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University of Pittsburgh Protocol Record STUDY23080154I, Improving PCP Advance Care Planning for People With ADRD

Improving Primary Care Clinicians' Advance Care Planning for Alzheimer's Disease and Related Dementias

PROTOCOL

National Clinical Trial (NCT) Identified Number: <Number, once assigned by CT.gov>

Principal Investigator*: Christine Kistler

Sponsor: University of Pittsburgh

Brief Grant Title: Improving PCP Advance Care Planning for People With ADRD (AD-ACP)

Grant Number*: 1R01AG083828

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February 3, 2026

CONFIDENTIALITY STATEMENT

This document is confidential communication. Acceptance of this document constitutes agreement by the recipient that no unpublished information contained herein will be published or disclosed without prior approval of the Principal Investigator or other participating study leadership and as consistent with the NIH (National Institutes of Health) terms of award.

Table of Contents

STATEMENT OF COMPLIANCE

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

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

National Institutes of Health (NIH)-funded investigators and clinical trial site staff who are responsible for the conduct, management, or oversight of NIH-funded clinical trials have completed Human Subjects Protection and ICH GCP Training.

INVESTIGATOR'S SIGNATURE

The signature below constitutes the approval of this protocol and provides the necessary assurances that this study will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements and applicable US federal regulations and ICH guidelines, as described in the *Statement of Compliance* above.

Principal Investigator or Clinical Site Investigator:

Signed: Christine E Kistler Digitally signed by Christine E Kistler Date: 2026.02.12 14:49:05 -05'00' Date: _____

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

Signed: Laura C. Hanson MD MPH Digitally signed by Laura C. Hanson MD MPH Date: 2026.02.12 14:56:50 -05'00' Date: _____

Name: Laura C. Hanson, MD, MPH

Title: Professor of Medicine, Vice Chief of Research

Affiliation: The University of North Carolina at Chapel Hill

1 PROTOCOL SUMMARY

1.1 SYNOPSIS

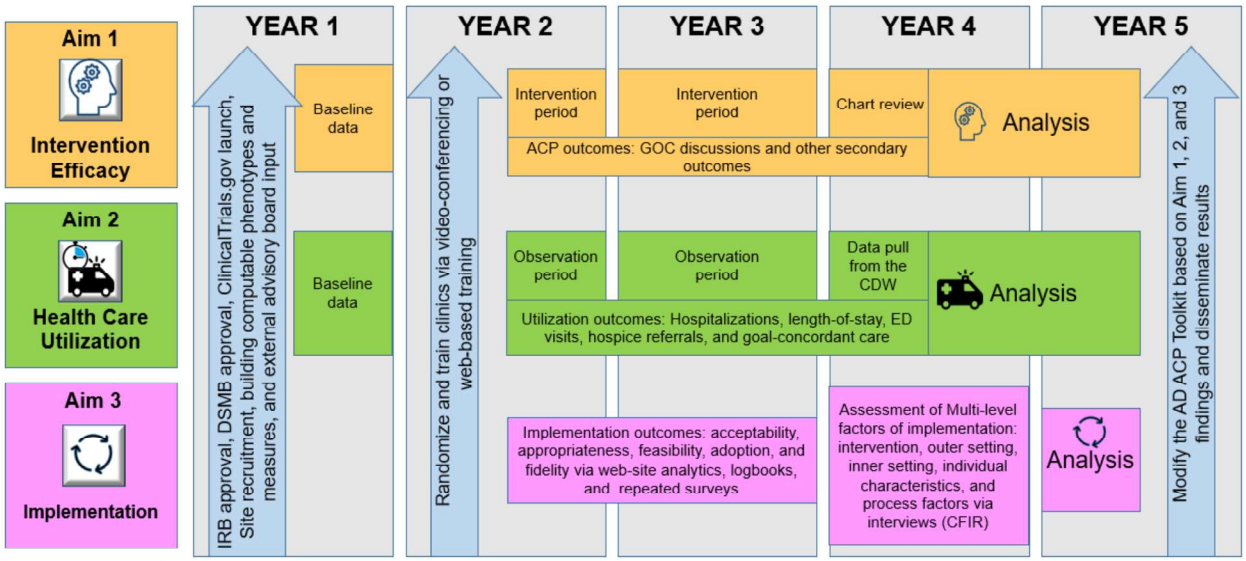
Title:	Improving Primary Care Clinicians' Advance Care Planning for Alzheimer's Disease and Related Dementias
Grant Number:	1R01AG083828
Study Description:	This project will test an advance care planning (ACP) toolkit for primary care teams caring for patients living with Alzheimer's Disease and related dementias (AD/ADRD) in a cluster randomized control trial. In 20 primary clinics, we will examine the advance care planning practices, including goals of care (GOC) discussions as our primary outcome, health care utilization, and implementation outcomes.
Objectives*:	**Primary Objectives** **Aim 1. Intervention Efficacy Outcomes:** To conduct a cluster RCT trial to compare the efficacy of the AD ACP Toolkit (intervention) vs usual care (control) on GOC discussions (primary outcome) in 800 people living with dementia (PLwD) in 20 primary care clinics, and other ACP practices such as preferred surrogate, decisional capacity, and portable ACP orders (secondary outcomes) over 18 months. Hypothesis: All outcomes will increase for intervention compared to control group. **Secondary Objectives** **Aim 2. Healthcare Utilization Outcomes:** To compare healthcare utilization outcomes (hospitalization/ emergency department visits, length-of-stay, hospice/ palliative care referrals, goal-concordant care), utilizing a large health care system's clinical data warehouse for PLwD with ≥50% 5-year all-cause mortality risk in intervention vs control clinics over 18 months. We will conduct pre-specified subgroup analyses by race, ethnicity, and clinic location. *Hypothesis*: For high-risk PLwD, the intervention will reduce healthcare utilization for PLwD at increased risk of mortality and reduce observed differences in utilization between subgroups of at-risk PLwD. **Aim 3. Implementation Outcomes:** We will assess implementation outcomes and explore multilevel barriers and facilitators to explain variations in those outcomes. We will use both quantitative methods to assess outcomes (acceptability, appropriateness, feasibility, adoption, and fidelity) as well as qualitative methods. Guided by the Consolidated Framework for Implementation Research (CFIR), we will collect qualitative interview data to explore barriers and facilitators to achieving those outcomes at each of the 10 intervention clinics.

