ED-to-community care transitions for persons living with dementia and care partners: development, implementation, and pilot testing of a novel artificial intelligence + care coach intervention

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1	02/19/2022
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Synopsis

Primary Objective The primary objective is develop and test NeuViCare AI + care coach as an intervention for ED-to-community care transitions for PLWD and their care partners, offering a potential solution to the lack of existing ED care transition interventions.
Secondary Objective (if applicable) N/A
Study Duration August 2022 – February 2024
Study Design Overall, we will use a sequential exploratory mixed-methods approach with integration of Specific Aims at the study design level. We will use a two-phase qualitative approach within Specific Aim 1, including: 1) semi-structured interviews with stakeholders, and 2) AI design optimization through a design thinking workshop. Specific Aim 2 will use a quantitative approach to assess implementation and patient-centered outcomes in a quantitative survey-based fashion through a one-arm open-labeled trial to primarily assess functionality and usability.
Number of Study Sites EDs at York St. Campus, Saint Raphael Campus, Shoreline Campus, and Bridgeport Campus
Study Population For the older adult participants, the inclusion criteria will be: 1) age ≥65 years with a diagnosis of ADRD or dementia within the electronic health record OR new cognitive impairment identified during an ED visit, 2) be fluent in English or Spanish, 3) discharge to the community setting after an ED visit, and 4) be willing to engage in discussions regarding the implementation of a novel AI technology. Primary care partners of PLWD must possess a smart device (either a phone, tablet, or computer) that has internet access to utilize and interact with NeuViCare AI services.
Number of Participants 55
Primary Outcome Variables After in-ED enrollment, we will collect baseline measurements of PLWD and their care partners. Particularly, at time 0 this will include domain assessments of validated tools

addressing dementia knowledge, PLWD self-efficacy, psychological well-being, social connectedness, and caregiver experience. After ED- or hospital-community care transition, a virtual session led by the care coach will build upon discharge instructions by developing a comprehensive transdisciplinary care plan and integrating the use of NeuViCare AI technology. Subsequent sessions with the PLWD and their care partner will assess knowledge translation of NeuviCare AI, follow through with care plan, and the development of sustainable skills for preventing crisis and recidivism. At follow-up time points of 7 days, 30 days, and 3 months, participants will be contacted to reassess responses to above domains of interest (primary outcome).
Secondary and Exploratory Outcome Variables (if applicable) Participants will be measured regarding their healthcare utilization, including ED visits, hospitalizations and care plan adherence with follow-up in the outpatient setting (secondary outcome). Finally, implementation outcomes of the NeuViCare AI technology will be assessed through validated surveys of acceptability, appropriateness, feasibility, and usability (secondary outcome).

Abbreviations

Abbreviation	Explanation

Glossary of Terms

Glossary	Explanation

APPROVED BY THE YALE UNIVERSITY IRB 6/11/2023

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1 Introduction

1.1 Introductory Statement

This document is a protocol for a human research study. The purpose of this protocol is to ensure that this study is to be conducted according to ICH GCP guidelines, and according to CFR 21 Part 812, other applicable government regulations, and Institutional research policies and procedures.

2 Background

2.1.1 Device Preclinical Experience

As a way to address many of these unmet caregivers' needs and poor patient outcomes, Amicus Brain Innovations, Inc. a technology *s*tart-up company, has created NeuViCare, which is a soon-to-be commercially available AI-led, assistive and decision support online service application that can be accessed from a smart phone, tablet or computer by clinicians, patients and caregivers. It was designed to reduce caregiver load and increase patient adherence rates for better quality of life.

NeuViCare's multifunctional platform services are designed to impact caregiver load, while addressing their unmet needs and patients' quality of life through AI-led technology. NeuViCare Task-Support Service will increase care plan adherence rates and allow for more timely diagnoses by providing an interactive, appointment reminder service. NeuViCare Resource Advisor will educate caregivers about available resources and reduce their time spent on this task by providing context-sensitive, task-support services to reliable community resources. NeuViCare Community will provide a secure, online forum that will provide peer-support and increase caregivers knowledge on challenging behaviors by administering weekly educational series and just-in time answers provided by AI. Amicus Brain will provide technical support and troubleshoot any issues with the community software.

2.1.2 Device Clinical Experience

Given the potential impact of NeuViCare in improving quality of care, Amicus Brain and Yale Memory Clinic have previously partnered together to successfully pilot test NeuViCare’s impact on patient care in the outpatient Neurology setting.

