DUHS IRB Application (Version 1.98) - Document Date 14AUG2025

General Information

*Please enter the full title of your protocol:		
Duke Alzheimer's Disease Center Clinical Cohort (Duke as Single IRB of Record)		
***Please enter the Short Title you would like to use to reference the study:**		
ADRC Clinical Cohort (Duke as Single IRB) * This field allows you to enter an abbreviated version of the Study Title to quickly identify this study.		

Add Study Organization(s):

List Study Organizations associated with this protocol:

Primary Dept?	Department Name
○	**DUHS** - Behavioral Neurology
◆	**DUHS** - Center for Study of Aging
○	**DUHS** - Geriatric Behavioral Health
○	**DUHS** - Medicine-General Internal Medicine

Assign key study personnel (KSP) access to the protocol

*** Please add a Principal Investigator for the study:**

(Note: Before this study application can be submitted, the PI MUST have completed CITI training)

Whitson, Heather

3.1 If applicable, please select the Key Study personnel: (Note: Before this study application can be submitted, all Key Personnel MUST have completed CITI training)
*** Denotes roles that are not recognized in OnCore. Please select an appropriate role that is recognized in all clinical research applications (iRIS, OnCore, eREG, etc.)**

A) Additional Investigators, Primary Study Coordinator (CRC), and the Primary Regulatory Coordinator (PRC):

B) All Other Key Personnel

Ayoub, Chakib
Sub-Investigator
Bauer, Melissa
Sub-Investigator

Beakas, Jenna Ashley
Study Coordinator (CRC/CRNC/RPL)
Blach, Colette
Analyst*
Bottiger, Brandi
Sub-Investigator
Bullock, William
Sub-Investigator
Carlson, Jessica
Clinical Research Specialist/Study Assistant
Cherry, Anne
Sub-Investigator
Chesnut, Blair
Analyst*
Cobb, Sandra
Nurse Practitioner
Connolly, Erin
Clinical Research Specialist/Study Assistant
Davis, Scott
Data Manager
Devinney, Michael
Sub-Investigator
Dewees, Rachel
Clinical Research Specialist/Study Assistant
Dooley, Joshua
Sub-Investigator
Einhorn, Lisa
Sub-Investigator
Eleswarpu, Sarada
Sub-Investigator
Ervin, John
Analyst*
Fekrat, Sharon
Collaborator
Fleenor, Julie
Clinical Research Specialist/Study Assistant
Gadde, Syam
Analyst*
Gadsden, Jeffrey
Sub-Investigator
Ghosh, Dhrubajyoti
Analyst*
Ghosh, Dhrubajyoti
Statistician
Habib, Ashraf
Sub-Investigator
Hauser, Elizabeth
Analyst*
Hecker, Emily
Study Coordinator (CRC/CRNC/RPL)
Hennon, Leila
Study Coordinator (CRC/CRNC/RPL)
Hinnant, Brittany
Clinical Research Specialist/Study Assistant
Hsia, Bethany

Laboratory Manager
Johnson, Kim
Sub-Investigator
Jones, Rodney
Analyst*
Kent, Michael
Sub-Investigator
Klinger, Rebecca
Sub-Investigator
Koner, Salil
Statistician
Krom, Russell-John
Sub-Investigator
Ladner, Kelcey
Study Coordinator (CRC/CRNC/RPL)
Liu, Andrew
Sub-Investigator
Luo, Sheng
Analyst*
Lutz, Michael
Sub-Investigator
MacDonald, Heather
Data Manager
Melcher, Jennifer
Graduate Student
Meng, Marie-Louise
Sub-Investigator
Merenstein, Jenna
Collaborator
Miller, Marshall
Study Coordinator (CRC/CRNC/RPL)
Moretti, Eugene
Sub-Investigator
O'Brien, Richard
Sub-Investigator
Ohlendorf, Brian
Sub-Investigator
Patillo, Sara
Study Coordinator (CRC/CRNC/RPL)
Plassman, Brenda
Sub-Investigator
Potter, Guy
Sub-Investigator
Rodgers, Beverly
Study Coordinator (CRC/CRNC/RPL)
Sasannejad, Cina
Sub-Investigator
Serbanescu, Mara
Sub-Investigator
Shields, Thomas
Study Coordinator (CRC/CRNC/RPL)
Song, Allen
Sub-Investigator
Songdechakraiwut, Tananun
Analyst*

Tunstall, LeeAnne
Study Coordinator (CRC/CRNC/RPL)
Wang, Shih-Hsiu
Sub-Investigator
Welsh-Bohmer, Kathleen
Collaborator
Williams, Cierra
Study Coordinator (CRC/CRNC/RPL)
Williams, Cierra
Regulatory Coordinator
Young, Christopher
Sub-Investigator
Yurashevich, Mary
Sub-Investigator
Zhao, Wufan
Clinical Research Specialist/Study Assistant

***Please add a Study Contact:**

Hennon, Leila
Hinnant, Brittany
Johnson, Kim
Ladner, Kelcey
Patillo, Sara
Whitson, Heather
Williams, Cierra

The Study Contact(s) will receive all important system notifications along with the Principal Investigator. (e.g., The study contact(s) are typically the Principal Investigator, Study Coordinator, and Regulatory Coordinator.)

Oncore

Please select the Library for your Protocol:

This field is used in OnCore and determines the Reference Lists, Forms, Protocol Annotations, Notifications, and Signoffs available for the protocol. Protocols that require reporting to the NCI (National Cancer Institute), must select the Oncology library.

- ○ Oncology
- ◉ Non-Oncology

Protocol Application Type

Select the type of protocol you are creating:

Please see additional criteria and information in the policy titled, "Reliance on the IRB of Another Institution, Organization, or an Independent IRB", on the **IRB web site**.

- ◉ Regular Study Application - Most common. The IRB will determine if the study is eligible for expedited review or requires full board review upon submission.
- ○ Application for Exemption from IRB Review - Includes Exempt, Not Human Subject Research, & Not Research.
- ○ External IRB Application - Any study using an external IRB as the IRB-of-Record.
- ○ Trainee Research While Away from Duke - Research conducted by medical students overseen by the Office of Curriculum & other student/trainee research away from Duke.

○ Individual Patient Expanded Access, Including Emergency Use - Use of an investigational product under expanded access, including emergency use of an investigational drug or biologic or emergency use of an unapproved device.

Conflict of Interest

Are any key personnel an inventor of any of the drugs, devices or technologies used in this research?

○ Yes ◉ No

Do any key personnel have a conflict of interest management plan issued by DOSI-COI related to this research?

○ Yes ◉ No

Oversight Organization Selection

CRU (Clinical Research Unit) or Oversight Organization Selection:

Please select the CRU.

Medicine

The Clinical Research Unit that takes responsibility for this study.

- Please select **Medicine** as the CRU **only** if the PI is in one of these Divisions or Institutes: Endocrinology, Gastroenterology, General Internal Medicine, Geriatrics, Hematology, Infectious Diseases, Nephrology, Pulmonary, Rheumatology & Immunology, Center for Applied Genomics and Precision Medicine, Center for the Study of Aging and Human Development, Duke Molecular Physiology Institute.
- More information on CRUs can be found on the Duke Office of Clinical Research (DOCR) website, **http://docr.som.duke.edu**
- Questions concerning CRU selection should be directed to docr.help@dm.duke.edu.
- For questions about the Campus Oversight Organization, please visit **Campus Oversight Organization**.

EXTERNAL KEY PERSONNEL (KP) TOOL

Use the following External KP Tool to determine each time you consider adding outside Key Personnel. You will need to clear your responses to the following 2 questions each time.

List all Key Personnel on the study who are outside Duke if they are engaged in research and relying on the DUHS IRB: (Consider these questions every time you add external key personnel)

If you have additional personnel, use the External KP Tool as a guide to determine if the personnel are engaged in research. Only people ENGAGED IN RESEARCH should be added as external key personnel.

Are the personnel intervening or interacting with the participant?

○ Yes ○ No

Are the personnel obtaining or receiving identifiable private information or protected health information (PHI)?

○ Yes ○ No

Entry 1

Confirm by checking this box, the person you are adding to this section is engaged in the research based upon the two questions above.	☑
Name	Dr. Heidi Roth
Study Role	Sub-Investigator
Email Address	Hroth@neurology.unc.edu
Institution / Organization	UNC-CH

Entry 2

Confirm by checking this box, the person you are adding to this section is engaged in the research based upon the two questions above.	☑
Name	Robert Huynh
Study Role	UNC PET SubI
Email Address	rhuynh@med.unc.edu
Institution / Organization	UNC - Radiation Safety Committee Chair

Entry 3

Confirm by checking this box, the person you are adding to this section is engaged in the research based upon the two questions above.	☑
Name	Weili Lin
Study Role	UNC SubI
Email Address	weili_lin@med.unc.edu
Institution / Organization	UNC, Biomedical Research Imaging Center (BRIC)

Entry 4

Confirm by checking this box, the person you are adding to this section is engaged in the research based upon the two questions above.	☑

Name	Gwenn Garden
Study Role	Co-Investigator - Center Director at UNC
Email Address	gagarden@email.unc.edu
Institution / Organization	UNC-CH

Entry 5

Confirm by checking this box, the person you are adding to this section is engaged in the research based upon the two questions above.	☑
Name	Andrea Bozoki
Study Role	Co-Investigator
Email Address	abozoki@unc.edu
Institution / Organization	UNC-CH

Entry 6

Confirm by checking this box, the person you are adding to this section is engaged in the research based upon the two questions above.	☑
Name	Mason Morgan
Study Role	Psychometrist
Email Address	morganm@neurology.unc.edu
Institution / Organization	UNC-CH

Entry 7

Confirm by checking this box, the person you are adding to this section is engaged in the research based upon the two questions above.	☑
Name	Patrick Smith
Study Role	Sub-Investigator
Email Address	smith562@mc.duke.edu
Institution / Organization	UNC-CH

Entry 8

Confirm by checking this box, the person you are adding to this section is engaged in the research based upon the two questions above.	☑
Name	Tiffany Kollah
Study Role	CRC
Email Address	tkolla@unc.edu
Institution / Organization	UNC-CH

Entry 9

Confirm by checking this box, the person you are adding to this section is engaged in the research based upon the two questions above.	☑
Name	Indira Lujano
Study Role	Research Assistant
Email Address	indira@live.unc.edu
Institution / Organization	UNC-CH

Entry 10

Confirm by checking this box, the person you are adding to this section is engaged in the research based upon the two questions above.	☑
Name	Jessica Ferrall
Study Role	Study Coordinator
Email Address	jferrall@neurology.unc.edu
Institution / Organization	UNC-CH

Entry 11

Confirm by checking this box, the person you are adding to this section is engaged in the research based upon the two questions above.	☑
Name	Indira Lujano
Study Role	Study Coordinator

