, and as CAMCI is not yet an FDA-cleared tool for clinical assessment, computer test scores collected or reported by the CAMCI will not be released or discussed.

4.7 Data and Safety Monitoring Plan. The PI, Co-Investigators, and DSMB will monitor the study at all stages. Throughout the study, the research personnel will minimally meet monthly to discuss recruitment and conduct of the study. Any instances of adverse events will be reported immediately to the NIA, DSMB, and Copernicus Group IRB using the standard forms and/or procedures that have been established for the clinical trial. The yearly IRB renewal for this study will include a summary report of the Data and Safety Monitoring Plan findings from the prior year.

4.8 Confidentiality. Participants will be required to sign a Subject Information and Consent form. All information collected for this study will be coded and remain confidential to the extent provided by law. The principal investigator will routinely review the methods of data collection and storage to ensure that no breach of confidentiality occurs. If the results of this study are submitted for publication, confidentiality of records will be maintained. Research records will be kept for a period of at least 5 years after the study ends.

4.9 Alternative Treatments. Not Applicable.

4.10 New Information. Participants will be promptly notified if any new information, either good or bad, develops during the course of this study that may cause a change of mind about continuing to participate.

4.11 Costs and Payments. There are no costs for participating in this study. Participants receive payment for completion of each portion of the study in which they participate (see table below).

Protocol 1:

Phase	***# subjects***	***Payment***

Baseline	420	$100*
Follow-Up (6 months)	280	$75
Follow-Up (12 months)	420	$75
Follow-Up (24 months)	140	$75

** $50 if a valid neuropsychological assessment is available allowing the protocol to be shortened*

Protocol 2:

Phase	***# subjects***	***Payment***
Baseline	400	$100*

** $50 if a valid neuropsychological assessment is available allowing the protocol to be shortened*

Protocol 3:

Phase	***# subjects***	***Payment***
Report Validation	60	$100

4.12 Conflict of Interest. The Principal Investigator, Amy Eschman, is employed by Psychology Software Tools (PST) and may be perceived to be affected by the outcome of the research study. Therefore, each Subject Information and Consent form discloses this relationship where it is stated "PST employs Amy Eschman, the principal investigator, who might benefit from commercial use of this product."

This project is part of a National Institutes of Health Small Business Innovation Research (NIH SBIR) award. SBIR grants are given to profit-making firms in order to develop new products. This grant has been awarded to Psychology Software Tools, of Pittsburgh, which is owned by Dr. Walter Schneider and Anthony Zuccolotto. The goal of this project is to commercialize CAMCI as a valid assessment tool for quickly screening cognitive impairment. Some of the data may be reported at scientific conferences or in scientific journals. Drs. Morrow, Saxton, and Ratcliff may also benefit from commercialization of this product.

Appendix A. Neuropsychologists

Lisa Morrow, PhD: Co-Investigator. Dr. Morrow is an Associate Professor of Psychiatry at Western Psychiatric Institute and Clinic with extensive research experience studying neuropsychological and psychiatric functioning in patients with neurological injury, including neurotoxic exposure, (e.g., lead, solvents), trauma, visuospatial deficits associated with stroke, as well as normal aging and dementia. She has published over 65 papers in major journals and chapters, and has over 40 presentations to national and international meetings. She has tested over 1,000 patients to assess cognitive deficits and helped to develop and publish several normative studies of neuropsychological tests and test batteries, including the Pittsburgh Occupational Exposures Test Battery, a Continuous Performance Test, the Four-Word Short-Term Memory Test and the CAMCI (Beers & Levine, 2008; Ryan et. al, 1987; Morrow et al., 1992; Morrow & Ryan, 2002).

Judith Saxton, PhD: Co-Investigator. Dr. Saxton is a neuropsychologist with over 20 years experience assessing patients with dementia. She is a clinical neuropsychologist in private practice, recently retired from the position of Director of the Training and Information Core, and Associate Director of the Clinical Core, of the Alzheimer's Disease Research Center and has been a PI or Co-Investigator on more than fifteen studies of cognitive functioning in older individuals. Dr. Judith Saxton is the author of the Severe Impairment Battery (SIB) a test of cognitive function in severe dementia (used in the USA, UK, Canada, Germany, France, Italy, Spain, Belgium, Holland, Japan, Korea, Argentina, Israel) and a co-developer of the CAMCI.

Graham Ratcliff, PhD. Co-Investigator. Dr. Ratcliff is a clinical neuropsychologist in private practice. He has over 25 years experience of neuropsychological assessment, and is the author or co-author of over 70 publications dealing with the effects of cerebral lesions on aspects of cognitive function, notably visuo-spatial ability, the effects of aging on memory, and the long-term consequences of head injury. He was PI of a federally funded study of Age Associated Memory Impairment, and has been a co-investigator on several community-based studies of dementia epidemiology.