2.2 Background/prevalence of research topic

As the nation’s older adult population grows, Alzheimer’s Disease and Alzheimer’s Disease-Related Dementias (AD/ADRD) is projected to affect an estimated 12.7 million people by 2050. Attention has been drawn to the growing population of persons living with dementia (PLWD) and their care partners through the National Plan to Address AD, yet physical, psychological, and financial burdens have persisted for the estimated 21.6 million unpaid informal care partners (e.g. family, friends). Often at considerable personal cost, care partners play an integral role in ensuring success of care transitions across healthcare settings, particularly involving the emergency department (ED). With the majority of PLWDs being discharged from the ED, care partners subsequently provide a significant amount of hands-on care and navigation of health-related and social needs within this vulnerable time period. Highlighting the inadequacies of current care transition efforts, PLWDs visit the ED at a higher rate and also have higher ED return and mortality rates after an initial ED visit in comparison to their non-cognitively impaired counterparts. The prioritization of ED dementia

care research by the American Geriatrics Society, the widespread dissemination of the 2014 consensus geriatric ED guidelines, and the 2018 launch of a geriatric ED accreditation program have highlighted the need for evidence with best practices for PLWD and their care partners. All prioritize the importance of ED-to-community care transitions, yet effective interventions focusing on patient- and care partner-centered outcomes are largely lacking. With uncertainty regarding treatment options for PLWD, there is an urgent need and opportunity to develop interventions addressing ED-to-community care transitions.

To date, little data exist on effective interventions to improve ED-to-community care transitions for older adults with ADRD or cognitive impairment. Attempts have primarily focused on cognitively intact older adults and considered the use of comprehensive geriatric assessments, enhanced discharge planning, referrals to specialist services, or community paramedics with variable impact on ED revisits and overall limited attention to patient-centered outcomes. Traditionally, some of these ‘high touch’ modalities involve frequent check-ins by healthcare personnel to ensure care plan adherence, but are resource-intensive, and therefore may have limitations in the way of scalability and affordability. Technology, including artificial intelligence (AI), has been shown to be a ‘high tech’ advancement that offers the potential to benefit older adults by promoting self-service and independence. AI has proven to be acceptable and used by older adults and care partners in relation to healthcare needs, but has been incorporated less within ED populations.

3 Rationale/Significance

3.1 Problem Statement

As the nation's older adult population grows, Alzheimer's Disease and Alzheimer's Disease-Related Dementias (AD/ADRD) is projected to affect an estimated 12.7 million people by 2050. With the majority of PLWDs being discharged from the ED,[14] care partners subsequently provide a significant amount of hands-on care and navigation of health-related and social needs within this vulnerable time period. To date, little data exist on effective interventions to improve ED-to-community care transitions for older adults with ADRD or cognitive impairment. Technology, including artificial intelligence (AI), has been shown to be a 'high tech' advancement that offers the potential to benefit older adults by promoting self-service and independence. AI has proven to be acceptable and used by older adults and care partners in relation to healthcare needs, but has been incorporated less within ED populations.

3.2 Purpose of Study/Potential Impact

Incorporation of AI-led technology among PLWD and their care partners will provide new insights into ways in which the ED discharge process can be improved. Additionally, this work will provide information regarding the optimal interaction between AI + care coaching to support this essential population during ED-to-community care transitions. Together, the proposed research will provide high-quality evidence regarding the design optimization and feasibility of implementing a novel 'high tech – high touch' ED-to-community care transition intervention among PLWD and their care partners.

3.2.1 Potential Risks

This risks to human subjects in the proposed research are minimal. Specific Aim 1 involves qualitative interviews and a design thinking workshop with various stakeholders regarding the role of AI + care coaching during ED-to-home community care transitions. Specific Aim 2 involves the pilot testing of the NeuViCare AI. Psychologically, there is a risk that participants will find the interviews and engagement with the AI + care coach burdensome or distressing. There is also a risk of inadvertent release of potentially identifying information. Other physical, social, cultural, financial, and legal risks are minimal. Data collection, management, and analytic processes outlined in the proposal are designed to ensure that participant privacy and confidentiality will be maintained.

3.2.2 Potential Benefits

Results from this study will help us learn more about ED-to-community care transitions of PLWD and their care partners. We believe that the possible benefits for clinical care outweigh the minimal risks of the proposed research. A small incentive will be provided, and the participants may benefit directly from the AI + care coach intervention, particularly if the

hypothesis is proven correct. This could be due to increased access to support and manifest in the way of increased engagement in the care plan, reduced care partner burden, and reduced health utilization in the following 30 days.