Email Address	indara@live.unc.edu
Institution / Organization	UNC-CH

Entry 12

Confirm by checking this box, the person you are adding to this section is engaged in the research based upon the two questions above.	☑
Name	Mackenna Moore
Study Role	Duke - CRISP Intern
Email Address	mackenna.moore@duke.edu
Institution / Organization	Durham Technical Community College

Entry 13

Confirm by checking this box, the person you are adding to this section is engaged in the research based upon the two questions above.	☑
Name	Mary Sutton Sallenger
Study Role	CRC
Email Address	sallengers@neurology.unc.edu
Institution / Organization	UNC-CH

Entry 14

Confirm by checking this box, the person you are adding to this section is engaged in the research based upon the two questions above.	☑
Name	Anna Brey
Study Role	Physician Assistant
Email Address	abrey@email.unc.edu
Institution / Organization	UNC-CH

Entry 15

Confirm by checking this box, the person you are adding to this section is	☑

engaged in the research based upon the two questions above.	
Name	Madelyn Vavrousek
Study Role	CRC
Email Address	vavrousekm@neurology.unc.edu
Institution / Organization	UNC-CH

Entry 16

Confirm by checking this box, the person you are adding to this section is engaged in the research based upon the two questions above.	☑
Name	Julianne Key
Study Role	Regulatory Monitor
Email Address	keyj@neurology.unc.edu
Institution / Organization	UNC-CH

Describe Role of External Personnel:

Tiffany Kollah, Mary Sutton Sallenger, and Madelyn Vavrousek will be assisting with Subject Recruitment from UNC clinics, as well as collaborating with Duke staff regarding subjects doing assessments at UNC. They are being assisted by additional primary research assistants who will be included as listed external KP as well. Dr. Heidi Roth is presently involved as a SubI/Collaborator. All PHI data sharing will be in accordance with executed data agreements, as well as any related language in the study consents, RDSP, and study application regarding that sharing, specifically between Duke and UNC as part of their ADRC collaboration. The primary intent is that Duke and UNC be able to share subject data/information for purposes of coordinated recruitment efforts as well as Clinical Case Consultations.

Drs. Weili Lin and Robert Huynh are both acting SubIs at UNC, assisting with activities related to imaging at the BRIC.

Drs. Gwenn Garden, Patrick Smith, and Andrea Bozoki are all SubIs based at UNC, and Mason Morgan is based at UNC and has the role of Psychometrist.

Mackenna Moore is a Durham Technical Community College, Clinical Research Student, who will be interning at the ADRC for Summer 2025. She will be observing study visits and aiding in managing study resources (e.g., creating blood collection kits, printing documents for data collection, etc.)

Anna Brey is a Physician Assistant as a study clinician. She will complete neurological exams at UNC-CH.

Julianne Key is a regulatory monitor at UNC-CH. She will be completing regulatory monitoring at UNC-CH.

Indicate the Protocol source below:

The protocol source is the author of the protocol. If the protocol is a joint authorship between multiple sources, select the primary author.

An IRB fee may be assessed for all research that is supported by for-profit entities and requires full board review. For additional information, see the **IRB fees section of the IRB web site**.

- (●) Duke PI initiated
- ( ) Commercial / Industry (for-profit entity) initiated
- ( ) Federal Government initiated
- ( ) Cooperative Group Initiated
- ( ) Foundation (non-profit group) initiated
- ( ) Other

Sponsor and Funding Source

Add all funding sources for this study: (Select 'Duke University' if you do not have funding or a sponsor for your study).

View Details	Sponsor Name	Sponsor Type	Contract Type:	Project Number	Award Number
⊟	Duke University	Institutional	Grant		

Sponsor Name:	Duke University
Sponsor Type:	Institutional
Sponsor Role:	Funding
Grant/Contract Number:	
Project Period:	From:08/30/2019 to:09/30/2020
Is Institution the Primary Grant Holder:	No
if No, then who is the Primary Grantee?	Neuroscience Translating Duke Health grant
Contract Type:	Grant
Project Number:	
Award Number:	
Grant Title:	Creating a clinical core model for the Alzheimer's Disease Research Center
PI Name: (If PI is not the same as identified on the study.)	
Explain Any Significant Discrepancy:	

⊟	National Institute on Aging	Federal Government	Grant		1P30AG072958-01

Sponsor Name:	National Institute on Aging
Sponsor Type:	Federal Government
Sponsor Role:	Funding
Grant/Contract Number:	
Project Period:	From:09/01/2021 to:06/30/2026
Is Institution the Primary Grant Holder:	Yes
Contract Type:	Grant
Project Number:	
Award Number:	1P30AG072958-01
Grant Title:	Duke/UNC Alzheimer's Disease Research Center
PI Name:	

(If PI is not the same as identified on the study.)	
Explain Any Significant Discrepancy:	

Is this a federally funded study?

(•) Yes ( ) No

Does this study have any of the following?

- Industry sponsored protocol
- Industry funded Duke protocol
- Industry funded sub-contract from another institution
- Industry provided drug/device/biologic
- SBIR/STTR funded protocol

( ) Yes (•) No

As part of this study, will any samples or PHI be transferred to/from Duke to/from anyone other than the Sponsor, a Sponsor subcontractor, or a Funding Source?

(•) Yes ( ) No

Is the Department of Defense (DOD) a funding source?

( ) Yes (•) No

For Federally funded studies:

Is your funding subject to, and does it comply with, the funding agency's policy for data sharing?

(•) Yes ( ) No

Check all that apply:

- [ ] NIH Genome Sharing - dbGaP
- [ ] NIH Genome Sharing - GWAS
- [ ] NIH Genome Sharing - NCI databases
- [ ] NIH Genome Sharing - other
- [ ] Non-NIH Genomic
- [x] General Data Sharing

Enter the Grant Number or Other Federal Agency Proposal or Application Number:

1P30AG072958-01

Note: The Federal Funding Agency ID Number is the Sponsor's grant number assigned to your project and available on your Notice of Award (example: R01HL012345).

If known, enter the SPS (Sponsored Projects System) number if applicable:

0

In the Initial Submission Packet, attach the following:
(1) The entire grant, or an explanation of why a grant is not needed.
(2) NIH institutional Certificate form related to data sharing (if applicable).

Mobile Devices and Software

Does this study involve the use of a software or a mobile application?

(●) Yes ( ) No

Please describe the following:

- The developer of the mobile app and how the app will be obtained.
- What PHI will be collected via the app.
- Where the data will be stored and who will have access to it.

N/A

List all software, including third party (non-Duke) and mobile apps, that will be utilized for ascertainment, recruitment, or conduct of the research/project: (eg, MaestroCare, DEDUCE):

Duke Qualtric
Duke Drop Box
Duke REDCap
PEDIGENE (part of ARENA data management system)
Duke MaestroCare
Sony ICD-UX560 or ICD-PX470 Stereo Digital Voice Recorder (or other similarly encrypted alternatives)
GlobalApp
VRFCAT (utilizing company provided iPads)

Are you using FCAP (Federated Clinical Analytics Platform) for this study?

( ) Yes (●) No

Multi-site Research

Is this a multi-site study?

(●) Yes ( ) No

Is the Duke PI/Co-PI the lead investigator or primary grant awardee?

(●) Yes ( ) No

Is the primary grant awardee a Duke employee?

(•) Yes ( ) No

Is a Duke employee the holder of the IND or IDE?

( ) Yes
( ) No
(•) N/A

Is Duke the central coordinating center for this study?

(•) Yes ( ) No

Is Duke serving as a central statistical center for this study?

(•) Yes ( ) No

Is Duke serving as a central laboratory, reading center, analysis center or other central resource for this study?

(•) Yes ( ) No

Do you have ten or more sites?

( ) Yes (•) No

Complete for each site if Duke is the Primary grant awardee or coordinating center:

Entry 1

Site Name:	UNC-CH
City:	Chapel Hill
State/Province:	NC
Country:	USA
	Site Contact Information
Primary Contact Name:	Weili Lin
Primary Contact Phone:	919-843-8120
Primary Contact Email:	weili_lin@med.unc.edu
	Site Details

Does the site have an IRB?	(•) Yes ( ) No
Site IRB approval expiration date:	01/29/2026
If date not provided, explanation of why:	
Has the site granted permission for the research to be conducted?	(•) Yes ( ) No
Does the site plan to rely on the DUHS IRB for review?	(•) Yes ( ) No
What is the status of the study at this site?	(•) Open ( ) Closed
Site approval letters or site personnel lists:	Attach site approval letters, site closure letters (if applicable), or site personnel lists in the Initial Submission Packet.

Provide a description of the procedures that will be used to inform sites of unanticipated problems involving risks to subjects or others, interim results, protocol modifications and other information that may be relevant to the protection of subjects:

The PI at Duke (Dr. Whitson) will be the centralized contact to coordinate communication between the sIRB at Duke and other sites/local IRBs. She will spearhead monthly conference calls attended by the PIs at each site, as well as weekly meetings with the Clinical teams and Core Leaders. As relevant, additional team members, including Project Coordinators, will participate in such meetings. An agenda item will be included during each call for discussion or update regarding the single IRB arrangement. Participating sites will provide necessary information, assurances or adverse events to the Duke study team for submission to the Duke IRB and the respective local IRB. The Duke IRB office will communicate directly with the Duke PI and study team, with regular meetings to go over IRB-related issues. When appropriate, the Duke IRB office will communicate directly with the relying sites' Human Research Protection Program offices.
Relying site (UNC) will follow local procedures to coordinate, collect, verify, and locally distribute information
such as:
• Local context
• Conflict of Interest disclosure and management
• Completion of ancillary reviews
• Training and qualifications of study team (IRB, ethics)
• Continuing Review or Closure information
• Reportable Events

How will you ensure that management, data analysis, and data safety and monitoring systems are adequate, given the nature of the research involved?

The Duke Data Center (DDC) will work closely with the PIs and will oversee consistent application of scientific standards and methodological rigor for data collection, processing, entry, cleaning, and analytics. This will be accomplished by intensive training of all study staff, the development of well-defined study specific procedures (SSPs), and Manuals of Procedures (MOPs) with detailed instructions for procedures involved in data acquisition, processing, and upload to the REDCap platform. Fidelity to research procedures will be accomplished by the development of well-defined protocols and internal audits.

How will you ensure that sample protocols and informed consent documents are developed and distributed to each collaborating institution?

The Duke Site will:
Submit IRB application to sIRB. Distribute copies of IRB-approved documents to sites for editing and submission to local IRBs. Oversee and collect all required documentation and assurances (e.g., FWA to OHRP and reliance agreements) from sites for sIRB. Review and assist in site IRB applications for study as needed. Maintain records of IRB submissions, approvals, and expiration dates for all study sites. Provide guidance on IRB forms and track annual continuing reviews. Post IRB documents and regulator

documentation to central website. Distribute approved protocol changes/amendments to sites and develop SOPs to assure updates are distributed and receive IRB approval prior to initiation of any changes.