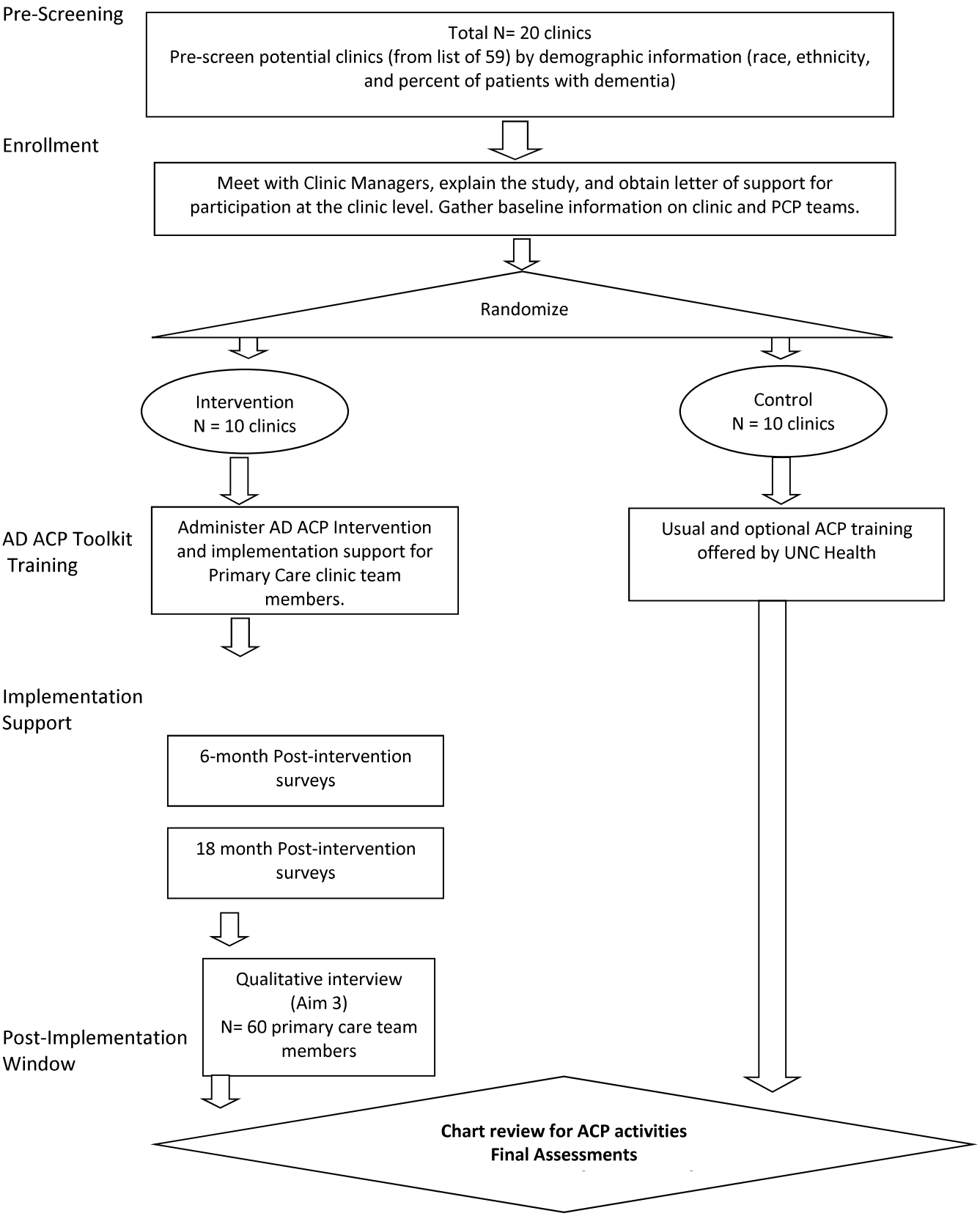
Endpoints/Outcomes:	Primary outcome: AD/ADRD GOC Discussions- Documented discussions identified via the Carolina Data Warehouse (CDW) and chart review including the primary care team member (PTCTM) with the PLwD or their surrogate decision-maker; must include a) communication about dementia stage or prognosis AND b) decision-making for at least one major treatment: CPR/mechanical ventilation, hospitalization, treatments for infections, artificial/feeding/hydration, OR hospice (Aim 1). Secondary outcomes: • ACP practices (Aim 1); Frequency of 1) documented choice of a surrogate decision-maker for the PLwD, 2) assessment and report of decision-making capacity for the PLwD, 3) completion of portable ACP orders using a state-approved Do Not Resuscitate (DNR) or Physician Orders for Life-Sustaining Treatment (POLST) form, and 4) documented discussion of prognosis or future medical complications of AD/ADRD during the 18-month intervention period via Electronic Health Record (EHR) chart review. • Hospitalizations and emergency department visits (Aim 2) • Length-of-Stay (Aim 2) • Referral to community palliative care or hospice (Aim 2) • Goal-concordant care (Aim 2) • Acceptability, Appropriateness, and Feasibility (Aim 3) measured in repeated surveys to assess the acceptability of the AD ACP intervention, including the approval, welcome, appeal, and likeability of the intervention • Adoption (Aim 3) measured as the frequency with which training is completed • Fidelity (Aim 3) measured by primary care team members' scores on post-intervention and post-implementation quizzes, participation in clinic-level and primary care team member-level ACP audit-and-feedback, refresher sessions and in-services, periodic coaching from the research team
Study Population:	• Intervention efficacy outcomes (Aim 1): primary care team participants from 20 primary care clinics serving a diverse older adult population with chart reviews of 40 randomly selected PLwD at each site (N=800). • Health utilization outcomes (Aim 2): PLwD with a >50% mortality risk over 5 years seen by the primary care team participants in the 18-month intervention period in Aim 1 • Implementation outcomes (Aim 3): Intervention-trained primary care team members who will complete implementation surveys. • Implementation outcomes (Aim 3): Up to 6 intervention-trained primary care team members at each site will complete post-intervention interviews.
Phase* or Stage:	NIH Behavior Change Stage III

Description of Sites/Facilities Enrolling **Participants:**	Study sites are at least 20 University of North Carolina (UNC) HEALTH primary care clinics, located in North Carolina.
Description of Study Intervention:	The AD ACP Toolkit intervention consists of 1) primary care team member training and 2) implementation support. Initial training includes 5 modules; an introduction and then modules devoted to four stages of dementia. The modules are based on current best-evidence for ACP communication skills specific to PLwD. Modules incorporate problem-based learning techniques and group interaction to promote content uptake. Each training module takes about 30 minutes and consists of a 15-minute didactic portion comprised of key dementia stage education and relevant communication skills, a 5-10-minute video scenario modeling stage-specific AD/ADRD ACP communication skills, and a 5-10 minute Q&A session. Group interaction is promoted during two skill-building practice roleplay exercises using stage-specific clinical vignettes. Videos include diverse actors representing healthcare professionals, people with AD/ADRD, and their families in primary care clinic settings. Didactic and roleplay content reflect communication skills such as active listening and respect for family and cultural norms. Modules provide information about how to incorporate ACP practices in clinical operations and practical resources to facilitate implementation. They include tools to help operationalize their training in clinical care such as ACP billing codes, chart documentation templates, POLST forms, and scheduling approaches to provide sufficient time for GOC discussions. At the end of the training, participants complete an action plan for practice improvement, a strategy found to change physician behavior in diabetes care focusing on how they will put that knowledge into practice. The entire training takes 3 hours and can be delivered in-person or via video conferencing. The second part of the intervention is implementation support including clinic and primary care team feedback reports on ACP practices, periodic coaching, access to refresher sessions and web-based recordings of the AD ACP Toolkit training, as well as local champions. Current processes at UNC HEALTH routinely provide quality metric feedback to clinics; we will utilize this existing system to provide trained clinics' (Medical Doctor/Advanced-Practice Providers (MD/APPs) and their teams with monthly audit-and-feedback on ACP practices using data from the UNC HEALTH ACP Dashboard. We will coordinate periodic lunch-and-learn sessions to discuss ACP challenges and facilitate ACP implementation by the primary care teams. Refresher sessions and as needed clinical in-services on requested topics will be held bi-monthly by Dr. Hanson and our team. Intervention MD/APPs and their teams will be re-offered training at 6 months. Each intervention clinic will identify and engage a local champion to support ACP activities.

Study Duration*:	60 months
Participant Duration:	Aims 1 and 2 participants will be primary care teams and their patients with dementia. The primary care team members will be recruited, trained, and provided implementation support over approximately 2 years. The teams' performance will be measured using data extracted in a one-time data pull. We will provide implementation guidance including audit-and-feedback alternating with lunch-and-learn sessions to the primary care clinics in the intervention arm on an alternating monthly basis over 18 months. The PLwD participants will participate in a one-time medical record review and data extraction. Aim 3 participants will be primary care team members who participated in the AD ACP Toolkit training session and follow-up for between 18 and 30 months. Aim 1 and 2 participants (primary care team members) – Ongoing implementation support Aim 1 and 2 participants (PLwD) – one-time medical record data extraction Aim 3 participants (primary care team members) – 18-30 months

1.2 SCHEMA




Pre-Screening
Total N= 20 clinics
Pre-screen potential clinics (from list of 59) by demographic information (race, ethnicity, and percent of patients with dementia)
Enrollment
Meet with Clinic Managers, explain the study, and obtain letter of support for participation at the clinic level. Gather baseline information on clinic and PCP teams.
Randomize
Intervention
N = 10 clinics
Control
N = 10 clinics
AD ACP Toolkit Training
Administer AD ACP Intervention and implementation support for Primary Care clinic team members.
Usual and optional ACP training offered by UNC Health
Implementation Support
6-month Post-intervention surveys
18 month Post-intervention surveys
Post-Implementation Window
Qualitative interview (Aim 3)
N= 60 primary care team members
Chart review for ACP activities
Final Assessments

1.3 SCHEDULE OF ACTIVITIES

	Pre-Screening and Recruitment	Enrollment	Intervention/ Toolkit Training	6 month	18 month	End of Study
Primary Care Clinic Selection	X					
Primary care team member Recruitment	X					
Clinic Randomization		X				
AD ACP Intervention			X			
AC ACP Implementation Support			X	X	X	X
Primary Care Team Member Baseline Data			X			
Post-Intervention Survey				X	X	
Qualitative Interviews						X
Outcome Evaluation						
Primary Outcome GOC Discussions (Aim 1 Efficacy)					X	
ACP Practices					X	
Healthcare Utilization					X	
Implementation			X	X	X	X

2 INTRODUCTION

2.1 STUDY RATIONALE

Advance care planning (ACP) practices are difficult for older adults and their primary care providers. Dementia further complicates this process. Alzheimer's disease and Alzheimer's disease related dementias (AD/ADRD) are incurable and progressive, and have unparalleled impact globally, including on the US healthcare system, patients, and families. Over 5 million Americans live with AD/ADRD, which profoundly affects their lives and the lives of their families who act as caregivers and surrogates making life-or-death healthcare decisions. Because persons living with dementia (PLwD) lose decision-making capacity over years, primary care primary care team members must be able to both discern when and how PLwD can express valid treatment preferences and how to communicate with PLwD and their families across all stages of AD/ADRD.