4 Study Objectives

4.1 Hypothesis

Specific Aim 1: We will optimize the NeuViCare AI + care coach intervention, for subsequent pilot testing.

Specific Aim 2: We will demonstrate: 1) feasible and acceptable implementation of NeuViCare AI + care coach intervention, 2) care plan adherence and NeuViCare AI engagement, and 3) reduced 30-day care partner burden and PLWD healthcare utilization.

4.2 Primary Objective

The primary objective is develop and test NeuViCare AI + care coach as an intervention for ED-to-community care transitions for PLWD and their care partners, offering a potential solution to the lack of existing ED care transition interventions.

4.3 Secondary Objectives (if applicable)

N/A

5 Study Design

5.1 General Design Description

Overall, we will use a sequential exploratory mixed-methods approach with integration of Specific Aims at the study design level. The rationale for the use of this approach is based on evidence that has shown the mixed-methods approach to be well-suited for the investigation of novel technology incorporation within healthcare settings by linking stakeholder's perspectives (qualitative) with implementation and patient-centered outcomes (quantitative). As performed by other user-centered design approaches, we will use a two-phase qualitative approach within Specific Aim 1, including: 1) semi-structured interviews with stakeholders, and 2) AI design optimization through a design thinking workshop. Specific Aim 2 will use a quantitative approach to assess implementation and patient-centered outcomes in a quantitative survey-based fashion.

5.1.1 Study Date Range and Duration

August 2022 – February 2024

5.1.2 Number of Study Sites

EDs at York St. Campus, Saint Raphael Campus, Shoreline Campus, and Bridgeport Campus

5.2 Outcome Variables

5.2.1 Primary Outcome Variables

After in-ED enrollment, we will collect baseline measurements of PLWD and their care partners. Particularly, at time 0 this will include domain assessments of validated tools addressing dementia knowledge, PLWD self-efficacy, psychological well-being, social connectedness, and caregiver experience. After ED- or hospital-community care transition, a virtual session led by the care coach will build upon discharge instructions by developing a comprehensive transdisciplinary care plan and integrating the use of NeuViCare AI technology. Subsequent sessions with the PLWD and their care partner will assess knowledge translation of NeuviCare AI, follow through with care plan, and the development of sustainable skills for preventing crisis and recidivism. At follow-up time points of 7 days, 30 days, and 3 months, participants will be contacted to reassess responses to above domains of interest (primary outcome).

5.2.2 Secondary and Exploratory Outcome Variables (if applicable)

Participants will be measured regarding their healthcare utilization, including ED visits, hospitalizations and care plan adherence with follow-up in the outpatient setting (secondary outcome). Finally, implementation outcomes of the NeuViCare AI technology will be

assessed through validated surveys of acceptability, appropriateness, feasibility, and usability (secondary outcome).

5.3 Study Population

For the older adult participants, the inclusion criteria will be: 1) age ≥65 years with a diagnosis of ADRD or dementia within the electronic health record OR new cognitive impairment identified during an ED visit, 2) be fluent in English or Spanish, 3) discharge to the community setting after an ED visit, and 4) be willing to engage in discussions regarding the implementation of a novel AI technology. Primary care partners of PLWD must possess a smart device (either a phone, tablet, or computer) that has internet access to utilize and interact with NeuViCare AI services.

5.3.1 Number of Participants

Phase 1 (qualitative interviews) – approximately 15

Phase 2 (Design Thinking Workshop) – approximately 15

Pilot Implementation – approximately 25

5.3.2 Eligibility Criteria/Vulnerable Populations

For the older adult participants, the inclusion criteria will be: 1) age ≥65 years with a diagnosis of ADRD or dementia within the electronic health record OR new cognitive impairment identified during an ED visit, 2) be fluent in English or Spanish, 3) discharge to the community setting after an ED visit, and 4) be willing to engage in discussions regarding the implementation of a novel AI technology. Primary care partners of PLWD must possess a smart device (either a phone, tablet, or computer) that has internet access to utilize and interact with NeuViCare AI services.

6 Methods

6.1 Treatment – Device

6.1.1 Intended Use for Device (provide the following information for each device being investigated in the study)

Building upon prior work in the outpatient Neurology setting, NeuViCare AI will include variations of its 5 components: 1) NeuViCare Planner - enables review of ordered tests and external resources recommended by the care provider; 2) NeuViCare Task-Support Service - provides context-sensitive, personalized SMS text-based assistance to help patients' complete care plan captured in the NeuViCare Planner; 3) NeuViCare Resource Advisor - presents trusted, unbiased advice to locate nearby resources listed within their care plan; 4) NeuViCare Advisor - educates and trains PLWD and their care partners at the moment of need; and 5) NeuViCare Community Hub - a safe virtual space which enables care partners to interact with other peer care partners to gain their experiential knowledge and emotional support.