How will you ensure that each collaborating institution holds an applicable OHRP-approved Assurance?

Ongoing current proof of Site-specific IRB Assurance will be collected (and updated as warranted) from each site, and maintained at Duke.

How will you ensure that each protocol is reviewed and approved by the IRB at the collaborating institution prior to the enrollment of subjects?

Ongoing current proof of Site-specific IRB approval will be collected (and updated as warranted) from each site, and maintained at Duke. These approvals will be uploaded as part of continuing review submissions to the Duke IRB.

How will you ensure that any substantive modification by the collaborating institution of sample consent information related to risks or alternative procedures is appropriately justified?

Collaborating institution (UNC) will provide all approved consent versions back to the Duke site, and any significant modifications from the Duke provided template will be shared with the Duke IRB to confirm appropriateness prior to use with subjects.

How will you ensure that informed consent is obtained from each subject in compliance with DHHS regulations?

Subject consent will occur either electronically, stored directly in REDCap, or when completed on paper, will be scanned and uploaded into REDCap to allow for coordinating site consent review QC activities.

Research Abstract

Please type your Research Abstract here:

The Research Abstract should summarize the main points of your study in one paragraph. The following guidelines may help you:

1. Purpose and objective (1-2 sentences)
2. Study activities and population group (2-4 sentences)
3. Data analysis and risk/safety issues (1-2 sentences)

The purpose of the study is to establish a clinical cohort for the Duke/UNC Alzheimer's Disease Research Center (ADRC). The cohort will be composed of subjects ages 25 to 44 at enrollment with normal cognition and subjects ages 45 to 80 at enrollment with normal cognition, mild cognitive impairment and a dementia diagnosis. Initial data including demographics, medical and family history, physical exam, neuropsychological testing will be obtained. Participants will most likely be asked to contribute a blood and urine sample, a cerebrospinal fluid sample, and undergo a MRI scan. The cohort ages 45 to 80 will be seen yearly until death to evaluate medical status, undergo neuropsychological testing and possibly collect additional samples or undergo additional imaging. All data will be de-identified and stored by the ADRC.

Research Summary

State your primary study objectives

The primary objective is to create a clinical cohort for the Duke/UNC ADRC, enrolling 100 subjects per year until recruitment goals are met; thereafter we will enroll new participants only to replenish the cohort following subject death, withdrawal or loss to follow-up. The ages of the cohort will be 25 to 44 and 45 to 80 at the time of enrollment. Subjects ages 45 to 80 must have a project partner as part of the study. The cohort will undergo baseline data collection according to the current guidelines of the Uniform Data Set, set forth by the National Alzheimer's Coordinating Center including medical and family history, socioeconomic demographics, physical exam, neuropsychological testing, blood and urine sample, cerebrospinal fluid sample, and brain MRI. A subject's project partner can be substituted for another one,

and if so, the new potential project partner will be consented into the study. Subjects in the ages 45 to 80 group will be re-evaluated every year with a medical history update, physical exam and neuropsychological testing.

Additional blood, fluid or imaging may be requested at later dates. As part of their enrollment in the cohort the subjects will be presented yearly to a consensus committee to confirm diagnosis. A subset of the cohort ages 45 to 80, unable or unwilling to have the Lumbar Puncture, may alternately be offered to supplement a PET Scan to confirm diagnosis if/when AD symptoms are present.

The Duke/UNC ADRC obtained funding from the National Institute of Aging (NIA) in September 2021 and is an NIA designated ADRC program.

State your secondary study objectives

- n/a

Please select your research summary form:

Standard Research Summary Template

This is the regular (generic) research summary template which is required for all regular applications (unless your protocol fits under the other research summary templates in this category). Use of these instructions is helpful for ensuring that the research summary contains all necessary elements.

Standard Research Summary

Purpose of the Study

- Objectives & hypotheses to be tested

The purpose of the study is to build a clinical cohort of adult research subjects with normal cognition, mild cognitive impairment (MCI) and dementia due to Alzheimer's disease and other related dementias (ADRD). The primary objective of this cohort will be to advance research on neurodegenerative brain disorders and the role of age, sex and genetics (especially APOE genotype) on their manifestation.

Background & Significance

- Should support the scientific aims of the research

Approximately 5 million Americans are currently suffering from Alzheimer's disease and related dementias (ADRD) with twice that number affected by mild cognitive impairment. Currently over $100 million per year is spent on direct and indirect costs of caring for people with ADRD. Unless effective interventions are found the numbers of people with ADRD will continue to increase as the population ages.

Alzheimer's Disease Research Centers have been in existence since 1984 when Congress directed the National Institutes of Health (NIH) and the National Institute on Aging (NIA) to increase research on dementia. Dementia research continues to be a national priority. In 2011 Congress passed the National Alzheimer's Project Act with the primary goal of preventing and effectively treating ADRD by 2025. This act created increased funding opportunities for Alzheimer's Disease Centers to increase advances in the field through research and resource generation and sharing. In 2017, strategic planning by the NIA resulted in

recommendations including establishing new cohorts to build predictive models of disease and wellness and sharing of data, disease models and biological specimens for research purposes. Participants in a cohort should be well characterized with standardized clinical data collection and followed yearly until death.

As an NIA designated Alzheimer's Disease Research Center, the Duke/UNC ADRC is establishing a clinical cohort of research participants ages 25 to 44 who have a one time set of visit and a clinical cohort of research participants ages 45 to 80 who have a baseline set of visits and are followed yearly. Both groups will contribute biological samples kept in the ADRC repository.

This project will establish a clinical cohort at Duke and UNC with standard clinical data gathering and biological samples that can be used for current and future research studies at Duke and in the future, as part of collaboration with other Alzheimer's Disease Centers and national and international research projects including the National Central Repository for Alzheimer's Disease and Related Dementias (NCRAD) and the National Institute on Aging Genetics of Alzheimer's Disease Data Storage Site (NIAGADS).

Design & Procedures

- Describe the study, providing details regarding the study intervention (drug, device, physical procedures, manipulation of the subject or the subject's environment, etc.). Discuss justifications for placebo control, discontinuation or delay of standard therapies, and washout periods if applicable. Identify procedures, tests and interventions performed exclusively for research purposes or more frequently than standard of care. Include alternative therapies, concurrent therapies discontinued per protocol, risk benefit ratio, and use of tissue/specimens. Discuss monitoring during washout periods if applicable. Include brief description of follow-up, if any.

Subjects with normal cognition, mild cognitive impairment and dementia diagnosis will be recruited from clinical visits at the Duke Neurology Memory Disorders Clinic at Morreene Road. Subjects will also be enrolled by self-referral and active recruitment through participation in existing studies, registries, educational talks at community organizations and community health fairs. Subjects in the ages 45-80 cohort must have a dedicated project partner of their choice at time of enrollment. The project partner is an individual who knows the participant well, preferably a family member (e.g. spouse, adult child). Written informed consent will be obtained from all participants and their project partners (via paper or via eConsent). Besides answering questions about the participant, we are mandated to ask the project partners very basic demographic information about themselves. For example; race, ethnic background, gender, month & year of birth, years of education, relationship to participant, and type & frequency of contact with the participant. A potential subject screening log will be securely maintained, including potential subject Name, Contact Info (Email and Preferred Phone Number), Age (aggregated 89+), Race, Zip Code, Sex, Years of Education, Referral Source, and reason for non-enrollment (when applicable). The maintaining of a basic screening log is to ensure that we do not contact people multiple times, and to ensure equitable recruitment of people among race and education levels (via aggregate analyses).

Subjects will have an initial visit with information/history gathering, physical exam, neuropsychological testing and blood draw. The project partner will be asked questions about the participant's activities of daily living (ADL's), mood, and day to day behaviors. Subjects will have follow up visits coordinating imaging, lumbar puncture and donation of other biological samples. Either Lorazepam (0.5 to 1mg) or Alprazolam (0.25 to 0.5mg) will be prescribed at the request of the participant to help mitigate anxiety during the MRI and/or lumbar puncture. Both medications are taken by mouth, and subject will be informed they must have a driver present if they decide to take this medication prior to either of these procedures. Subjects also have the option to undergo an MRI simulation that closely mimics a real MRI scanner in terms of appearance, sensation, and sound. It features an automated table, lights, and a fan to enhance the realism of the experience. Additionally, the simulator can display tasks and playback MRI sounds, ensuring subjects are well-prepared and comfortable for the actual MRI scan.

Subjects and project partners in the ages 45 to 80 cohort will have an annual follow up visit as long as they are able to participate, preferably in person, but may also occur over the telephone if necessary.

All information gathered at the initial visit and annual follow up will be entered into the the current version of the Uniform Data Set (UDS), a longitudinal data set that is submitted to the National Alzheimer's Coordinating Center (NACC). At baseline and at yearly follow up, a consensus committee will meet to make a diagnosis based upon history and presentation, neuropsychological testing, imaging, and biomarker information.

All activities are research related. Subjects ages 25 to 44 and ages 45 to 80 will have a baseline visit which may contain tests including:

At Baseline Visits (typically over 3 visits, completed within 60 days of initial visit)

- Informed consent will be obtained from subject and project partner (if not otherwise already obtained remotely)
- Subjects will be assigned a coded research identification number used for the UDS and biological specimens in the repository
- Demographics and project partner demographics
- Family history, medical history and current medications
- General physical and neurological exam, including sensory and motor testing
- Vital signs
- Blood sample will be collected for genetic testing and distributed into aliquots, which will be stored at Duke for future unspecified research on cognition and disorders associated with altered cognition with blood processed and stored by Substrate Services. For females aged 45-60, additional 10ml blood draw for ReproSURE test, processed and frozen, then sent to LabCorp for testing.
- Urine sample
- Neuropsychological testing including
  - Montreal Cognitive Assessment (MoCA)
  - Clinical Dementia Rating (CDR)
  - Craft Story 21 Recall - Immediate
  - Benson Complex Figure Copy,
  - Number Span
  - Test Forward,
  - Number Span Test Backward
  - Category Fluency
  - Trails A and B
  - Craft Story 21 Recall – Delay
  - Benson Complex Figure Recall
  - Multilingual Naming Test (MINT)
  - Verbal Fluency – Phonemic Test
  - Rey Auditory Verbal Learning Test (RAVLT)
  - Benton Judgement of Line Orientation (JoLO)
  - Virtual Reality Functional Capacity Test - short version (*VRFCAT-SLx)*

Note: To increase subject safety and reduce subject travel/time burden, portions of this visit may be conducted remotely via phone/video chat, particularly pertaining to the Uniform Data Set (UDS), version 3 which includes demographics and project partner demographics, family history, medical history, current medications and neuropsychological testing.

- Retinal imaging (non-invasive screening of subject's eyes to look for potential signs of Alzheimer's or related disorders)
- Additional testing of subject's memory, thought processes and recognition, including the PHQ8 and GAD 7. We will also assess menopause status on appropriate female subjects using the Menopause Specific Quality of Life (MENQOL) questionnaire and the Stages of Reproductive Aging Workshop (STRAW) + 10 staging system (STRAW-10).