Most AD/ADRD care is provided by primary care. Among Medicare recipients, 85% of PLwD are diagnosed by primary care team members without dementia expertise; only 1/3 receive specialty dementia care. Primary care teams – nurses, medical assistants, physicians, advance practice providers

(APPs), and social workers, etc. – are well-positioned to empower PLwD and families in ACP yet lack the dementia-specific education, ACP communication skills, and clinical implementation guidance to meet this need. As a result, PLwD continue to receive high-intensity medical treatments poorly aligned with goals and preferences. Recent primary care ACP interventions do not primarily focus on PLwD and thus exclude the voice of PLwD.

Limited evidence exists to address the gap in AD/ADRD specific ACP practices in primary care. To fill this gap, our experienced investigative team developed an AD/ADRD ACP practice improvement intervention ("AD ACP Toolkit") for primary care, for PLwD across all stages of AD/ADRD. The AD ACP Toolkit contains 5 modules: an introduction and modules about early, moderate, late, and end-stage AD/ADRD. *Each module includes AD/ADRD education, ACP communication skills, and clinical implementation guidance.* The AD ACP Toolkit includes ongoing clinical implementation guidance including audit-and-feedback and local champions. In a 6-month pre-post evaluation, the Toolkit improved multiple ACP practices, including doubling goals of care (GOC) discussions with PLwD (17% to 32%, $p<0.005$), and reduced hospitalizations and emergency department visits.

2.2 BACKGROUND

Increasing rates of Alzheimer's Disease and Alzheimer's Disease Related Dementias (AD/ADRD). Globally, the number of persons living with dementia (PLwD) is expected to rise from 36 million in 2010 to 66 million by 2030 and cost almost $1 trillion annually, leading the World Health Organization to call dementia research a public health priority. In the US alone, AD/ADRD affects at least 5 million people, costs $305 billion annually, and contributes to 1 in 3 US deaths. With the rise in numbers of PLwD nationally and globally comes an increase in the importance of planning for medical decision-making around these deaths.

High quality advanced care planning (ACP) requires skilled communication and ongoing care. To be effective in serious illness such as AD/ADRD, ACP is an ongoing process of skilled communication between medical providers and patients, designed to share and document personal values, goals and preferences regarding future medical care, and facilitate medical care matched to those goals.

High quality ACP is especially important and underutilized for PLwD and their families. In July 2021, the American Association of Neurology issued a position statement that noted "Caring for patients with dementia requires respecting patient autonomy while acknowledging progressively diminishing decisional capacity and continuing to provide care in accordance with other core ethical principles (beneficence, justice, and nonmaleficence)." Due to the time constraints and other barriers in primary care, most primary care teams choose to delay communication and often fail to address ACP for PLwD because it is perceived as time-consuming and emotionally draining. PLwD and their families rarely receive ACP that spans the full trajectory of the disease.

Most AD/ADRD care is provided by primary care teams, yet they lack training and expertise in dementia-specific ACP. Among Medicare recipients, 85% of PLwD are diagnosed by teams without dementia expertise; only 1/3 receive any specialty dementia care. Primary care teams – physicians, advance practice providers (APPs), nurses, medical assistants, and social workers, etc. – are well positioned to empower PLwD and their families to engage in ACP. However, they lack high-quality training to support ACP in AD/ADRD care. As a result, they struggle to engage in ACP discussions, citing knowledge

deficits, emotional barriers, time constraints, documentation issues, changing preferences, and lack of skills. 10-12 Provider-focused ACP training tools are available, but they are not responsive to the needs of all primary care team members working with PLwD. Even those with mild dementia require dementia-specific ACP communication approaches, such as assessing capacity or discussing plans for the future.

Our long-term goal is to ensure that all PLwD receive goal-concordant care. Because PLwD receive most of their healthcare in primary care rather than specialty care, our primary research objective is to address the critical scientific gap in AD/ADRD ACP practices in primary care.

2.3 RISK/BENEFIT ASSESSMENT

2.3.1 KNOWN POTENTIAL RISKS

The potential risks of study participation are similar to routine care. The AD ACP Toolkit intervention has minimal risk, based on evidence from the pilot Randomized Control Trial (RCT) and other AD ACP trainings in other settings such as nursing homes and hospitals which have not demonstrated any adverse effects. Elements of the AD ACP Toolkit – dementia education, communication skills training, and clinical operation information – have all been previously established as evidence-based care to improve outcomes for other serious illness populations.

The only expected potential risk to participants attributable to the research study is a risk of breach of confidentiality.

For Aims 1 and 2, the potential risk is the breach of confidentiality of personal health information for PLwD, as patient level data will be collected, though it will be done via large data extraction to develop a de-identified cohort that will be stored behind robust firewalls with data safety protocols. However, procedures will be taken to minimize the possibility of a breach in confidentiality, and we have a data safety monitoring plan to explicitly address this potential risk. Additionally, no participants will be identified in any publication or report of this study.

For Aim 3, a primary care team participant's potential risk is breach of confidentiality. However, as clinical care team members in primary care are often surveyed about a variety of primary care initiatives, participation in coaching calls, the web-based analytics data, the surveys, and interviews pose minimal risk of disclosure or disruption to the primary care clinics. There is a very small risk of breach of confidentiality in Aim 3, as we will have survey and interview data, as well as records of coaching calls and track web-site utilization with web-based analytics.

We will have an External Advisory Board from the start of the study to advise on these issues and a Data Safety Monitoring Board to monitor for study protocol deviations and adverse events. We will develop a formal data safety monitoring plan to protect against breaches. An implementation specialist, Dr. Leeman, will also advise on implementation to prevent this issue and include information about this in the Toolkit currently.

To protect against this risk, all collected data, including Personal Health Information (PHI), will be defined by the research protocol, and limited to research purposes. We will protect confidential medical information from Electronic Health Record (EHR) reviews by abstracting data directly into a secure

database or onto coded paper forms separated from personal identifiers. Data will be entered in a password protected secure database, and all paper documentation will be maintained in double- locked files. The Sheps Information Technology group enables standard operating procedures required to secure the network and databases, including operational and technical controls. All servers are located within a hardened data center. Modes of communication between the study coordinating center at the University of North Carolina, and between Site-Clinical Research Coordinator (CRC), Site-Principal Investigator (PI and others will be restricted to encrypted e-mail, secure text messages, or secure verbal communication to protect confidential health information. NC TraCS and UNC Sheps IT will work with Dr. Subashan Perera to ensure the data access, transfer, and storage are secure.

2.3.2 KNOWN POTENTIAL BENEFITS

This work will test the efficacy of an intervention to improve ACP with PLwD in primary care settings and provide data on barriers and facilitators to implementing the toolkit in primary care that will inform future NIH Stage IV research. If successful, the design of the AD ACP Toolkit will enhance its sustainability, allow for rapid changes as indicated by advances in evidence, and facilitate dissemination. It may be adaptable to other outpatient specialty practices such as oncology or cardiology, and other care settings, such as the nursing home, where AD/ADRD-specific ACP interventions have shown little benefit.

2.3.3 ASSESSMENT OF POTENTIAL RISKS AND BENEFITS

The benefit to risk ratio is highly favorable in this study. First, the AD ACP toolkit has low risk of harms, as it is composed of evidence-based and minimal-risk interventions which are shown to improve outcomes for other serious illness populations. Second, there are significant potential benefits to participants in both study arms.