6.1.2 Device Administration and Schedule

If interested and consented to joint the study, the PLWD and/or care partner will be given introductory instructions regarding the use of NeuViCare by the RA in the ED prior to discharge. Post-ED education will be performed by occupational therapy care coaches who will focus on incorporating NeuViCare AI technology to problem solve and build skills to empower PLWD and their care partners with knowledge and capacity to reduce severity of crisis escalations that result in healthcare utilization.

6.1.3 Method of Assignment/Randomization (if applicable)

N/A

6.1.4 Device Calibration

N/A

6.1.5 Storage Conditions

N/A

6.1.6 Concomitant therapy

N/A

6.1.7 Restrictions

There are no restrictions.

6.2 Assessments

6.2.1 Efficacy

Implementation outcomes of the NeuViCare AI technology will be assessed through validated surveys of acceptability, appropriateness, feasibility, and usability. *Acceptability* is defined as the perception that a given innovation is agreeable, palatable, or satisfactory. Acceptability will be measured by the Acceptability of Intervention Measure (AIM). *Appropriateness* is defined as the perceived fit, relevance, or compatibility of the innovation for a given setting or consumer, and/or perceived fit of the innovation to address a particular issue or problem. Appropriateness will be measured by the Intervention Appropriateness Measure (IAM). *Feasibility* is defined as the extent to which a new innovation can be successfully used or carried out within a given setting, and will be measured by the Feasibility of Intervention Measure (FIM). Finally, *usability* encapsulates several aspects including subjective assessments of effectiveness, efficiency, and satisfaction, and will be measured using the System Usability Scale (SUS). All measures identified are psychometrically valid and readable (Table).

Table 1: Implementation outcomes to be assessed
Note: All responses will be scored on a 5-point Likert scale from 'Completely Disagree' to 'Completely Agree'.

Acceptability of Intervention Measure (AIM)
1. NeuviCare AI meets my approval.
2. NeuviCare AI is appealing to me.
3. I like NeuviCare AI.
4. I welcome NeuviCare AI.
Intervention Appropriateness Measure (IAM)
5. NeuviCare AI seems fitting.
6. NeuviCare AI seems suitable.
7. NeuviCare AI seems applicable.
8. NeuviCare AI seems like a good match.
Feasibility of Intervention Measure (FIM)
9. NeuviCare AI seems implementable.
10. NeuviCare AI seems possible.
11. NeuviCare AI seems doable.
12. NeuviCare AI seems easy to use.
System Usability Scale (SUS)
13. I think that I would like to use this system frequently.
14. I found the system unnecessarily complex.
15. I thought the system was easy to use.
16. I think that I would need the support of a technical person to be able to use this system.
17. I found the various functions in this system were well integrated.
18. I thought there was too much inconsistency in this system.
19. I would imagine that most people would learn to use this system very quickly.
20. I found the system very awkward to use.
21. I felt very confident using the system.
22. I needed to learn a lot of things before I could get going with this system.

6.2.2 Safety

N/A

6.2.3 Adverse Events Definition and Reporting

The PI will take all possible measures to minimize any risks that may occur as a consequence of participation in this investigation. Adverse events will be recorded and noted by the PI, and reported to the Yale University Human Research Protection Program. While we feel that such events are very unlikely, we will follow all until resolution if adverse events occur.

6.2.4 Pharmacokinetics (if applicable)

N/A

6.2.5 Biomarkers (if applicable)

N/A

6.3 Study Procedures

6.3.1 Study Schedule

Table 2: Timeline for completion of Specific Aims and dissemination of results						
	2022-2023					
	July – Aug	Sep – Oct	Nov – Dec	Jan – Feb	Mar – Apr	May – June
Specific Aim 1						
Hire and train research assistants	X					
Phase 1 – Qualitative interviews	X	X				
Phase 2 – Design thinking workshop		X				
Adaptation of ED-specific NeuViCare AI			X			
Specific Aim 2						
In-ED enrollment for pilot implementation and testing				X	X	X
Data analysis						X
Manuscript preparation			X			X
Preparation of NIH/NIA K76, K23, or NIH STTR application					X	X
Dissemination of results at national meetings						X