- MRI of the brain will be performed at Duke.
- (except when not applicable) LP will be performed in the Morreene Road Clinic as well as the ADRC offices in the Hock Plaza Building (2424 Erwin Road, Suite 103), by a neurologist or in the PACU or Medicine Pavillion by an anesthesiologist proficient in the task. Subjects will be informed about the risk of Lumbar Puncture (LP) and a procedure consent signed. The LP will be done using standard aseptic technique in a lower lumbar intervertebral interspace. No more than 15 ml's of CSF will be collected in vials containing a bar coded label indicating the subjects ADRC ID number, but no PHI. Samples will be frozen on dry ice and transported to the Duke Substrate Services Core Research Support, for processing and storage. If the study doctors believe that a Blood Patch is necessary, this may be conducted by a study physician.
- A member of the Duke ADRC team will call subjects 1-3 days after the LP to discuss their health and confirm any AEs.
- Where applicable, PET scans will be obtained (in accordance with ADRC parameters) at either Duke or the UNC Biomedical Research Imaging Center (BRIC).

Information gathering, neuropsychological testing, blood sample, and urine sample will be done at the Duke Neurology Outpatient Office at Morreene Road, as well as the ADRC offices in the Hock Plaza Building (2424 Erwin Road, Suite 103). Lumbar puncture will be conducted at these offices, but may also be conducted at the Duke North PACU at the discretion of the PI. MRI will be done at Duke Radiology.

Responses will be recorded as subjects respond to various cognitive testing questions. We will record the audio with a Sony digital voice recorder, or other secure audio recording device and software. Subjects will be told that their voice is being recorded and that no additional personally identifying information will be on the saved recording, beyond their voice alone. All recordings will be given a unique identifier before

they are uploaded to Duke Box. Once the upload is complete, all data will be deleted from the voice recorder. No PHI will ever be stored on the digital voice recording device. The data will be used for testing scoring purposes, and may be shared for research purposes only if participants give their consent to do so, as indicated on their consent form.

Yearly evaluations

Subjects and project partners in the ages 45 to 80 cohort will be contacted approximately every 12 months for a follow-up evaluation. At the yearly follow up evaluation we will update medical information and perform neuropsychological testing. We may also collect additional blood or CSF and additional imaging. These follow-up evaluations are done ideally in person but also can be conducted over the telephone. Participants will be asked to participate in yearly evaluations until the time of death. Participants can withdraw from the study at any time without concern for the future of their care.

Engagement Activities
Participants will have the opportunity to attend occasional engagement events that may include updates on the study and Alzheimer's Disease research, as well as information on brain health and aging.

Consensus Committee Diagnosis

After data collection is completed, a consensus committee composed of representatives from neurology, neuropsychology and imaging will meet on a bi-weekly to monthly basis to review information on each subject and come to a consensus diagnosis. Each subject will be reviewed at baseline and yearly.

Storage of data

All data gathered as part of the UDS will be stored in Redcap on a secure server.

Storage of samples

Blood and CSF samples will be stored in a freezer at -80°C at the Duke Substrate Services (SSCRS) under the direction of the Duke ADRC. Substrate Services Core Research Support (SSCRS) serves as a centralized processing core and storehouse at Duke for research samples for large clinical, consortium-based collaborations and for basic, discovery science. Samples will not contain any PHI and will be assigned a Repository ID number. Study staff will maintain the link between the PHI and samples on a password protected server in the ADRC.

Samples are stored indefinitely or until samples are exhausted. Subjects can request to have their samples withdrawn by sending a written request to the PI.

Research and Specimen Sharing

We will share subject's coded biological samples and data with the National Cell Repository for Alzheimer's Disease and Related Dementias (NCRAD), a research facility at Indiana University that is supported by the National Institute on Aging to facilitate genetic research in Alzheimer disease, aging, and related disorders. All biological samples sent to NCRAD will also be stored indefinitely and processed at NCRAD for use by qualified scientists at other Alzheimer's Disease Centers and other research centers (including other academic and commercial laboratories studying Alzheimer's disease, aging, and other related disorders). In addition to the blood sample, some coded demographic information about the subject (age/year of birth, family history of dementia, and diagnosis) will be sent to NCRAD. Subject identity will not be shared with NCRAD or with any other outside investigators. Duke has an already established MTA with NCRAD. No data nor samples will be transferred, except while such an agreement is in effect.

Otherwise, all research data and specimens will be made available only to DUHS and UNC Faculty, DUHS and UNC study coordinators, and external investigators that can provide proof of current IRB approval and that have also submitted a proposal to the Principal Investigator, Dr. Heather Whitson. Investigators wishing to gain access to these data and/or samples will be required to submit a separate IRB application and consent (or proof of waiver) for this purpose. All proposals must be internally reviewed to assure appropriate use of the data/specimens and to determine feasibility and availability of resources. All requests and approvals for usage are tracked internally. We also request copies of any publications from all investigators that resulted from, or included, data/specimens from our database/repository.

It must be emphasized that all data/specimens released from the Duke/UNC ADRC database/repository are de-identified (unless granted specific subject approval to also include potentially identifiable data /specimens such as audio recordings, DNA, and retinal images). All data/specimens are coded by a unique Duke/UNC ADRC ID number rather than by name. Data and specimen information are maintained in the database according to identifier number and not by name. All original (primary) data are stored in locked cabinets in a locked room or on a Duke IT secure server which is password protected and backed up regularly. Project staff strictly protects access. No specimens/data are ever released to third outside parties unless the subject (or the participant's legal representative) has requested and consented to data release (e.g. for medical purposes). A strict confidentiality policy is in place for all project staff. Access to

the data is restricted and protected as required by law and can only be accessed by authorized investigators and research staff. For information disclosed outside of Duke University Health System and /or UNC Health System, it will be assigned a unique Duke/UNC ADRC code number. The key to the code will be kept in a secured file on the database server and the Data Management team leader will keep a secure back-up copy.

The database/repository will be maintained indefinitely as long as funding is available or until the data /specimens are exhausted.

PET Sub-study
A subset of the total ages 45 to 80 cohort (up to 100 total subjects), unable or unwilling to have the Lumbar Puncture, may alternately be offered to supplement a PET Scan. This subset will sign a main consent (LP or non-LP) as well as a specific PET consent at the time of their scan. Some PET Scans will occur at the UNC Biomedical Research Imaging Center (BRIC) facility, with imaging and data shared with the Duke site in accordance with executed data agreements.

We will presently administer the Amyloid and Tau ligands to all subjects receiving PET, unless otherwise indicated. If 2 PET scans are to occur on the same day, this will be conducted in accordance with standard safety procedures at the BRIC regarding wash-out period.

At present, UNC is seeking an IND for the approved ligands. Until those INDs have been received, we have a cap of 30 subjects per ligand. Once IND is received, it will be submitted to the UNC RDRC and the Duke IRB alog with request to lift that cap of 30 subjects.

Duke/UNC ADRC Collaboration

As the federal grant has come through supporting the Duke/UNC ADRC, there will be elements of subject and data sharing between the institutions that are presently being contractually developed. This sharing will not commence until all related agreements have been fully executed, and this IRB application (and the RDSP) will be updated accordingly at that time to describe the specifics.

Per Subaward Attachment 7: "This project/protocol is part of a Joint Federally Grant-funded Duke/UNC Alzheimer's Disease Research Center (ADRC) and the clinical cohort protocol (Pro00103958) will be multi-site with Duke as the IRB of Record. Along with the general sharing of study data between the sites, there will also be coordination of subject visits between the sites requiring contact information sharing. Also, PET scans for all subjects will be taking place at UNC so transfer of any PET data and images back to Duke will need to be permitted. We expect to utilize the same transfer method currently used between the UNC Biomedical Research Imaging Center (BRIC) and the Duke Brain Imaging and Analysis Center (BIAC). Data sharing will be primarily via shared access to REDCap (with Data Access Groups used to minimize unnecessary sharing, where appropriate), and otherwise via Duke Box.

Data elements will include but is not limited to name, contact information, MRN's, and dates."

iMIND study (Pro00111831)
For subjects enrolled via consent into both this protocol as well as the iMIND study (Pro00111831), clinical consensus, apoe, and biomarker data will be shared with appropriate KP on the iMIND study, via REDCap and Locker Room access.

UDSv4 Sub-Study
From May 2024 to July 2024, a subset of active subjects (up to 5 subjects) may complete an additional visit in order to pilot the updated UDS (version 4). Active participants and their study partners that have completed a study visit with cognitive testing between March 2024 and July 2024 will be recruited to complete an additional visit within 3 months. Subjects will return to the Hock Plaza building for the UDS version 4 (UDSv4) and will be asked to provide feedback about the visit. Data will be entered into a separate project in REDCap and will be submitted to NACC. Portions of this visit may be conducted remotely via phone/video chat.

Selection of Subjects

- List inclusion/exclusion criteria and how subjects will be identified.

Inclusion Criteria for All Subjects

- Each subject must be ≥ 25 to ≤ 80 years of age.
- Each subject must be able to read at a 6th grade level, as determined by the investigator, and must have a history of academic achievement and/or employment sufficient to exclude significant intellectual disability.
- Each subject (or legal representative) must sign the informed consent form after the scope and nature of the investigation have been explained to them, and before screening assessments. Some consent may be obtained via phone script and REDCap eConsent.
- Each participant must be willing to have an MRI and a lumbar puncture, or alternately (to the lumbar puncture) a series of PET scans.
- Each participant ages 45 to 80 must have a study partner who agrees to participate in the study and who is able to read at a 6th grade level, as determined by the investigator, and must have a history of academic achievement and/or employment sufficient to exclude intellectual disability.

Exclusion Criteria

- Evidence of a clinically relevant or unstable neurological disorder including history of multiple head injuries, stroke or other CNS conditions (MS, Parkinson's disease, etc.)
- Evidence of a clinically relevant or unstable psychiatric disorder.
- Impairment that cannot be accommodated to be able to complete a valid Neuropsychological assessment. (vision or hearing impairment, eg.)
- History of alcoholism or drug dependency/abuse within the last 2 years before enrollment.
- Potential subjects are given PHQ8/GAD7 questionnaires as screening. For those that screen fail, their questionnaire results will be kept in RedCap and we are keeping this information to track reasons for screen failure. This information will be stored for study team use only and will not be shared outside of the Duke/UNC Collaborative ADRC. For those that pass the screening, the information from the questionnaires will be used in the study. Those with a GAD-7 score >9 and/or PHQ-8 score >9 will be considered ineligible.
- An ongoing uncontrolled, clinically significant medical condition such that, in the judgment of the investigator, a subject's participation in the trial would pose a significant medical risk to the subject.
- Contraindication or intolerance to 3T MRI investigations, including implanted devices
- Inability to have an MRI.
- Unwillingness to consent to data sharing between Duke and UNC.
- History of malignancy of any organ system, treated or untreated, within the past 24 months, regardless of whether there is evidence of local recurrence or metastases. However localized tumors not requiring systemic chemo- or radiotherapy, localized basal or squamous cell carcinoma of the skin, or in-situ cervical cancer are permitted.
- If CSF sampling is scheduled for this participant: Contraindication to lumbar puncture, history of back surgery (with the exception of microdiscectomy or laminectomy over one level), signs or symptoms of intracranial pressure, spinal deformities or other spinal conditions that in the judgment of the investigator would preclude a lumbar puncture; treatment with antiplatelet medication at the time of enrollment, including but not limited to Plavix; chronic treatment with anticoagulant medications including but not limited to Coumadin and direct oral anticoagulant drugs such as Eliquis and Xarelto.