3 OBJECTIVES AND ENDPOINTS

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS	PUTATIVE MECHANISMS OF ACTION
Primary			
To conduct a cluster RCT trial to compare the efficacy of the AD ACP Toolkit (**intervention**) vs usual care (**control**) on GOC discussions (**primary outcome**) in 800 PLwD, and other ACP practices such as preferred surrogate, decisional capacity, and portable ACP orders (**secondary outcomes**) over 18 months.	The AD ACP Toolkit, compared to usual care controls, will enable primary care teams to conduct more frequent and more effective ACP practices as evidenced by increased ACP outcomes over 18 months for 40 randomly sampled PLwD per clinic (N=800), from 20 randomized US primary care clinics.	Most AD/ADRD care is provided by primary care. Among Medicare recipients, 85% of PLwD are diagnosed by providers without dementia expertise; only 1/3 receive specialty dementia care. Primary care teams – nurses, medical assistants, physicians, advance practice providers (APPs), and social workers, etc. – are well-positioned to empower PLwD and families in ACP yet lack the dementia-specific education, ACP communication skills, and clinical implementation guidance to meet this need.	Training improves dual processing via System 1 and System 2.
Secondary			
To compare healthcare utilization outcomes (hospitalization/ emergency department visits, length-of-stay, hospice/ palliative care, goal-concordant care), utilizing a large health care system's clinical data warehouse for PLwD with ≥50% 5-year all-cause mortality risk in intervention vs control clinics over 18 months.	Number of hospitalization/ emergency department visits; length-of-stay of hospitalization/ emergency department visits; hospice/ palliative care utilization; goal-concordant care (ACP Y/N)– within 18 months	Hospital transfers are common for persons with more advanced AD/ADRD, and are burdensome and stressful for the person and their family caregivers. Some hospital transfers are avoidable because acute illness can be treated in lower intensity settings, OR because goals of care are more comfort-focused.	ACP aligns a PLwD's care plan with their values and shifts the default from "hospitalization" to "goal-concordant" care
Tertiary/Exploratory			
We will assess implementation outcomes and explore multilevel barriers and	We will assess toolkit (training and implementation guidance) impact on	In addition to training (dementia-specific education and ACP communication skills), primary care team	CFIR addresses multi-level fac-tors (barriers and facilitators) at the

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS	PUTATIVE MECHANISMS OF ACTION
facilitators to explain variations in those outcomes by collecting qualitative interview data to explore barriers and facilitators to achieving those outcomes at each of the 10 intervention clinics.	implementation, efficacy, and health care utilization outcomes. The perception that the innovation is acceptable (ie, agreeable, palatable, or satisfactory), appropriate (fit/relevance of the innovation to: a) the setting and b) address the problem), and feasible (the extent to which the innovation can be successfully enacted or carried out within the setting) to the participants	members need implementation guidance to integrate AD ACP into routine practice. The implementation guidance is designed to address these factors and includes clinic- and individual-level ACP audit-and-feedback, periodic coaching, refresher sessions and in-services, and designation of a local champion. To be successful, our intervention must be acceptable, feasible, and appropriate to achieve high levels of adoption by primary care teams. Primary care teams must implement the Toolkit with fidelity over time, using it to systematically instead of delivering scatter-shot ACP.	level of the intervention (e.g., complexity), primary care team members (e.g., attitudes, beliefs), and inner and outer settings (resources, culture, leadership, and wider context). Proctor's Implementation Outcomes Framework will guide evaluation of implementation outcomes in real-world primary care

4 STUDY DESIGN

4.1 OVERALL DESIGN

Study design is a NIH Behavior Change Stage III efficacy cluster randomized trial conforming to the Consolidated Standards of Reporting Trials (CONSORT) statements for trial methods and protocol. Our approach uses NIA standards for a community-based efficacy trial (NIH Behavior Change Stage III) of a protocolized behavioral intervention yet incorporates two implementation models to support efforts for wider dissemination. Study sites are 20 UNC HEALTH primary care clinics. Randomization is at the clinic level, and patient outcome assessment at the level of the PLwD. Primary care team members at the 10 intervention clinics will receive one 3-hour training session using the AD ACP Toolkit, followed by implementation coaching, monthly feedback from the UNC HEALTH ACP dashboard, and other implementation support. The 10 control sites will receive the usual and optional ACP training offered by UNC HEALTH. We will use a computable case finding algorithm to generate a random sample of 800 PLwD from the anticipated 20 clinics (40 per clinic site). Outcome assessments will be from structured EHR data pulls supplemented with EHR chart reviews done by research staff masked to study arm at 18 months. The primary outcome will be frequency of GOC discussions identified via chart review (**Aim 1)**. Secondary outcomes for **Aim 1** address GOC discussion content, including designation of surrogate decision-maker,

capacity assessment, complications of dementia, and completion of ACP documents. **Aim 2** will use 18-month data from all PLwD with >50% 5-year all-cause mortality risk seen in study clinics to compare rates of healthcare utilization outcomes (hospitalizations, length of stay, Emergency Department (ED) visits, hospice, and goal-concordant care) between arms. **Aim 3** will measure acceptability, appropriateness, feasibility, adoption, and fidelity assessed using brief surveys of primary care clinic team members at each AD ACP Toolkit training session, at the 6-month and 18-month time points after training, and a qualitative interview at study end (30 months). Additional implementation data will be collected via web-site tracking analytics, recorded logs of coaching calls and audit-and-feedback, and post-intervention period interviews to assess barriers and facilitators to implementation. Primary analyses will be on intention-to-treat basis, with pre-specified subgroup analyses of outcomes by key clinic and patient characteristics such as clinic location, race, ethnicity, and mortality risk. The study timeline covers 60 months. We will seek approval through the UNC Institutional Review Board (IRB) for this intervention prior to initiating research and will be subject to annual and other required reviews. The study design leverages a large public healthcare system with a sophisticated clinical data warehouse to test the AD ACP Toolkit in primary care for a diverse population of PLwD and their families.

4.2 SCIENTIFIC RATIONALE FOR STUDY DESIGN

Because patients in the same clinic may have dependent outcomes, we will use a clustered RCT design to help control confounding within clinics. Given minimal contamination between clinics, a clustered RCT is the best study design to assess the effect of the intervention v control. We will use a generalized estimating equations model with an exchangeable working correlation structure to account for a site (clinic) effect.

4.3 JUSTIFICATION FOR INTERVENTION

Dual Process Theory (DPT) provides a framework for understanding how decisions are actually, rather than ideally, made. DPT recognizes the natural human tendency to make decisions through both rapid, intuitive means (System 1), and more deliberative, analytical processes (e.g., System 2; carefully weighing one's options and their consequences). Usual communication and decision making too often rely on intuitive thinking, such as assuming full code status as the default and not discussing ACP until a medical crisis occurs. Through ACP skills training based on DPT, primary care teams improve performance by learning to deliberately engage in ACP (System 2- e.g. recognizing an ACP discussion is needed for a PLwD) while having short-cuts for communication, billing, and clinical practice (System 1; e.g. scheduling a specific ACP discussion, using patient-centered language, and having the correct billing codes), thus making ACP discussions more frequent AND more efficient. Using this model, our training shifts participants away from the path of least resistance (e.g., avoiding ACP discussions) and supports them as they tackle more cognitively taxing questions, such as : "What would my patient want for herself if she were able to tell me?" through simple and effective skills, such as, "Tell me more…". Because intuitive thinking is both easy and widespread, primary care teams need more than just support in understanding and applying evidence; they also need support in building appropriate short-cuts and heuristics and then implementing those in clinical care. Our outcomes measure both the frequency of ACP discussions (Aim 1) and the lived experience of the primary care teams (Aim 3) to demonstrate improvements in system 1 and system 2. Grounding the scenarios in dual process theory supports primary care team members as they access more deliberative cognitive processing, helping them to address the emotional process of AD/ADRD ACP. The ACP practice improvement toolkit (AD ACP Toolkit) is designed to help primary care

teams use more appropriate, evidence-based heuristics to engage PLwD and their family caregivers in decision-making. For example, for nutrition, we use a "comfort feeding" framework to shift the discussion from an apparent "care v. no care" to one that shows caring through assisted hand feeding rather than burdensome feeding tubes.