6.3.2 Informed Consent

Both Specific Aims 1 and 2 will prospectively enroll participants identified and recruited by the trained Research Assistant (RA). For Specific Aim 1, the RA will be present in real-time within the ED and evaluate all ED older adults by electronic medical record screening. Those with identified dementia in the electronic medical record will be candidates for inclusion, among others described further below. Prior to participation the RA will then approach the treating clinician and ask for their approval to speak with the patient and caregiver prior to engagement. Informed consent will be obtained by personnel with up-to-date Yale HIC-required human subject's protection and HIPAA trainings. Written informed consent will be targeted, but verbal informed consent by telephone may need to be used given several present care partner/visitor restriction policies in the ED. Participants will be informed of the purpose of the study, the likely length of the qualitative interview or design thinking workshop, and the possible risks and benefits of participation. In addition, procedures to protect confidentiality will be reviewed. Participants will be reminded that inclusion is voluntary and that they are free to end the interaction at any point they wish. There will be no coercion or undue influence to participate in the research. The semi-structured interview guide will be developed, refined, and then reviewed and approved by the Yale University Human Research Protection Program prior to the start of the study, as will recruitment and written informed consent procedures.

Specifically, the RA will first assess the potential participant's capacity given that this work will prioritize PLWD and their care partners. The goal will be to determine their genuine comprehension of the study, not their mere ability to read and repeat the consent text. This will be completed by first approaching the candidate patient participant using the validated UBACC Capacity 10 questions. A score of ≥14 will be required to denote capacity, and a 'best response' will be required to be noted for at least one item in the domains of understanding, appreciation, reasoning and choice. For those without capacity, we will operate under the premise of 'obtaining assent and respecting dissent'. The RA will ask the patient if they agree to participate in the research. Assent can be expressed or indicated

verbally (e.g., saying “yes”), behaviorally (e.g., acting agreeably), or emotionally (e.g., having a positive facial expression). Furthermore, the separate assent form will be presented to the candidate patient participant, requesting their signature. Conversely, dissent will be noted by a ‘verbal or non-verbal indication of unwillingness to participate in study procedures. This will be noted and the participant will not be questioned further. When the patient lacks capacity but provides assent, the RA will then reach out by telephone to the contact listed in the electronic medical record to obtain proxy informed consent, going through the separate caregiver consent form. The relation of the contact will be described and reported in terms of family member (relation), designated care partner, legally authorized representative, surrogate decision maker to ensure they have authority to provide consent.

In the case of older adults with proxy-informed consent or among those that have capacity and also provided consent/assent, the RA will perform the 4AT. The 4AT is scored from 0-12 and tests for delirium and cognitive impairment. A score of ≥4 suggests possible delirium, with these people to be excluded from our study. A score of 1-3 suggests possible cognitive impairment. A score of 0 suggests delirium or severe cognitive impairment is unlikely. Additionally, the RA will then perform the AD8 with the older adult as well as their care partner by telephone. The AD8 is more focused on dementia specifically for screening. As a gold standard, a score of ≥2 on the care partner-completed AD8 will be noted to suggest cognitive impairment. In cases where AD8 scores differ between patient and care partner, the care partner score will be the one that dictates the ‘true’ AD8 score and therefore whether the patient is concerning for cognitive impairment or not.

For Specific Aim 2 (pilot testing), similar in-ED recruitment strategies will be used as above for identification, consent, cognitive screening, follow-up scheduling, and nominal gift card incentivization, but an additional method of recruitment will also be employed in this phase of the research. To broaden our potential participant pool (particularly when the RA is not in the ED), we will work with the JDAT team to obtain a Dashboard/list of ED patients that meet inclusion criteria. The JDAT team will query the electronic medical record to identify patients with a problem list diagnosis of ‘dementia’ that were discharged from the ED sites. The Dashboard/list of patients will be securely provided to the research team’s RA. The research team’s RA will then use EPIC In-Basket function to contact one of three clinicians with a recent and/or longitudinal relationship with the patient and/or caregiver, outside of the treating ED physician. Clinician #1 is the patient’s PCP, clinician #2 is the ED case manager, and clinician #3 is the ED follow-up nurse. The ED case manager, if involved in the patient’s care, has a longitudinal relationship that lasts up to 72 hours beyond emergency care, in which the patient or caregiver is able to contact them to address issues. In their current role, the ED follow-up nurse already contacts all patients >65 years of age discharged from the ED within 24-48 hours. If the enrolling RA is not present in the ED, the ED case manager or ED follow-up nurse during their interaction will briefly mention the study goals and inquire if the research team’s RA can contact them by telephone to further discuss the study. If for some reason, the case manager or follow-up nurse did not meet with a patient with dementia

identified through the JDAT Dashboard, then we will ask the patient's PCP through EPIC In-Basket if acceptable to contact the patient and caregiver. The research team's RA will then contact the patient and/or caregiver, first informing them that one of the 3 listed clinicians stated it was acceptable for the RA to contact them, followed then by describing the study, identifying interest, and consenting the patient and/or caregiver as described previously (similar to in-ED enrollment from here forward).