Subject Recruitment and Compensation

- Describe recruitment procedures, including what method(s) will be used, when the study will be introduced to potential participants and by whom. If any follow-up contact is planned, describe the proposed method and timing. Describe how you will ensure that subject selection is equitable and all relevant demographic groups have access to study participation (per 45 CFR 46.111(a) (3)). Include information about how many DUHS participants will be recruited. If participants are to be compensated and/or reimbursed, provide specific prorated amounts to be provided for expenses such as travel and /or lost wages, and/or for inducement to participate.

Subjects will be recruited from the Alzheimer's Disease Prevention Registry, Genematch Registry, the North Carolina Registry for Brain Health and advertisements in social media and news platforms. Affiliates of the Duke/UNC ADRC will also speak about the study at community education events and health fairs. An outreach coordinator will assist with recruitment of individuals from diverse racial and socioeconomic groups.

Subjects with mild cognitive impairment or dementia (or eligible family members) will be recruited from the Memory Disorder Clinic held at the Morreene Road Clinic. A caregiver known to the patient and/or legally authorized representative (LAR) will introduce the study to subjects with dementia and the research team will only approach patients that express interest in participation. Participants will also be recruited

from UNC Memory Clinics with a flyer and the study introduced by their provider. Subjects recruited from UNC Memory clinics will be enrolled as Duke/UNC ADRC participants.

A goal is to recruit 100 subjects per year. Over the life of the current Federal grant, the anticipated recruitment numbers for the 45-80 cohort is projected to be 420 participants and they must have a project partner - so 420 project partners.

The 25-44 cohort is projected to be 120 participants. Altogether the maximum expected enrollment over this period is 960.

Subjects will receive:

- $50 upon completion of UDS4, blood draw
- $50 upon completion of each annual (yearly) follow up
- $100 upon completion of MRI
- $100 upon completion of each PET scan
- $100 upon completion of lumbar puncture

They will be paid by ClinCard.

UDSv4 Sub-Study

Active subjects that completed a study visit between March 2024 and July 2024 will be asked to return for an additional visit within 3 months. Up to 5 subjects will be enrolled in the study including at least 1 subjects with dementia, 1 subject with mild cognitive impairment and 1 subject with normal cognition.

Subjects will receive $50 upon completion of UDSv4 via ClinCard.

Consent Process

- Complete the consent section in the iRIS Submission Form.

Subject's Capacity to Give Legally Effective Consent

- If subjects who do not have the capacity to give legally effective consent are included, describe how diminished capacity will be assessed. Will a periodic reassessment occur? If so, when? Will the subject be consented if the decisional capacity improves?

Subjects with a diagnosis of dementia will be required to have informed consent signed by an LAR. Competency to sign consent will be addressed by the PI or treating physician for subjects with mild cognitive impairment. Periodic reassessment of competency will be assessed at the yearly evaluation based upon by history and cognitive testing. Dementia is a progressive disorder with no chance of improvement so there is no chance of improvement in decisional capacity.

Study Interventions

- If not already presented in the Design & Procedures section, describe study-related treatment or use of an investigational drug or biologic (with dosages), or device, or use of another form of intervention (i. e., either physical procedures or manipulation of the subject or the subject's environment) for research purposes.

There are no study interventions involved in this research.

Risk/Benefit Assessment

- Include a thorough description of how risks and discomforts will be minimized (per 45 CFR 46.111(a) (1 and 2)). Consider physical, psychological, legal, economic and social risks as applicable. If vulnerable populations are to be included (such as children, pregnant individuals, imprisoned persons or cognitively impaired adults), what special precautions will be used to minimize risks to these subjects? Also identify what available alternatives the person has if he/she chooses not to participate in the study. Describe the possible benefits to the subject. What is the importance of the knowledge expected to result from the research?

The risks to subjects in this study are related to the lumbar puncture (risk of fainting, bleeding, bruising, headache and infection), phlebotomy (fainting, bruising and infection), sensory and motor testing (muscle strain, dizziness, falls), MRI (risk of claustrophobia), PET Scan (risk of claustrophobia and radiation exposure), and loss of privacy.

Regarding PET Scan, 2 radioactive tracers are to be used, 11c-PiB, and 18F-MK-6240, manufactured by the UNC/BRIC Radiopharmaceutical Facility in accordance with cGMP standards, and under the requisite INDs and approval by the UNC Radioactive Drug Research Committee (RDRC).

The procedures will be explained in detail to the subjects and performed using aseptic technique by experienced clinicians. Particular care will be taken to explain the procedures to subjects with dementia to allay fear and assure that the subject assents to participation. Project partners will be present with patients with dementia to provide comfort, support and explain procedures.

Privacy will be protected by identifying subjects only through an assigned ID number. The code linking PHI and UDS, repository specimens and imaging will be stored on a password protected server in the Alzheimer Disease Research Center at Duke.

There is no direct benefit to subjects from participating in this study. There is the potential for indirect benefit from advancing knowledge about dementia. Dementia is one of the most common causes of death and no disease-modifying therapies are available, so the potential benefit is great.

Costs to the Subject

- Describe and justify any costs that the subject will incur as a result of participation; ordinarily, subjects should not be expected to pay for research without receiving direct benefit.

There is no cost to the subject for participation in the study.

Data Management, Analysis and Statistical Considerations

- Describe endpoints and power calculations. Provide a detailed description of how study data will be analyzed, including statistical methods used, and how ineligible subjects will be handled and which subjects will be included for analysis. Include planned sample size justification. Provide estimated time to target accrual and accrual rate. Describe interim analysis including plans to stop accrual during monitoring. Phase I studies, include dose escalation schema and criteria for dose escalation with definition of MTD and DLT.
- **For external collaborators/personnel** who are NOT ENGAGED in the research but are handling de-identified or a limited data set of **Duke** data, include their name, role and a description of the data.

A consensus committee will meet bi-weekly to monthly to review the clinical data gathered through the Uniform Data Set, imaging, and laboratory testing to determine a baseline consensus diagnosis for each subject enrolled in the cohort. Updated data on each subject will be reviewed yearly by the committee with an updated consensus diagnosis. Otherwise, there is no data analysis as part of the clinical cohort.

The goal is to enroll 100 subjects per year in the cohort, until recruitment goals are met. Thereafter, new participants will be recruited only to replenish the cohort due to death, withdrawal, or drop-out. Subjects

will otherwise participate in the clinical cohort until the time of death, withdrawal or drop-out. The purpose of this cohort and its collected data and samples is to serve as a resource for future study. There is no end point for the study.

Data & Safety Monitoring

- Summarize safety concerns, and describe the methods to monitor research subjects and their data to ensure their safety, including who will monitor the data, and the frequency of such monitoring. If a data monitoring committee will be used, describe its operation, including stopping rules and frequency of review, and if it is independent of the sponsor (per 45 CFR 46.111(a) (6)).

This protocol does not involve treatment of subjects. Lumbar puncture and phlebotomy are procedures that are done routinely in clinic. Although lumbar punctures are routinely performed in the clinic, they are considered greater-than-minimal risk procedures. MRI has no associated risks if subjects are screened for metal and other devices before the scan. Adverse events will be documented and reviewed by the PI. Further, the PI will report adverse events and problems to the IRB in accordance with institutional and HRPP policies.

The Clinical Research Unit (CRU) Quality Assurance coordinator will review the study annually for regulatory compliance and data quality.

Privacy, Data Storage & Confidentiality

- Complete the Privacy and Confidentiality section of the iRIS submission form.

Study Scope

Does this study have a cancer focus? Cancer focus includes studies that enroll >50% oncology or malignant hematology patients; or, preventing, detecting, and diagnosing cancer or understanding the impact of cancer on patients and their caretakers.

○ Yes ◉ No

Does this study involve the use of a drug, biologic, food, or dietary supplement?

◉ Yes ○ No

Does this study involve the use of a medical device, an algorithm (whether computer based or not), an in vitro diagnostic test, or samples to look for biomarkers?

○ Yes ◉ No

Does this study employ magnetic resonance, including imaging (MRI), spectroscopy (MRS), angiography (MRA) or elastography (MRE) beyond the standard of care?

◉ Yes ○ No

Does this study specify or require the performance of diagnostic procedures using ionizing radiation (x-rays, DEXA, CT scans, nuclear medicine scans, etc.) that are beyond the standard of care?

◉ Yes ○ No

Does this study specify or require the performance of therapeutic procedures using ionizing radiation (accelerator, brachytherapy or systemic radionuclide therapy) that are beyond the standard of care?

○ Yes ◉ No

Does this study specify or require the use of a laser system for diagnosis or therapy that is beyond the standard of care (excludes the use of lasers as a standard surgical instrument)?

○ Yes ◉ No

Will the participant be subjected to increased or decreased ambient pressure?

○ Yes ◉ No

Do you plan to recruit subjects from Duke Regional Hospital (DRH)?

○ Yes ◉ No

Do you plan to recruit participants from Duke Raleigh Hospital or any Wake County Clinic(s) that are governed by Duke Raleigh Hospital (e.g. Duke Cancer Centers located in Wake County)?

○ Yes ◉ No

Does this study include using the Duke logo in any advertisements?

◉ Yes ○ No

Is this study retrospective, prospective, or both?

"Retrospective" means that data or samples already in existence (collected prior to the study submission) will be used.
"Prospective" means there will be data or samples collected in this study for research purposes.

○ Retrospective
◉ Prospective
○ Retrospective and Prospective

If the study is both retrospective and prospective: Is this a review solely of information collected for non-research purposes (i.e. a review of medical records)?

○ Yes ○ No

Does this protocol include any research using botulinum toxin, including the FDA-approved clinical product (Botox)?

○ Yes ◉ No

Does this protocol involve the administration of any of the following materials to humans?