Implementation science developed to identify and address the factors that impede translation of efficacious interventions into actual practice change -- the so-called "science-to-service gap." These factors include unrealistic resource needs, low practitioner motivation, and time-intense training. To reduce the science-to-service gap, we include attention to implementation outcomes as part of this efficacy trial, with the goal of de-signing and interventions that are ready for widespread implementation once the trial is completed. To accelerate potential improvements in ACP in primary care, we will therefore measure and ground the AD ACP Toolkit in the key components of implementation. Proctor's Implementation Outcomes Framework outlines factors critical to integrating our intervention into real-world primary care. To be successful, our intervention must be sufficiently acceptable, feasible, and appropriate to achieve high levels of adoption by primary care team members. Primary care settings and team members must implement the Toolkit with fidelity over time, using it to systematically guide practice instead of delivering scatter-shot ACP, that may exacerbate health disparities in ACP. To plan for widespread implementation, evidence is also needed on factors that explain variation in implementation outcomes. The Consolidated Framework for Implementation Research identifies factors at the level of the intervention (e.g., complexity), primary care team (e.g., attitudes, beliefs), setting (resources, culture, leadership), and wider context that may accentuate or hinder implementation.

4.4 END-OF-STUDY DEFINITION

End of the study is defined as the completion of a one-time data pull for PLwD to meet Aims 1 and 2, 18 months after the last intervention site is trained. For approximately 120 primary care team members, the end of the study is defined as the completion of post-intervention brief surveys and, for the subset who participate in qualitative post-intervention interviews in Aim 3.

5 STUDY POPULATION

Clinics: Eligible clinics in UNC HEALTH must be primary care clinics with ≥60 PLwD encounters per year. Clinics will be geographically distant to minimize cross-contamination. If an individual primary care team member in a clinic participated in our pilot training, we will not exclude their clinic, given the randomized nature of the study. The main effect of any previously trained individuals in the control arm will be to dilute the efficacy of the intervention and a resulting trend towards the null hypothesis.

PLwD: For Aims 1 and 2, clinics will be the unit of randomization and PLwD will be the unit of analysis. Using data in the CDW, we will identify all PLwD seen by the intervention site's primary care teams via our AD/ADRD computable phenotype in the 18-month intervention window. As in our pilot, we will use a novel method to randomly select 40 eligible PLwD from each clinic and review their charts for Aim 1 outcomes. To ensure randomness in our chart review, we developed a novel identification method to randomly select participants throughout the intervention period. We have modified this process for the larger trial. We will divide the 18-month period into 40 equal time intervals and randomly select a visit occurring during each sub-interval ensuring visits are selected from 40 different patients meeting eligibility criteria. A goals of care discussion (as defined in the primary outcome section) occurring any time during the 18-month period in those 40 patients will be counted as an occurrence of the primary outcome. If more charts (e.g., 56) are to be reviewed from each clinic to increase statistical power in per

protocol analysis (per sample size section), the 18-month period will be divided into a greater number of sub-intervals (e.g., 56). This process removes the potential proximity bias that patients seen most proximal to training may receive more ACP discussions than those near the end of the intervention period. We will randomly sample PLwD to ensure balanced representation of ACP outcomes from all clinic clusters. PLwD will be eligible only after we confirm the presence of the AD/ADRD diagnosis. Approximately half of PLwD see their primary care providers within a year. Thus, if we target clinics with at least 60 encounters with PLwD, we expect 30 of them to be seen within a year and 45 in 18 months, thus easily attaining 40 encounters in the 18-month window. All PLwD with a ≥50% 5-year all-cause mortality risk seen over the 18-month intervention period will be eligible for the healthcare utilization analyses in Aim 2. We chose the 5-year cut-off point due to the increased health care costs seen during this period of time as compared to other serious illnesses and the potential to see an impact from the intervention.

Primary care team members: Within each intervention clinic, we will recruit all MD/APPs who see older adult patients, along with their associated clinical staff (e.g., nurses, social workers, medical assistant, etc.) for training. We will exclude primary care team members who do not care for older adults (e.g. pediatricians or lactation nurses), are employed at geriatric specialty or dementia specialty clinics, or are without a primary care panel (e.g., only urgent care). For control sites, we will match sites based on size and location and choose the primary care team members as eligible with the same criteria as above. For Aim 3, the intervention site primary care team members will be eligible for the implementation surveys (N= approximately 120) and interviews (n=60). We will also survey intervention and control clinics at the beginning and at completion of the implementation period for basic clinic and PCTM demographic data.

5.1 INCLUSION CRITERIA

Primary care team member eligibility: Must be an MD/APP, employed at a primary care clinic within UNC HEALTH clinics with ≥60 PLwD encounters per year, who sees older adult patients, along with their associated clinical staff (e.g., nurses, social workers, medical assistants, etc.) for training with AD ACP Toolkit. For **Aim 3**, only the trained intervention site primary care team members will be eligible for the implementation surveys.

PLwD eligibility: Must be a PLwD age 65 years or older seen by the intervention site's primary care teams in the 18-month intervention window for Aim 1. PLwD will be eligible only after we confirm the presence of the AD/ADRD diagnosis. All PLwD with a ≥50% 5-year all-cause mortality risk seen over the 18-month intervention period will be eligible for the healthcare utilization analyses in Aim 2.

5.2 EXCLUSION CRITERIA

Primary care team member exclusion criteria: We will exclude primary care team members who do not care for older adults (*e.g.* pediatricians or lactation nurses), are employed at geriatric specialty or dementia specialty clinics, or are without a primary care panel (*e.g.,* only urgent care).

PLwD exclusion criteria: Patients will be excluded if they have not been seen in the past 18 months by their primary care team, or if they do not have a diagnosis of ADRD.

5.3 LIFESTYLE CONSIDERATIONS

N/A

5.4 SCREEN FAILURES

Screen failures are defined as participants who registered for the training offered in this study but are not subsequently assigned to the study intervention or entered in the study. Individuals who do not meet the criteria for participation in this trial (screen failure) because of meeting one or more exclusion criteria that are likely to change over time may be rescreened. For example, if a primary care team MD/APP switches clinics from a control to intervention site, they will be offered training and once trained will be eligible for Aim 3. A screen failure would constitute interviewing a primary care team member who has not been trained as part of Aim 3. The participant's interview would not be used in subsequent analyses. Since PLwD are drawn from the clinic, screen failure is not possible for Aims 1 and 2.

5.5 STRATEGIES FOR RECRUITMENT AND RETENTION

Aims 1 and 2 Clinic Recruitment.

Recruitment and Consent. Primary care team members from clinic sites within UNC HEALTH and University of North Carolina Physicians Network (UNCPN) practices (see **Letters of Support**) will be recruited to participate. We will advertise for interested clinics in the monthly UNCPN newsletter; present the study at the monthly UNCPN medical directors meeting; and directly reach out to medical directors and clinic managers with the help of the UNCPN Research Committee and our co-investigators. Clinic sites will receive $3000 in incremental payments across the study period to facilitate recruitment and retention. Replicating procedures used in our pilot work, we will recruit UNCPN primary care clinic providers through direct outreach. We will draw on our UNCPN connections and our co-investigators, Drs. Hanson, Halpert, and Aragon, to recruit primary care team members from UNC HEALTH primary care clinics. We can also enlist Drs. Helton and Busby-Whitehead, the chairs of Family Medicine and Geriatric Medicine, respectively, for outreach. Dr. Ivester has also agreed to do direct outreach if needed.

We will work with the administrative teams at each of the 10 intervention sites to determine the optimal way to recruit primary care team participants, including remote options. We will work with each clinic to elicit volunteers for the study, providing a timeline of the research, answering questions, and providing other details as needed. We will also provide a call-back number and email address. We will purposively recruit from the entire pool of primary care team members, including social workers, nurses, case managers, medical assistants, etc. in addition to physicians and advance practice providers. All primary care team members from intervention sites will be approached and encouraged to participate in the 3-hour AD ACP Toolkit training. Training will be offered at convenient times, with the goal of reaching 70% of eligible primary care team physicians and APPs and will have it available online for training as well. While all primary care team members will be encouraged to participate in the training, MD/APP training completion rates will be used to determine fidelity. We will use similar recruitment methods as in our past study including email, letters, and networked outreach via clinic opinion leaders. Using our baseline data and our R56 results, we will explicitly target those primary care team members with the largest panels of adults aged ≥65, in the larger clinic sites for training. As per our prior protocol, training materials will be accessible online for asynchronous completion. For the control sites, primary care providers and staff will

be eligible with the same criteria as above. While we will apply for full IRB approval, our pilot study was IRB exempt due to its focus on team members and its use of deidentified data. We will post clinical trial information on ClinicalTrials.gov.