6.3.3 Screening

See 6.3.2.

6.3.4 Enrollment

See 6.3.2.

6.3.5 On Study Visits

Qualitative interviews will be conducted in Specific Aim 1, Phase 1, and will take approximately 30-45 minutes. A Design Thinking Workshop will be convened during Specific Aim 1, Phase 2 and will take approximately 2-4 hours. Pilot implementation in Specific Aim 2 will follow the PLWD and care partners for 3 months post-ED visit.

6.3.6 End of Study and Follow-up

Participants will be assessed up to 3 months post-ED visit regarding outcomes through surveys built into the AI platform. There is no in-person follow-up.

6.3.7 Removal of subjects

Engagement with the study is voluntary. If a participant wishes to withdraw, they will stop using the NeuViCare AI software and not complete follow-up surveys.

6.4 Statistical Method

6.4.1 Statistical Design

Recorded interviews will be professionally transcribed. We will perform coding throughout the study using a qualitative descriptive approach with thematic analysis. A draft code key will be generated through an inductive coding process. Interviews and coding will occur concurrently, and coding disagreements will be resolved by group consensus. We will use the final code key to analyze the remaining transcripts, and will then produce code reports and identify themes while maintaining an audit trail of coding decisions. NVivo, a specialized software package for qualitative research, will be used to facilitate data organization and theme identification.

Additionally, we will use a primarily inductive approach to content analysis whereby theoretical insights will be developed from the design thinking workshop data. Similar to prior qualitative work within design thinking workshops, themes and subthemes will be generated and grouped by common words, phrases, or ideas.

Regarding the DKAS and Zarit Caregiver burden scale, we will compare baseline and 30-day mean scores of the pilot group using the paired t-test.Given the proposal's pilot nature, descriptive statistics will be used to assess ED and hospitalization outcomes as well as survey data regarding implementation outcomes. A mean score of ≥4 using the FIM will be indicative of NeuviCare AI's feasibility. A mean score of ≥4 using the AIM will be indicative of NeuviCare AI's acceptability. A mean score of ≥4 (using the IAM will be indicative of NeuviCare AI's appropriateness. In analyzing usability data, the 10-item SUS has a possible original score of 0-40. After multiplication by 2.5 and conversion to a 0-100 scale, prior research suggests that above average usability are interventions with a score ≥68.

6.4.2 Sample Size Considerations

N/A

6.4.3 Planned Analysis

6.4.3.1 Primary Analyses

See 6.4.1.

6.4.3.2 Secondary Objectives Analyses

See 6.4.1.

6.4.3.3 Safety

N/A

6.4.3.4 Analysis of Subject Characteristics

We will present descriptive characteristics of cognition screening (to identify degree of ADRD), health literacy, chronic conditions, sociodemographic factors, and ED chief complaint.

6.4.3.5 Interim Analysis (if applicable)

N/A

6.4.3.6 Health economic evaluation

N/A

6.4.3.7 Other

N/A

6.4.4 Subsets and Covariates

N/A

6.4.5 Handling of Missing Data

Missing data will be considered missing at random and will not be imputed.

7 Trial Administration

7.1 Ethical Considerations: Informed Consent/Assent and HIPAA Authorization

Information sheets will be Institutional Review Board (IRB)-approved and the participant/legally authorized representative (LAR)/surrogate decision-maker will have the document read to them. The RA will explain the research study to the participant and answer any questions that may arise. This conversation will take place in a private room or via telephone if the caregiver is not present in the ED.

Participants/LAR/surrogate decision-makers will have the opportunity to carefully review the information sheet and ask questions. The participants/LAR should have the opportunity to discuss the study with their family or surrogates, or think about it prior to agreeing to participate. Participants/LAR must be informed that participation is voluntary and that they may withdraw from the study at any time, without prejudice. A copy of information sheet will be given to the participants/LAR/surrogate decision-makers for their records.

See additional information in 6.3.2.

7.2 Institutional Review Board (IRB) Review

The protocol will be submitted to the IRB for review and approval. Approval of the protocol must be obtained before initiating any research activity. Any change to the protocol or study team will require an approved IRB amendment before implementation. The IRB will determine whether informed consent and HIPAA authorization are required.