Category of Investigational Product	Examples

Any mRNA	Pfizer or Moderna COVID-19 vaccines
Any viral vector	AAV vector, adenoviral vector (e.g., J&J or Astrazeneca COVID-19 vaccine)
Any genetically-modified cells	CAR-T cells (e.g., Kymriah, or other autologous cells)
Any genetically-modified organisms (virus, bacterium, or other agents)	Oncolytic viruses (Imlygic, others), certain live attenuated vaccines, challenge viruses or challenge bacteria
Any plasmid DNA	DNA vaccines
Any other recombinant or synthetic nucleic acid (DNA, RNA, others)	

○ Yes ◉ No

Subject Population Groups and Enrollment

Population Groups (Select targeted population groups only):

- ☑ Adults
- ☐ Minors who are Wards of State
- ☐ Minors
- ☑ Duke Patients
- ☐ Pregnant individuals
- ☐ Fetuses
- ☐ Imprisoned Persons
- ☑ Adults incapable of giving consent
- ☑ Adults with diminished capacity
- ☐ Disabled subjects
- ☐ Students
- ☐ Employees
- ☑ Healthy Controls
- ☐ Deceased subjects
- ☐ Blanket Protocol

Please select any population groups excluded from participation in this study:

- ☑ Pregnant individuals

Will you administer a pregnancy test to eligible female subjects prior to the start of study activities?

◉ Yes ○ No

Maximum number of subjects to be consented at Duke:

Enter a single number. If you anticipate consenting a range of subjects, enter the **upper** limit of the range. The number should represent the maximum number of subjects for the life of the study.

960

Maximum number of subjects to be consented at all sites:

Enter a single number. If you anticipate consenting a range of subjects, enter the **upper** limit of the range. The number should represent the maximum number of subjects for the life of the study.

960

Subject Procedures and Costs

Biobank - Does this study involve the collection, use, tracking, banking (storage) or distribution of human biological specimens?

Human biological specimens include blood or its components, healthy or diseased tissue, bodily fluids, DNA /RNA or human stem cells.

(•) Yes ( ) No

Procedures

Check all that apply:

- [x] Genetic Testing
- [ ] Gene Transfer
- [x] DNA Banking
- [ ] Testing for Reportable Infectious Diseases
- [ ] Human Cell Banking
- [ ] *Use of Human Embryonic Stem Cells
- [ ] *Use of Human-induced Pluripotent Stem Cells
- [ ] *Use of Other Cells Derived from Human Embryos
- [ ] *Use of Human/Animal Chimeric Cells
- [ ] *Specialized Cell Populations for Cell Therapy
- [ ] Use of Human Tissue
- [x] Use of Bodily Fluids
- [x] Use of Blood (or its components)
- [ ] Not Applicable

Will blood be drawn in this study for research purposes?

(•) Yes ( ) No

Maximum amount to be drawn in any 8 week period (ml):

70

Number of blood draws per week:

0

Will the Operating Room be used in this study?

Include only research time, not clinical care time.

( ) Yes (•) No

Will there be extra costs to subjects or insurance as a result of the research (e.g. tests, hospitalization)?

○ Yes ◉ No

Will there be Subject Compensation?

◉ Yes ○ No

Compensation for Travel / Lost Income (in USD):

0

Other Subject Compensation:

Subject partner will be paid $50 (each) for each completed visit The subject will receive:
• $50 upon completion of Visit 1
• $50 upon completion of each annual (yearly) follow-up
• $100 upon completion of Visit 2
• $100 upon completion of Visit 3

UDSv4 Sub-Study: $50 upon completion of visit

Additional travel (mileage) compensation may be provided for distances of greater than 15 miles each way. We can provide reimbursement up to $250 for round-trip mileage from your home to each study visit at the current IRS rate. In the unlikely situation that an overnight stay near the research site is needed, we will provide accommodation at a local hotel and will reimburse meal expenses up to the Federal per diem rate, with receipts.

Subjects may additionally be provided:
1) up to $30 reimbursement ($15/person, $30 total if subject and caregiver), per visit, to aid with costs for meals during on-site visits.
2) a gift Totebag (value, less than $5 each) to each subject, to aid in confidential carrying of study related materials.

Subject Recruitment Materials

For each document to be reviewed, use the table below to provide the following information:

Attach a copy of each advertisement to be used with this study in the Initial Submission Packet. If any advertisement will have multiple wording variations, attach a copy of each version of the advertisement. For media materials (i.e., videos, radio ads, commercials), include transcripts and links.

If an advertisement includes the Duke logo, be sure to indicate "yes" in Study Scope section.

The IRB must approve all study advertisements used to recruit.

Types of subject recruitment materials include, but are not limited to, the following:

Direct Advertising
Posters
Billboards
Flyers
Brochures

Media Advertising
Newspaper Ads
Magazine Ads

Radio Ads
TV commericals / Video
Internet website
Social Media

Other Types of Advertising
Newsletter
Email
Postcards / Letters

(Note: Doctor-to-Doctor letters do not require IRB approval)

Document name	Material category	Location material displayed	Has this material previously been approved by the IRB?
ADRC Flyer 1	(•) Billboard / Flyer / Poster ( ) Brochure ( ) Internet website / Email ( ) Letter / Postcard ( ) Phonescript ( ) Radio ( ) Television / Video ( ) Newsletter / Newspaper / Magazine ( ) Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. For use in the Duke and UNC memory clinics, to recruit participants	( ) Yes (•) No
ADRC Flyer 2	(•) Billboard / Flyer / Poster ( ) Brochure ( ) Internet website / Email ( ) Letter / Postcard ( ) Phonescript ( ) Radio ( ) Television / Video ( ) Newsletter / Newspaper / Magazine ( ) Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. For use in the Duke and UNC memory clinics, to recruit participants	( ) Yes (•) No
ADRC Flyer - Multicultural	(•) Billboard / Flyer / Poster ( ) Brochure ( ) Internet website / Email ( ) Letter / Postcard ( ) Phonescript ( ) Radio ( ) Television / Video ( ) Newsletter / Newspaper / Magazine ( ) Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. For use in the Duke and UNC memory clinics, to recruit participants. May also be posted in Social Media.	( ) Yes (•) No

ADRC Flyer - Black Family	◉ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email ○ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. For use in the Duke and UNC memory clinics, to recruit participants. May also be posted in Social Media.	○ Yes ◉ No
ADRC Flyer - Hispanic Family	◉ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email ○ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. For use in the Duke and UNC memory clinics, to recruit participants. May also be posted in Social Media.	○ Yes ◉ No
ADRC Flyer - White Family	◉ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email ○ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. For use in the Duke and UNC memory clinics, to recruit participants. May also be posted in Social Media.	○ Yes ◉ No
Dr. Liu Message	○ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email ○ Letter / Postcard ○ Phonescript ○ Radio ◉	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Video can be access by this link:	○ Yes ◉ No

	○ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	https://duke.box.com/s/endgc5gsgxkk8uj7terfveuezzjiqhny Will be shown to or shared with prospective study subjects.	
MH Interview	○ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email ○ Letter / Postcard ○ Phonescript ○ Radio ◉ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Video can be access by this link: https://duke.box.com/s/l0e427zx1qo0pw1qddvo1briop6gwlp6 Will be shown to or shared with prospective study subjects.	○ Yes ◉ No
Genematch Member Letter	○ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email ◉ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Genematch will send a personal email to each potential participant	○ Yes ◉ No
Results Brochure	○ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email ○ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Provided to each participant during their results meeting in person or via zoom	○ Yes ◉ No
	○ Billboard / Flyer / Poster ○ Brochure	Please be specific. For example, "Duke"	

APOE Results slide presentation	○ Internet website / Email ○ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ◉ Other	would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. For use when providing APOE results to subjects	○ Yes ◉ No
MRI Disc label	○ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email ○ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ◉ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. On any MRI discs provided to subjects, there will be a warning label that "this MRI was done as part of a research study. The MRI images are research quality. Results should not be used for clinical purposes."	○ Yes ◉ No
DukeUNC Alzheimer's Disease Collaboration Flyers - Doc1	◉ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email ○ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Collection of flyers for use in community. Previously approved for use under another ADRC protocol.	◉ Yes ○ No
DukeUNC Alzheimer's Disease Collaboration Flyers - Doc2	◉ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email ○ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Collection of flyers	◉ Yes ○ No

	○ Newsletter / Newspaper / Magazine ○ Other	for use in community. Previously approved for use under another ADRC protocol.	
DukeUNC Alzheimer's Disease Collaboration Flyers - Doc3	◉ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email ○ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Collection of flyers for use in community. Previously approved for use under another ADRC protocol.	◉ Yes ○ No
DukeUNC Alzheimer's Disease Collaboration Flyers - Doc4	◉ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email ○ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Collection of flyers for use in community. Previously approved for use under another ADRC protocol.	◉ Yes ○ No
DukeUNC Alzheimer's Disease Collaboration Flyers - Doc5	◉ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email ○ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Collection of flyers for use in community. Previously approved for use under another ADRC protocol.	◉ Yes ○ No
	○ Billboard / Flyer /		

Hard to Reach letter	Poster ○ Brochure ○ Internet website / Email ◉ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Letter to be sent to subjects who have been difficult to reach.	◉ Yes ○ No
MRI Scan Prep video	○ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email ○ Letter / Postcard ○ Phonescript ○ Radio ◉ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Shown to participants, pre-MRI. Video can be accessed by this link: https://www.ypo.education/medical-tests/mri-t257/video/	○ Yes ◉ No
ADRC First Year Visits letter	○ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email ◉ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Provided to participants during pre-screening to help understand Year 1 participant expectations.	○ Yes ◉ No
ADRC First Year Visits NON LP letter	○ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email ◉ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Provided to	○ Yes ◉ No

	○ Newsletter / Newspaper / Magazine ○ Other	participants during pre-screening to help understand Year 1 participant expectations.	
Incidental MRI findings - Letter to participant	○ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email ◉ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Letter to provide to participant when neuro-radiologist finds a concerning finding on participant's MRI scan. Letter is sent after clinician contacts participant about finding.	○ Yes ◉ No
Incidental MRI findings - Letter to Medical Provider	○ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email ◉ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Letters to provide to participant's medical provider when neuro-radiologist finds a concerning finding on participant's MRI scan. Letter is sent after clinician contacts participant about finding.	○ Yes ◉ No

Consent Process

Attach draft consent forms in the Initial Review Submission Packet.

Consent forms must be MS Word documents and follow the specific format outlined by the IRB. **Click here** to download a copy of the consent form template.

Note: Please do not edit the section of the footer that contains the Protocol ID, Continuing Review and Reference Date fields. Those fields will be used to stamp the final consent form when it is approved by the IRB. If you want to add an internal version date, please put it in the header.

Who will conduct the consent process with prospective participants?

Provide their role(s) in this study (PI, Study Coordinator, etc.):

Designated key personnel will consent subject and the subject partner. This consent may either occur in person, or via phone (or approved, non-recorded method of video-call) utilizing a script as well as REDCap eConsent. Script will ask patients if sending them consent via email for discussion purposes is acceptable, prior to doing so.

Who will provide consent or permission?

(Select all that apply):

- [x] Participant
- [ ] Parent(s) or Legal Guardian(s)
- [x] Legally Authorized Representative (LAR)

How much time will the prospective participant (or legally authorized representative) have between being approached about participating in the study and needing to decide whether or not to participate?