Recruitment strategies used:

1. Recruitment Emails- recruitment email promoting the training and how the training is available: In-person Zoom training (along with dates and times available and sign-up link in email) vs. Asynchronous training.

2. Reminder Emails- Reminder emails were sent to continue to recruit those who have not yet taken the training along with a continued reminder for clinicians who have not completed the training. These reminder emails went out every 1-2 weeks, at maximum every 3 weeks depending on the calendar.

3. Leadership engagement- frequent discussion with clinic leadership through the medical director and clinic manager to continue to promote training. Clinic managers promoted training internally with internal emails and messages sent in the EPIC EHR to providers for some clinics. Clinic leaders also sent out letters written by the AD-ACP study team to clinicians for internal promotion of the study training.

4. Physical letters mailed to clinics- physical letters with wet signature from Site-PI written and mailed to clinicians for promotion of the study training as well as to serve as an additional reminder that the clinician was missing pieces of the training and encourage completion of these areas.

5. All Hands/Providers meetings- Co-investigators Halpert and Aragon attended Intervention clinics all hands/ providers meetings (at least 2 meetings per clinic) to promote taking the study training and/or study task completion.

Retention. We will use several successful site retention strategies drawn from our previous studies. First, during recruitment, the site Principal Investigator, Co-Investigators, Project Manager, and Research Assistants will provide all participants with study contact information and discuss the options for the AD ACP Toolkit training sessions and provide maximum flexibility. We will inform them of the Continuing Medical Education/Continuing Nursing Education (CME/CNE) for completing training, and collect contact information either email or telephone, whichever is preferred for Aim 3. Second, the Research Assistant will send a reminder email/and or telephone call/text to participants 2 working days before the session. They will also receive ongoing implementation guidance including bimonthly audit-and-feedback of their ACP note completion rates. They will be available to answer questions or personally visit with the clinics if indicated. If a clinic asks to withdraw participation, the reason for the request will be discussed, and if possible, remedied. We will compensate the clinics for their time with payments at the beginning and end of the study period and the intervention clinic's primary care team members with CME/CNE for their training time. Drs. Hanson, Halpert, and Aragon, ACP and dementia experts, will lead the 3-hour AD ACP Toolkit sessions for the 10 intervention clinics. To encourage continued ACP practices, we will provide audit-and-feedback, coaching, retraining, and other feedback about participants' performance compared to their peers using the UNC Epic ACP dashboard and via our outcome measure data pulls developed as part of our R56. We will perform a one-time data pull for the ACP practices at the end of the intervention,

randomly sampling 40 PLwD seen in each clinic over the 18-month period and therefore will not need to retain PLwD. We will provide all clinics with $3000 in incremental payments across the study period to facilitate recruitment and retention.

Aim 3 Participant Recruitment.

Recruitment and Consent. Replicating procedures used in our previous work, all intervention-trained primary care team members will be eligible for the implementation surveys. We will seek to include a diversity of primary care team member disciplines (including the physicians/APPs, Registered Nurses [RNs], or Licensed Clinical Social Workers [LCSWs]). To encourage participation, we will provide $50 gift cards to all participants from each intervention site for the initial round of surveys pre- and post-training, and all participants from each intervention site for the 6-month and 18-month surveys as well. Informed consent will not be required as the training, pre- and post-training surveys, and participation in coaching calls pose no more than minimal risk to participants. To understand the barriers and facilitators to the AD ACP Toolkit implementation, we will conduct individual interviews (N=60) with primary care team participants who will receive $50 for their time. We will provide a call-back number and email address.

Retention. We will use several successful retention strategies drawn from our previous intervention studies. First, during recruitment, the Principal Investigator, Project Manager, and Research Assistant will provide all participants with study contact information, discuss the timeline for the trial, inform them of compensation for completing data collection, and collect contact information either email or telephone, whichever is preferred. Second, the research assistant will contact them about the follow-up surveys to remind them about them prior to sending them out. Third, to encourage retention in implementation surveys, we will offer a small payment ($50) to incentivize participants for completing each survey ($50 for the pre-post surveys together as they will be taken at the time of training, and $50 for the 6-month and 18-month surveys). We will work with UNCPN to optimize survey delivery, with online via secure email, in-person, and written options to maximize survey completion. Fourth, we will provide our contact information for real-time assistance with the surveys, and the principal investigator and project coordinator will remain in contact with the clinic sites throughout the study. They will be available to answer questions or personally visit the clinics if indicated. If a clinician asks to withdraw participation, the reason for the request will be discussed, and if possible, remedied. For example, if there is concern about the time requirements of the participant in the surveys, research staff will work to minimize the questions in subsequent surveys. We will not need to provide retention for the one-time participation in the implementation interviews given the one-time nature of the interviews.

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

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

6.1.1 STUDY INTERVENTION OR EXPERIMENTAL MANIPULATION DESCRIPTION

Intervention Condition: The AD ACP Toolkit intervention consists of primary care team member training supported by implementation guidance. Initial training includes a 15-minute introduction module followed by 4 modules devoted to the four stages of dementia. Design is grounded in decision science and implementation science theory. The modules are based on current best-evidence for ACP communication skills specific to PLwD. Modules incorporate problem-based learning techniques and group interaction to promote content uptake. Each training module takes about 30 minutes and consists of a 15-minute didactic portion comprised of key dementia stage education and relevant communication skills, a 5-10-minute video scenario modeling stage-specific AD/ADRD ACP communication skills, and a 5–10-minute Q&A session. Group interaction is promoted during two skill-building practice roleplay exercises using stage-specific clinical vignettes. Videos include diverse actors representing healthcare professionals, people with AD/ADRD, and their families in primary care clinic settings. Didactic and roleplay content reflect communication skills such as active listening and respect for family and cultural norms. Modules provide information about how to incorporate ACP practices in clinical operations and practical resources to facilitate implementation. They include tools to help operationalize their training in clinical care such as ACP billing codes, chart documentation templates, POLST forms, and scheduling approaches to provide sufficient time for GOC discussions. At the end of the training, participants complete an action plan for practice improvement, a strategy found to change physician behavior in diabetes care. At the end of the training, participants complete an action plan focusing on how they will put that knowledge into practice. The entire training takes 3 hours and can be delivered in-person or via video conferencing. We will also offer a self-directed web-based version of the training for team participants unable to attend the real-time training sessions.

Table 5. Four modules' components with screenshot of 2 video scenarios above (GDS 2-3 and GDS 4-6)

1. ACP in early dementia (GDS 2-3): This module promotes skills in facilitating goal-concordant care in the future as patients experience cognitive decline, including determining a preferred surrogate healthcare decision-maker and considering completion of advance directives such as living wills.

2. Decision-making capacity in moderate dementia (GDS 3-4): This module focuses on how to assess decision-making capacity in primary care and communicate with sensitivity and respect for the ACP needs of both the PLwD and their family.

3. Using the POLST in late-stage dementia (GDS 4-6): This module provided techniques to communicate around the issues of resuscitation, level of treatment, infection treatment, and nutrition decisions with families of people with late-stage dementia.

4. Hospice and hospitalization in end-stage dementia (GDS 7): This module includes communication techniques for discussing hospice and how that relates to ongoing hospitalization

To guide ongoing clinical implementation, the intervention includes clinic and primary care team feedback reports on ACP practices, periodic coaching, access to refresher sessions and web-based recordings of the AD ACP Toolkit training, as well as local champions. The intervention's implementation guidance is based in current best evidence. Current processes at UNC HEALTH routinely provide quality metric feedback to clinics; we will utilize this existing system to provide trained clinics' MD/APPs and their teams with bimonthly audit-and-feedback on ACP practices using data from the UNC HEALTH ACP Dashboard and lunch-and-learn sessions. We will coordinate periodic coaching sessions to discuss ACP challenges and facilitate ACP implementation by the primary care teams. Refresher sessions and as needed clinical in-services on requested topics will be held bi-monthly by Dr. Hanson and our team. Intervention MD/APPs and their teams will be re-offered training at 6 months. Each intervention clinic will identify and engage a local champion to support ACP activities.