A study closure report will be submitted to the IRB after all research activities have been completed.

7.3 Subject Confidentiality

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, and the sponsor(s) and their interventions. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party without prior written approval of the sponsor.

All research activities will be conducted in as private a setting as possible.

The study monitor, representatives of the Institutional Review Board (IRB), or regulatory agencies may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) for the participants in this study. The clinical study site will permit access to such records.

The study participant's contact information will be securely stored at each clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by the reviewing IRB, Institutional policies, or, if applicable, sponsor requirements.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored at the [insert location]. This will not include the participant's contact or identifying information. Rather, individual participants and their research data will be identified by a unique study identification number. The study data entry and study management systems used will be secured and password protected. At the end of the study, all study databases will be de-identified and archived at the Yale School of Medicine.

7.4 Deviations/Unanticipated Problems

A protocol deviation is any noncompliance with the study protocol. 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 are to be developed by the site and implemented promptly.

It is the responsibility of the site investigator to identify and report deviations within 5 working days of identification of the protocol deviation. All deviations must be addressed in study source documents, reported to the study sponsor, and the reviewing Institutional Review Board (IRB) per their policies.

Unanticipated problems involving risks to participants or others 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.

The investigator will report unanticipated problems (UPs) to the reviewing Institutional Review Board (IRB) and to the study sponsor. 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 study sponsor, if applicable within 5 days in accordance with of the investigator becoming aware of the event.
- Any other UP will be reported to the IRB and study sponsor within 10 days of the investigator becoming aware of the problem.
- All UPs should 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 & 10 days of the IRB's receipt of the report of the problem from the investigator.

7.5 Data Collection

Data will be collected using the NeuViCare AI app.

7.6 Data Quality Assurance

Participant Safeguards: For Specific Aim 1, telephone qualitative interviews and cognitive debriefing processes will be conducted by personnel with interview experience among PLWD and their care partners. In the unlikely event that a participant experiences distress, study personnel will be instructed to terminate the interview, listen to the concerns of the participants, and provide reflective statements so that the participant knows that his or her concerns were heard. Such events will also be documented by Dr Gettel as part of the audit trail standard in qualitative research.

NeuViCare AI: The application is implemented on the HIPAA compliant Google Compute Platform (GCP), also called Google Cloud. Hence, NeuViCare’s computing, network, and data storage services are all on the cloud. All data collected and stored by the NeuViCare application is guaranteed to be only stored on the Cloud, encrypted at rest. For more information, you can visit the following website:

https://cloud.google.com/security/compliance/hipaa-compliance/. Amicus Brain has secured HIPAA Business Associate Agreement (BAA) from Google; thus, ensuring that all parties maintain HIPAA security and overall HIPAA compliance. Additional data safety measures include the following:

- Use of HTTPS 128-bit encryption for all data transfers using Secure Socket Layer transmission
- All data stored in Google Cloud is encrypted at the storage level using AES256 (a 256-bit key) file encryption
- Ensuring study data is only accessible to authorized users
- Using only servers in a secure private, HIPAA-compliant cloud environment provisioned from GCP
- Amicus Brain has instituted physical safeguards and cyber security safeguards including separation of environments and separation of roles to protect the Production cloud environment where the NeuViCare application is hosted.

Confidentiality and Data Safeguards: To minimize the risks to data confidentiality, data will be stored and accessed on secure servers, and access will be limited to members of the research team. For the step involving chart review, minimal personnel will be used, and no sections of the chart will be printed. Once variables that require access to protected health information have been constructed, a deidentified data set will be created for analysis, with each participant assigned a unique random number. Additionally, recorded interviews will not contain any identifying information. Access to the deidentified data set and qualitative interview transcripts will be limited and maintained on password protected computer systems in locked offices.

Adverse Events: The PI will take all possible measures to minimize any risks that may occur as a consequence of participation in this investigation. Adverse events will be recorded and noted by the PI, and reported to the Yale University Human Research Protection Program. While we feel that such events are very unlikely, we will follow all until resolution if adverse events occur.

7.7 Study Records

Interviews records, surveys completed.

7.8 Access to Source

Source data will be maintained per Medical Records policy in a password protected, secure, Health Insurance Portability and Accountability Act (HIPAA) compliant, web-based electronic database with a built-in audit trail.

Only Institutional Review Board (IRB) approved research team members who have current HIPAA and Collaborative Institutional Training Initiative (CITI) Good Clinical Practice (GCP) and human subjects protection training will be authorized to access records.