If you are not giving the person overnight to consider whether or not to participate, please justify.

As much time as needed will be given for potential subjects and their study partner to decide about study participation.

Where will the consent process occur?

The in-person consent process will occur in the Duke Neurology clinics or at the ADRC offices in the Hock Plaza Building (2424 Erwin Road, Suite 103).

Alternately, it may occur via phone/video utilizing the Screening/Consent script, as well as REDCap eConsent. Potential Subjects (and Caregivers) will be sent an email containing a link to REDCap, allowing them to create individual credentials, then read through the consent online while it is being discussed with them. Finally, the subjects/caregivers will be able to sign their consents electronically.

Finally, if potential subjects contacted by phone do not have email/internet access, consent could be mailed to them prior to review by phone, then signed consent could be returned at Visit 1.

Regarding subject re-consent related to the data sharing between Duke and UNC, it will be specifically sought during a given subject's next research/clinic visit, if not sooner.

What steps will be taken in that location to protect the privacy of the prospective participant?

Any potential subject and their study partner will be taken to a private setting to discuss participation in the research.

How much time will be allocated for conducting the initial consent discussion, including presenting the information in the consent document and answering questions, with each prospective participant?

At least 1 hour will be designated for the consent process. However, if subject or subject partner have additional questions time will be made to address questions or concerns. Subjects and their study partners will also be given instructions regarding who to contact if they have additional questions after the consent process.

What arrangements will be in place for answering participant questions before and after the consent is signed?

Subjects and their study partners will also be given instructions regarding who to contact if they have additional questions after the consent process.

Describe the steps taken to minimize the possibility of coercion or undue influence.

Subjects and their study partners will be given as much time as needed to decide whether they wish to participate in the research. They will also be reminded that their participation is voluntary and that they may withdraw at any time. Because of the potential for diminished cognitive capacity in this population, enrolled subjects will be evaluated yearly for decision making capacity and will be asked to give assent if appropriate and necessary.

What provisions will be in place to obtain consent from participants who do not read, are blind or who do not read/understand English?

Currently, there are no plans to obtain consent from participants who do not read, are blind or who do not read /understand English.

Do you plan to obtain written consent for the conduct of research?

(●) Yes ( ) No

Protected Health Information (PHI)

Indicate how you intend to use potential subjects' Protected Health Information (PHI):

( ) I will review, but not record, PHI prior to consent.
(●) I will record PHI prior to consent.
( ) I do not intend to use PHI prior to consent.
( ) I will record PHI without consent. (decedent research, database repository, chart review)

Request for Waiver or Alteration of Consent and/or HIPAA Authorization

Will the population include deceased individuals?

(●) Yes ( ) No

This waiver request applies to the following research activity or activities:

☑ Scheduling of research activities in MaestroCare and/or the recording of PHI via telephone for screening purposes prior to obtaining written consent for the research. Scheduling of research activities in MaestroCare and/or the recording of PHI via telephone for screening purposes prior to obtaining written consent for the research.
☑ Ascertainment (identification, selection) and/or recruitment of potential subjects while recording identifiable private information, such as protected health information (PHI), prior to obtaining the subject's consent.
☐ Conduct of the research project without obtaining verbal or written consent and authorization.

Note: Answer the questions below as they pertain solely to PHI collected prior to consent.

Provide the following information:

List the elements of informed consent and/or HIPAA authorization for which waiver or alteration is requested:

- Provide the rationale for each.

We are requesting a waiver of all elements of consent and HIPAA. Subjects will be recruited from the Alzheimer's Disease Prevention Registry, the North Carolina Registry for Brain Health and other registries, as well as from the Duke and UNC Neurology and primary care clinics. Subjects have given prior consent to be part of these registries. The project partner will not be recruited, as this will be someone familiar to the potential subject.

List the specific protected health information (PHI) to be collected and its source(s):

- (Note: PHI = health information + identifiers)

Name, age, sex, pertinent health information and past medical evaluations related to cognition will be collected from potential research subjects or their legally authorized representative. A screening log will be securely and separately maintained from the enrollment log and subject database, including potential subject Name, Contact Info (Email and Preferred Phone Number), Age (aggregated 89+), Race, Zip Code, Sex, Years of Education, Referral Source, and reason for non-enrollment (when applicable). Contact info is included here to keep this information centralized and secure, yet remotely accessible to study staff so that they do not need to keep contact information in less secure locations. Access to this screening log will be limited to study team members with appropriate REDCap access rights.

Criteria for Waiver: The DUHS IRB may waive the requirement for informed consent and authorization if all of the following criteria are met:

- Please respond to each item in the space below using protocol-specific language to provide justification:

a) The research or clinical investigation involves no more than minimal risk to subjects:

The information will be gathered by Duke/UNC ADRC research staff in a secure location and will only be shared with investigators. There is no more than minimal risk to subjects to identify potential subjects for this research.

b) The waiver or alteration will not adversely affect the rights and welfare of the subjects. Include a description of any measures to be taken to ensure that the rights and welfare of subjects will be protected:

This waiver will not adversely affect the rights or welfare of potential subjects. All efforts will be made to protect subject confidentiality as we use this waiver to ascertain potential subjects.

c) Whenever appropriate, the subjects will be provided with additional pertinent information after participation:

There will be no information to report to subjects, as this is a registry.

d) If this research activity relates to research involving deception, explain how subjects will be provided with additional pertinent information after study participation and what information will be provided. Otherwise indicate "not applicable":

Not applicable.

e) The use or disclosure of protected health information involves no more than minimal risk to the privacy of individuals, based on, at least, the presence of the following elements (e1. and e2.)

Demonstrate that the use or disclosure of PHI involves no more than minimal risk to the privacy of subjects by describing the plans requested below:

e1) An adequate plan to protect the identifiers from improper use and disclosure. Describe the plan (how protection will be accomplished) and indicate where the PHI will be stored and who will have access:

Only Duke/UNC ADRC staff will record or have access to PHI through EPIC, Duke REDCap, or through phone calls. Whenever possible we will use the minimum necessary PHI to ascertain potential subjects. Any PHI will be stored on a secure shared drive maintained by Duke IT and the Duke/UNC ADRC, or in Duke REDCap. Subject consents will be either uploaded into REDCap, or entered there directly via eConsent.

e2) An adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law.

Describe the plan (how and when identifiers will be destroyed and by whom). If there is a health or research justification for retaining the identifiers or such retention is otherwise required by law, provide the reason to retain identifiers:

Subject identifiers used for identification and ascertainment of subjects will be destroyed at the earliest possible date, consistent with the conduct of the research. This will be done by designated member(s) of the study team. A screening log will be securely maintained, including potential subject Name, Contact Info (Email and Preferred Phone Number), Age (aggregated 89+), Race, Zip Code, Sex, Years of Education, Referral Source, and reason for non-enrollment (when applicable). As it is being maintained to ensure that we do not contact people multiple times and to ensure equitable recruitment of people among race and education levels (via aggregate analyses), this log will be destroyed at the conclusion of subject enrollment. Contact info is included here to keep this information centralized and secure, yet remotely accessible to study staff so that they do not need to keep contact information in less secure locations.

e3) Adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity except (i) as required by law, (ii) for authorized oversight of the research study, or (iii) for other research for which the use or disclosure of PHI would be permitted by the HIPAA Privacy Rule. By electronically signing this submission, the PI provides this written assurance:

Acknowledged.

f) The research could not practicably be conducted or carried out without the waiver or alteration:

- Explain why informed consent/authorization can not be obtained from subjects.

It would be impractical to consent subjects who have not been identified or to re-consent subject who have already given prior consent to be part of a registry. The study does not have the resources or the bandwidth to contact a large number of subjects for screening and ascertainment.

g) The research could not practicably be conducted or carried out without access to and use of the protected health information:

It is necessary and respectful of subjects' time to be able to identify them as potentially eligible prior to contacting with them.

h) For research using biospecimens or identifiable information, the research could not practicably be carried out without access to and use of the protected health information:

Aggregate data are not appropriate for this research. We need patient level data to identify potential subjects. The maintaining of a basic screening log is needed to ensure that we do not contact people multiple times and to ensure equitable recruitment of people among race and education levels (via aggregate analyses). Contact info is included in the secure Duke REDCap screening log to keep this information centralized and secure, yet remotely accessible to study staff so that they do not need to keep contact information in less secure locations.

Waiver of Documentation of Consent and HIPAA Authorization for Scheduling in MaestroCare and/or the recording of PHI via telephone for screening purposes:

These research activities prior to obtaining written consent for the study presents no more than minimal risk of harm to subjects:

- (●) True
- ( ) False

These are procedures for which written consent is normally not required outside of the research context:

- (●) True
- ( ) False

An IRB-approved phone script will be used to obtain verbal consent from subjects for scheduling and/or screening prior to obtaining written consent for the study:

- (•) True
- ( ) False

IRB Notification of Decedent Research

In accordance with 45CFR164.512(i)(1)(iii), the IRB must approve research involving decedent's private health information. In order for the IRB to make the determination, please respond to each item in the allotted space below, using protocol-specific language to provide justification.

Provide a brief, meaningful description of the protected health information for which use or access has been determined to be necessary:

While it is not the intent to directly engage in decedent research, there is the possibility that subjects will expire while enrolled in this research and we will want to get information regarding their death. We would access name, address, date of birth and date of death.

Check each statement below to attest to your knowledge that:

- [x] The PHI to be used will be used solely for research.
- [x] All subjects to whom this form applies will be dead.
- [x] The PHI is necessary for the research.

- ( ) You will not disclose such PHI (share with anyone from outside DUHS or the SOM/SON) without first removing all direct identifiers, and also all indirect identifiers including information about the patient's age if greater than 89 years (state instead that the age is 90+ years), any dates of health-related events, and any patient's address more specific than state or 3 digit zip code (thus the data become de-identified).
- (•) Alternatively, you may choose to disclose this PHI, but, if so, you declare that you will maintain an accounting of this disclosure (commonly referred to as "tracking" the disclosure) for the patient's next of kin if requested.

Drugs, Biologics, and Other Substances

Select Protocol Phase (for studies with FDA regulated drugs or biologics only). Choose only one:

- ( ) Phase 0
- ( ) Phase I
- ( ) Phase I/II
- ( ) Phase II
- ( ) Phase II/III
- ( ) Phase III
- ( ) Phase IV
- (•) N/A
- ( ) Pilot

Drugs, biologics, or other substances being evaluated as a part of this research study:

Add all drugs, biologics, or other substances being evaluated as a part of this research study for which an IND is provided for the indication used in this study.
Also add any other drugs, biologics or other substances here that are being used as a part of this research study, for which an IND is not provided.

List every other drug, biologic or other substance for which side effects are described in the consent form.