The Elements, Content, and Method of Delivery of Each AD ACP Toolkit component

Elements	Content	Method for Delivery
Dementia-specific education	Stage-specific findings and challenges, including AD/ADRD staging, capacity assessment, symptom burden, hospice guidelines, etc.	10-minute didactics, delivered via video conferencing and via the website
ACP communication skills	Context-specific skills and tips on how to slow down, set the communication stage, active listening, respect for personhood and cultural norms, and common, useful language to prepare patients and families	10-minute didactics, either via video or on the website; 4 stage-specific videos to demonstrate the techniques, and 15-minute role-playing exercises; a fillable action plan, EHR ACP templates
Clinical implementation support	Coding and billing information for ACP and ACP templates, an action plan for each team member participant, monthly ACP audit-and-feedback to participants alternating with educational lunch-and-learns, and coaching sessions, site champion, refresher sessionsas needed	Resources at the end of the training session, available on the website, monthly feedback reports on ACP practices, periodic coaching

An intervention clinic will be considered active and in the implementation phase once 50% of its physicians and APPs are trained. Given the delay in receipt of the feedback from the Data Safety and Monitoring Board (DSMB) in October 2025 due to unforeseen and uncontrollable circumstances, and the fact that 2 sites achieved 50% training over the summer of 2025, the implementation start date for the 2 sites will be the date of receipt of the DSMB approval (1/20/26). The study team will continue to recruit additional PCTMs to reach 70%. Additionally, the start of the implementation period will begin 9 months after the first trained provider completed training at each clinic or once 50% of the clinic's providers are trained, whichever comes first. If a clinic fails to train any provider by the time the last trained clinic starts its implementation period, the implementation period will start at the time of last trained clinic date to synchronize data collection. This start date will allow for ongoing implementation support and feedback.

Control condition: Clinics randomized to the control arm will have access to voluntary, routine ACP training sessions provided by UNC HEALTH. We will provide the control clinics summary reports of their ACP practice outcomes at the end of the 18-month follow-up period, which can be used in future practice improvement efforts. Control clinics will be surveyed before the start of the implementation period and at the end of the implementation period for basic clinic and PCTM data.

6.1.2 ADMINISTRATION AND/OR DOSING

Intervention will be administered via a one-time real-time web-based training or via a self-directed on-line version with bi-monthly audit-and-feedback and lunch-and-learn sessions and dosing will include completion of the full training and bi-monthly updates.

6.2 FIDELITY

6.2.1 INTERVENTIONIST TRAINING AND TRACKING

Intervention site tracking and coaching support: Using the UNC HEALTH ACP Dashboard, research staff, and Dr. Aragon will review monthly reports of ACP activities. They will also review Toolkit training completion. The ACP Dashboard is a structured section in the Epic EHR that allows for reports to be run in real-time. Educational lunch-and-learn sessionswill be tailored to clinic-specific barriers to ACP activities, with emphasis on impactful in-depth GOC discussions and related operational strategies. Topics covered may include: a) sharing of success stories and facilitators of success, b) review of training content and ACP Dashboard data, and c) strategies to overcome implementation barriers. We will take notes of all lunch-and-learn sessions or coaching teleconferences and keep record of what was discussed at each coaching call. Because we will randomize training at the level of clinics, we will continue to offer and track web-based training throughout the intervention period as part of our implementation outcomes. Transcripts and training data will be used to meet Aim 3.

The proposed project uses the NIH Behavior Change Consortium standards for fidelity, addressing each of its 5 components in the following ways:
Study Design: An evidence-based and conceptually-grounded intervention has been standardized and protocolized to ensure consistent delivery. The AD ACP Toolkit uses standardized templates and tools to reinforce delivery of all components.
Primary care team training: Investigators will deliver standardized training to intervention primary care teams based on the previously developed and piloted AD ACP Toolkit. Refresher sessions will be offered to all intervention participants to boost fidelity.
Intervention delivery: Training data will be reviewed by Dr. Hanson who will work with intervention sites to optimize training participation by all eligible primary care team members; training will be offered 10 times initially to facilitate delivery.
Receipt of Intervention: Team members will take a post-training test, and can continue to retake the testing until they score ≥80%. One-to-one re-training will be offered as will booster sessions to ensure full uptake of the intervention, and for any new primary care team members added to the clinics.
Intervention enactment: We will monitor and provide feedback to the trained team members on the frequency of ACP by their team from the ACP Dash-board Epic EHR report monthly with comparisons to other sites, and ongoing coaching calls as indicated. Our External Advisory Board (EAB) and DSMB will assist throughout this entire process providing important input and oversight.

Implementation data collection: Primary care team members who participate in the AD ACP Training will be asked to provide de-identified demographic data but will not be identified by name. They will complete surveys pre- and post-training, 6 months, and 18 months after training. Surveys will be tailored to the team member's ACP role. Interviews will be conducted using a structured interview guide developed based on best practices of qualitative research (e.g., open-ended, non-leading questions) to reduce the risk of bias and elicit detailed responses and will be reviewed with the team for clarity and completeness. After the implementation period is completed, interviewers (Drs. Kistler and Leeman) will recruit primary care team members to consent to a one-time interview to elicit input on barriers and facilitators to engaging with the Toolkit and ACP. Each interview will last 30-60 minutes and be conducted at a location convenient to the participants. Recordings, audio files, and transcripts will be stored on a secure, password-protected server and destroyed once analyses are complete. Drs. Kistler and Leeman have extensive experience in conducting qualitative interviews.

6.3 MEASURES TO MINIMIZE BIAS: RANDOMIZATION AND BLINDING

Site recruitment, consent, randomization, masking, Primary care team members will be recruited from UNC HEALTH and UNCPN practices. We will advertise for interested primary care team members at clinic sites in the monthly UNCPN newsletter, the monthly UNCPN medical directors meeting, and direct outreach to clinic primary care team members with the help of the UNCPN Research Committee and our co-investigators. We will target primary care team members in clinics identified in our R56 as having the largest older adult patient panels and thus likely to have the largest expected AD/ADRD panels. The External Advisory Board, clinic medical directors, and managers will review study protocols and the medical directors will agree to their site's participation. Randomization will be at the clinic level and will occur once primary care team members at all 20 primary care clinics have been recruited and 6 months of pre-intervention baseline data on their ACP practices has been collected. The study biostatistician will randomize clinic sites in a 1:1 ratio, to the extent possible, ensuring an even distribution by size between intervention and control sites. Specifically, we feel clinic size and social vulnerability of patients served are the most important characteristics to be balanced between the groups. Clinic size will be operationally quantified using the older adult (age 65+) census. Social vulnerability will be operationalized as high or low based on whether Social Access Index Score (SAIS) developed by co-investigator Dr. Khairat is above or below the median. The SAIS uses a combined social inequity score, which uses 7 independent social determinant scores, and an access inequity score, which uses four independent access factors, to create a composite social access index score.[1] We will consider all 92,378 possibilities for assigning the 20 clinics to two groups (A and B, per se) of 10, and compute Endo's distance metric (based on Kullback-Leibler divergence) for each possibility.[2] We will then choose the possibility with the smallest distance where the total census difference between groups is no more than 10% of the smaller group census, as we feel clinic size is the more important factor. In case of an unlikely event with equally small distances, we will select one combination at random. Once we arrive at a final grouping A and B of clinics, we will randomly assign one to the active intervention and one to usual care. Dr. Kistler and all personnel involved in the outcomes assessment will remain masked to study arm assignment, while co-investigators Hanson, Halpert, and Aragon will deliver training and feedback reports to intervention sites.

6.4 STUDY INTERVENTION/EXPERIMENTAL MANIPULATION ADHERENCE

Types of Fidelity	Procedures to Ensure Fidelity	Adherence Monitoring
Study Design	• Intervention based on a well-defined protocol • Standardized tools and templates	• Templates assigned to primary care teams • Training toolkit reviewed by EAB
Primary Care Team Training	• Training of co-Is on study protocol and SOPs • Training of PCP teams to deliver ADRD ACP • Audio-recorded training modules for consistent re-training or for new personnel	• 50% of physician/APPs completed training • Post-training evaluation for PCP teams (threshold score 80%) • Delivery of 10 training sessions

Intervention Delivery, receipt, and enactment	• Bi-monthly audit-and-feedback to clinics and PCP teams and lunch-and learn sessions • Testing for each dementia stage	• Completion of audit-and-feedback alternating with lunch-and learn sessions every other month • Participants retake the testing until they score ≥80%. Clinic specific feedback when fidelity drops below threshold.