7.9 Data or Specimen Storage/Security

To minimize the risks to data confidentiality, data will be stored and accessed on secure servers, and access will be limited to members of the research team. For the step involving chart review, minimal personnel will be used, and no sections of the chart will be printed. Once variables that require access to protected health information have been constructed, a deidentified data set will be created for analysis, with each participant assigned a unique random number. Additionally, recorded interviews will not contain any identifying information. Access to the deidentified data set and qualitative interview transcripts will be limited and maintained on password protected computer systems in locked offices.

7.10 Retention of Records

Study records retained for 1 year, then destroyed.

7.11 Study Monitoring

As stated in the NIH Resource Sharing Plan guideline, our plan will disseminate project results to the wider scientific and healthcare community and thereby *'expedite the translation of the research results into knowledge, products, and procedures to improve human health.'* Research resources generated with funds from this grant will be freely distributed, as available, to qualified academic investigators for non-commercial research. Yale University and the PI will adhere to the NIH Grants Policy on Sharing of Unique Research Resources including the "Sharing of Biomedical Research Resources: Principles and Guidelines for Recipients of NIH Grants and Contracts" issued in December 1999. We recognize that the public dissemination of our scientific results facilitates the creation of collaborative efforts, with outside investigators playing an important role in the ultimate development of additional original research. These critical objectives will be achieved by disclosing our research findings and conclusions in oral or poster presentations at national and international meetings and in publications in refereed scientific journals. We also respect the rights of our collaborators in this regard. Published manuscripts will be deposited to the NIH manuscript service as required. Should any intellectual property arise which requires a patent, we would ensure that the technology remains widely available to the research community in accordance with the NIH Principles and Guidelines document. Moreover, we plan to share resources with broad availability of policies, practices, materials, and tools to facilitate collaboration, reuse, and replication. Making project materials, databases, results, and algorithms available will facilitate collaboration and reuse and allow for verification or replication by other researchers.

7.12 Data Safety Monitoring Plan

The principal investigator is responsible for monitoring the data, assuring protocol compliance, and conducting the safety reviews quarterly. During the review process the principal investigator will evaluate whether the study should continue unchanged, require modification/amendment, or close to enrollment.

The principal investigator and the Institutional Review Board (IRB) have the authority to stop or suspend the study or require modifications.

This protocol presents minimal risks to the subjects and Unanticipated Problems Involving Risks to Subjects or Others (UPIRSOs), including adverse events, are not anticipated. In the unlikely event that such events occur, Reportable Events (which are events that are serious or life-threatening and unanticipated (or anticipated but occurring with a greater frequency than expected) and possibly, probably, or definitely related) or Unanticipated Problems Involving Risks to Subjects or Others that may require a temporary or permanent interruption of study activities will be reported immediately (if possible), followed by a written report within 5 calendar days of the Principal Investigator becoming aware of the event to the IRB (using the appropriate forms from the website) and any appropriate funding and regulatory agencies. The investigator will apprise fellow investigators and study personnel of all UPIRSOs and adverse events that occur during the conduct of this research project via email as they are reviewed by the principal investigator. The protocol's research monitor(s), e.g., study sponsors, funding and regulatory agencies, and regulatory and decision-making bodies will be informed of adverse events within 5 days of the event becoming known to the principal investigator.

7.13 Study Modification

Study will be modified as needed and reported through the IRB as needs arise.

7.14 Study Discontinuation

Study will be discontinued if significant adverse events are noted to participants.

7.15 Study Completion

February 2024

7.16 Conflict of Interest Policy

The independence of this study from any actual or perceived influence, such as by the pharmaceutical industry, is critical. Therefore, 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 trial. The study leadership in conjunction with the appropriate conflict of interest review committee 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.

Any investigator who has a conflict of interest with this study (patent ownership, royalties, or financial gain greater than the minimum allowable by their institution, etc.) must have the conflict reviewed by the Yale Provost's Committee on Conflict of Interest with a Committee-sanctioned conflict management plan that has been reviewed and approved by the study sponsor prior to participation in this study. All investigators will follow the applicable conflict of interest policies.

7.17 Funding Source

Geriatric Emergency care Applied Research Network 2.0 / Emergency Medicine Foundation / West Health Institute

7.18 Publication Plan

The PI hold primary responsibility for publishing the results, which will be targeted after research study completion. The PI will adhere to the publication guide provided by funding sponsors.

8 Appendices

Appendix #	Title	Section	Topic

9 List of Tables