View	Drug Name	FDA Approved	A new drug or a new use of	IND Number

Details			approved drug:	
⊟	**Drug/Biologic /Substance Generic Name:** Alprazolam **Generic Drug Name:** **Investigational Drug Name:**	Yes	No	

Drug/Biologic/Substance Generic Name:	Alprazolam
Generic Drug Name:	
Investigational Drug Name:	
Drug/Biologic/Substance Source:	
Is the drug/substance being provided to the subject free-of-charge?	Yes
Is the Drug FDA Approved?:	Yes
Is this drug/biologic or other chemical, metabolite, nutritional substance or other substance to be used in this research subject to the provisions of the Controlled Substances Act?	No
Does this Drug have an IND Number?	No
IND Number	
IND Holder:	N/A
IND details:	
If FDA Approved and an IND is not required, Please provide a rationale for exemption:	This drug is used only for anxiety related to MRI and/or lumbar puncture. It is not being studied for safety and/or efficacy and is used according to its label.
Will drug/substance be shipped from Duke to external locations	No
Dose Range:	0.25-0.5 mg
Frequency:	once
Will this drug, biologic, chemical, metabolite, nutritional substance or other substance be manufactured or compounded at Duke?	No
Drug Storage Restrictions (including temperature, etc.):	None
As indicated in the Investigator's Brochure or other available documentation, what is the highest FDA Use-in-Pregnancy Rating for drug used for research purposes in this study?:	Category D

⊟	**Drug/Biologic /Substance Generic Name:** Lorazepam **Generic Drug Name:** **Investigational Drug Name:**	Yes	No	

Drug/Biologic/Substance Generic Name:	Lorazepam
Generic Drug Name:	
Investigational Drug Name:	
Drug/Biologic/Substance Source:	
Is the drug/substance being provided to the subject free-of-charge?	Yes
Is the Drug FDA Approved?:	Yes
Is this drug/biologic or other chemical, metabolite, nutritional substance or other substance to be used in this research subject to the provisions of the Controlled Substances Act?	No
Does this Drug have an IND Number?	No
IND Number	
IND Holder:	N/A
IND details:	
If FDA Approved and an IND is not required, Please provide a rationale for exemption:	This drug is not being studied for safety and/or efficacy. It will be used according to label and provided to subjects who may require an anxiolytic for MRI and/or lumbar puncture
Will drug/substance be shipped from Duke to external locations	No
Dose Range:	0.5 mg
Frequency:	once
Will this drug, biologic, chemical, metabolite, nutritional substance or other substance be manufactured or compounded at Duke?	No
Drug Storage Restrictions (including temperature, etc.):	None
As indicated in the Investigator's Brochure or other available documentation, what is the highest FDA Use-in-Pregnancy Rating for drug used for research purposes in this study?:	Category D

⊟	**Drug/Biologic/Substance Generic Name:** PiB C11 **Generic Drug Name:** **Investigational Drug Name:**	No	No	

Drug/Biologic/Substance Generic Name:	PiB C11
Generic Drug Name:	
Investigational Drug Name:	
Drug/Biologic/Substance Source:	UNC BRIC Radiochemistry Core
Is the drug/substance being	

provided to the subject free-of-charge?	Yes
Is the Drug FDA Approved?:	No
Is this drug/biologic or other chemical, metabolite, nutritional substance or other substance to be used in this research subject to the provisions of the Controlled Substances Act?	No
Does this Drug have an IND Number?	No
IND Number	
IND Holder:	N/A
IND details:	UNC Radioactive Drug Research Committee (RDRC) approval has been obtained and has been attached.
If FDA Approved and an IND is not required, Please provide a rationale for exemption:	
Will drug/substance be shipped from Duke to external locations	No
Dose Range:	
Frequency:	
Will this drug, biologic, chemical, metabolite, nutritional substance or other substance be manufactured or compounded at Duke?	No
Drug Storage Restrictions (including temperature, etc.):	
As indicated in the Investigator's Brochure or other available documentation, what is the highest FDA Use-in-Pregnancy Rating for drug used for research purposes in this study?:	

⊟	**Drug/Biologic/Substance Generic Name:** F-MK6240 **Generic Drug Name:** **Investigational Drug Name:**	No	No	

Drug/Biologic/Substance Generic Name:	F-MK6240
Generic Drug Name:	
Investigational Drug Name:	
Drug/Biologic/Substance Source:	UNC BRIC Radiochemistry Core
Is the drug/substance being provided to the subject free-of-charge?	Yes
Is the Drug FDA Approved?:	No
Is this drug/biologic or other chemical, metabolite, nutritional substance or other substance to be used in this research subject to	No

the provisions of the Controlled Substances Act?	
Does this Drug have an IND Number?	No
IND Number	
IND Holder:	N/A
IND details:	UNC Radioactive Drug Research Committee (RDRC) approval has been obtained and has been attached.
If FDA Approved and an IND is not required, Please provide a rationale for exemption:	
Will drug/substance be shipped from Duke to external locations	No
Dose Range:	
Frequency:	
Will this drug, biologic, chemical, metabolite, nutritional substance or other substance be manufactured or compounded at Duke?	No
Drug Storage Restrictions (including temperature, etc.):	
As indicated in the Investigator's Brochure or other available documentation, what is the highest FDA Use-in-Pregnancy Rating for drug used for research purposes in this study?:	

Are you using an investigational pharmacy at Duke?

Please be aware that inpatient administration of an investigational drug requires the use of the Duke IDS or Oncology ICS, as per Department of Pharmacy policy.

○ Yes ◉ No

Who will be responsible for the storage, inventory and control of the drug/biologic or other chemical, metabolite, nutritional substance or other substance to be evaluated in this research?

The IDS is available to assist any investigator (upon request) with storage and control of investigational drugs in the outpatient setting

This drug will be prescribed to participants as needed for anxiety related to MRI and/or lumbar puncture. They will pick it up from their pharmacy as they would their usual prescriptions. The study will provide the drug free of charge to those who require this.

Where will the drug/biologic or other chemical, metabolite, nutritional substance, or other substance to be evaluated in this research be stored?

N/A - drugs not being evaluated. Patient with get from their local pharmacy

From where will the drug/biologic or other chemical, metabolite, nutritional substance or other substance to be evaluated in this research be dispensed?

Patient with get from their local pharmacy

At the completion of this research study, what will be done with the unused or returned investigational drug /biologic or other chemical, metabolite, nutritional substance or other substance?

N/A - drugs not subject of this research

Privacy and Confidentiality

Explain how you will ensure that the subject's privacy will be protected:

Consider privacy interests regarding time and place where subjects provide information, the nature of the information they provide, and the type of experience they will be asked to participate in during the research.

All clinical history and exams will take place at Duke and UNC sites including: Duke Neurology Outpatient Clinic at Morreene Road, the ADRC offices in the Hock Plaza Building (2424 Erwin Road, Suite 103), appropriate UNC sites/clinics and also the PACU area where anesthesiologists can conduct the lumbar punctures or blood patches in a secure and confidential clinical and research setting (or as otherwise approved via phone/video interview). All procedures and imaging will take place in a secure and confidential clinical and research setting. The information provided is part of the UDS, a national standardized tool.

Describe how research data will be stored and secured to ensure confidentiality:

How will the research records and data be protected against inappropriate use or disclosure, or malicious or accidental loss or destruction? Records and data include, for example, informed consent documents, case report forms or study flow sheets, survey instruments, database or spreadsheets, screening logs or telephone eligibility sheets, web based information gathering tools, audio/video/photo recordings of subjects, labeled specimens, data about subjects, and subject identifiers such as social security number.

The Duke/UNC ADRC is an NIA designated ADRC program. Data gathered as part of the Uniform Data Set (UDS) will be managed by core data personnel in the Duke/UNC ADRC and stored in Redcap at Duke. Redcap will transmit the data securely to NACC. Imaging data will be stored on secure servers within the Duke/UNC ADRC. Subject consents will be either uploaded into REDCap, or entered there directly via eConsent.

Data previously collected under the Bryan ADRC protocols for venipuncture and CSF is stored on a secure server in the Duke ADRC.

All data for the UDS will be collected electronically and transmitted into Redcap where it will be stored.

MRI images will be stored on Duke Radiology and Duke-UNC Brain Imaging and Analysis Center (BIAC) servers.

VRFCAT-SLx is run off an i-pad tablet device. It is a single user interface with each user being provided their own log-in credentials and PIN by the Duke study team. The software will already be preloaded onto the i-pad and are initiated by the participant when they are ready to begin the assessment. All digital assessment files will be coded and stored with participant identification numbers only; no personally identifying information will be attached to the files. These data files will be electronically transmitted to WCG servers in Cary NC via their secure web-based portal.
Data will be processed and cleaned at WCG. Quarterly data transfers will occur back to the Duke/UNC ADRC through a secure portal (Duke Box). VRFCAT use with participants will begin now that all required data agreements have been completed between Duke/UNC and WCG-VeriSci.

All data/specimens released from the Duke/UNC ADRC database/repository are de-identified or represent data elements that cannot be de-identified (retinal images, voice recordings, whole genome data or DNA) but these data are not connected to other PHI and are released only with permission (opt in) of the participant.

Every effort will be made to secure participants identity, health information and research results. The study will assign each participant a unique global ID (UGID) and use additional consistent ID’s to link UDS data, images, and biomarkers stored by Substrate Services Core Research Support (SSCRS). All information will be stored in the ARENA, a data management system with multi-layered security levels, which will ensure participant confidentiality during all phases of the study. The ARENA integrates several

platforms including REDCap and PEDIGENE (an ORACLE-based system for managing complex genetic and –omic data) and links to EPIC and other secure servers to allow data transfer between Duke and outside entities in a secure manner. The ARENA will transmit data securely to NACC.

All data/specimens are coded by a unique Duke/UNC ADRC global ID number rather than by name. Data and specimen information are maintained in the ARENA database according to identifier number and not by name. All data/specimens released from the ARENA database and biorepository managed by Substrate Services Core Research Support (SSCRS) are de-identified [or represent data elements that cannot be de-identified (retinal images, voice recordings, whole genome data or DNA) but these data are not connected to other PHI and are released only with permission (opt in) of the participant] and given a unique ID number linked to the global ID number. All original (primary) data are stored in locked cabinets in a locked room with access strictly controlled by ADRC research staff. No specimens/data are ever released to third outside parties unless the participant (or the participant's legal representative) has requested and consented to data release (e.g. for medical purposes). A strict confidentiality policy is in place for all ADRC research staff. Access to the data is restricted and protected as required by law and can only be accessed by authorized investigators and research staff. The database/repository will be maintained indefinitely as long as funding is available or until the data/specimens are exhausted.

The basic screening and enrollment logs, maintained securely in Duke REDCap, will have access limited to appropriate ADRC study team members, via REDCap roles and credentialing.

Application Questions Complete

Please click Save & Continue to proceed to the Initial Submission Packet.

The Initial Submission Packet is a short form filled out after the protocol application has been completed. This is an area to attach protocol-related documents, consent forms, and review the application.