6.5 CONCOMITANT THERAPY

We will survey participants in the intervention arm whether they have received other ACP training in their repeat surveys.

6.5.1 RESCUE THERAPY

N/A

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

7.1 DISCONTINUATION OF STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

When a participant discontinues from the AD ACP Toolkit but not from the study, remaining study procedures will be completed as indicated by the study protocol. If a clinically significant finding is identified (including, but not limited to changes from baseline) after enrollment, the investigator or qualified designee will determine if any change in participant management is needed. Any new clinically relevant finding will be reported as an adverse event (AE).

The data to be collected at the time of study intervention discontinuation will include the following:

- The reason(s) for discontinuing the participant from the intervention, and methods for determining the need to discontinue.
- If the participant is due to be eligible for further surveys or interviews or periodic coaching as part of the study intervention, those assessments will be administered at the time of discontinuation

No interim analyses for safety, efficacy or futility are planned except for routine reports to the DSMB of adverse events stratified intervention arm as a part of the ongoing study monitoring by the DSMB.

7.2 PARTICIPANT DISCONTINUATION/WITHDRAWAL FROM THE STUDY

Participants are free to withdraw from participation in the study at any time upon request. An investigator may discontinue a participant (i.e. a primary care team member) from the study for the following reasons:

- Significant study intervention non-compliance, unless varying compliance is an aspect of the study objectives

- Lost-to-follow up; unable to contact participant
- Any event or medical condition or situation occurs such that continued collection of follow-up study data would not be in the best interest of the participant or might require an additional treatment that would confound the interpretation of the study
- The participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation such as a change of clinic or type of clinical role.

The reason for participant discontinuation or withdrawal from the study will be recorded in the electronic data collection form. Subjects who are randomized but do not receive the study intervention may be replaced. Subjects who are randomized and receive the study intervention, and subsequently withdraw, or are discontinued from the study, will be replaced.

7.3 LOST TO FOLLOW-UP

A participant will be considered lost to follow-up if he or she fails to complete the repeated measures survey and study staff are unable to contact the participant after at least 3 attempts.

The following actions must be taken if a participant fails to complete a survey:

- The site will attempt to contact the participant, encourage the participant to complete the surveys, and counsel the participant on the importance of completing the surveys and ascertain if the participant wishes to and/or should continue in the study
- Before a participant is deemed lost to follow-up, the investigator or designee will make every effort to regain contact with the participant (where possible, 3 telephone calls and, if necessary, a certified letter to the participant's last known mailing address or local equivalent methods). These contact attempts will be documented in the participant's medical record or study file.
- Should the participant continue to be unreachable, he or she will be considered to have withdrawn from the study with a primary reason of lost to follow-up]

8 STUDY ASSESSMENTS AND PROCEDURES

8.1 ENDPOINT AND OTHER NON-SAFETY ASSESSMENTS

List of measures, definitions, and sources

Measure	Definition	Source
PRIMARY OUTCOME		
GOC discussions	Documented discussions including the primary care team member with the PLwD or their surrogate decision-maker; must include a) communication about dementia stage or prognosis AND b) decision-making for at least one major treatment: CPR/mechanical ventilation, hospitalization, treatments for infections, artificial/feeding/hydration, OR hospice.	EHR review
SECONDARY OUTCOMES Aim 1		

ACP practices	1) documented choice of surrogate healthcare decision-maker 2) documented assessment of decision-making capacity for the PLwD 3) completion of portable ACP orders with DNR or POLST forms 4) documented discussion of prognosis or future medical complications of dementia during the 18-month period after training	EHR review
HEALTHCARE UTILIZATION OUTCOMES Aim 2		
Hospitalizations + Emergency Department visits	Admission to a UNC HEALTH hospital for an inpatient or observation stay or a visit to a UNC HEALTH emergency department (inclusive of hospitalization)	CDW data extraction
Length of stay	Duration of hospitalizations from day of admission to day of discharge	CDW data extraction
Hospice or palliative care referral	Chart order in the EHR to refer a PLwD to hospice or palliative care	CDW data extraction
Hospice Disenrollment	Insurance status for Centers for Medicare/Medicaid Services (CMS) billing.	CDW data extraction
Goal-concordant care	Documented code status in EHR	CDW data extraction augmented with EHR review
IMPLEMENTATION OUTCOMES Aim 3		
Acceptability, Appropriateness, and Feasibility of the Intervention	The perception that the innovation is acceptable (ie, agreeable, palatable, or satisfactory), appropriate (fit/relevance of the innovation to: a) the setting and b) address the problem), and feasible (the extent to which the innovation can be successfully enacted or carried out within the setting) to the participants	Pre-post and 6-month and 18-month surveys
Adoption	The intention, decision, or action to try the intervention	Web-based analytics, logbooks
Fidelity	The degree to which the innovation was implemented as intended	Web-based analytics, logbooks

While the clinics will be the unit of randomization and the primary care team member is the unit of the intervention, the PLwD will be the unit of analysis. Data collection will be identical for both arms. **Aim 1** data will be obtained from EHR reviews at 18 months post-intervention of 40 randomly selected PLwD from the MD/APPs at each intervention site and 40 PLwD from the MD/APPs at the control sites using the CDW. **Aim 2** data will focus on a large data set of all PLwD with ≥50% 5-year all-cause mortality seen by the MD/APPs in the intervention versus the control arm. For **Aim 3**, data will be obtained from repeated mixed-method surveys, ongoing web-based analytics, study logbooks, documented notes of coaching calls, and interviews at 18 months.

Implementation data collection: Primary care team members who participate in the AD ACP Training will be asked to provide de-identified demographic data but will not be identified by name. They will complete surveys pre- and post-training, 6-months, and 18-months after training. Surveys will be tailored to the team member's ACP role. Interviews will be conducted using a structured interview guide developed based on best practices of qualitative research (e.g., open-ended, non-leading questions) to reduce the risk of bias and elicit detailed responses and will be reviewed with the team for clarity and completeness. After the implementation period is completed, interviewers (Drs. Kistler and Leeman) will recruit primary

care team members to consent to a one-time interview to elicit input on barriers and facilitators to engage with the Toolkit and ACP. Each interview will last 30-60 minutes and be conducted at a location convenient to the participants. Recordings, audio files, and transcripts will be stored on a secure, password-protected server and destroyed once analyses are complete. Drs. Kistler and Leeman have extensive experience in conducting qualitative interviews.

Primary outcome: AD/ADRD GOC Discussions. GOC discussions are assessed in a medical record review. An AD/ADRD GOC discussion is present if a member of the primary care team documents a discussion of the dementia stage or prognosis, plus decision-making for one or more of five common items discussed across all AD/ADRD stages: CPR/mechanical ventilation, hospitalization, treatments for infections, artificial feeding/hydration, and hospice. Our GOC outcome aligns with recent definitions of successful ACP, and has been used in our prior research, including the pilot study of this intervention. Though charts will be chosen using a discrete clinic visit, the entire period from the point the clinic is trained through 18 months will be reviewed for GOC discussions. We will review each intervention and control clinic's charts for these elements over an 18-month period.

Secondary outcomes.

- **ACP practices (Aim 1)** will be measured as the frequency of 1) documented choice of a surrogate decision-maker for the PLwD, 2) assessment and report of decision-making capacity for the PLwD, 3) completion of portable ACP orders using a state-approved DNR or POLST form, and 4) documented discussion of prognosis or future medical complications of AD/ADRD during the 18-month intervention period via chart review.
- **Hospitalizations and emergency department visits (Aim 2)** will be measured as the frequency of hospitalizations for observation or inpatient stay using validated EHR chart review methods and the CDW data extraction. Hospitalizations are important markers of cost, both to patients and families and to the larger healthcare system. They also represent disruptions in the normal guidance offered by primary care providers. **Emergency department visits** will be measured as the frequency of emergency department evaluation, obtained via the CDW data extraction. ACP interventions in other populations and patients with advanced dementia have demonstrated reductions in hospitalization and emergency department visits.
- **Length-of-Stay (Aim 2)** will be measured as the length of each admission and observational stay in days, which will be obtained via CDW data extraction.
- **Use of community palliative care or hospice (Aim 2)** will be measured in the presence of a referral in the EHR and obtained via the CDW data extraction; referrals will be used rather than encounters, since service providers are frequently external to the UNC HEALTH system for these services.
- **Goal-concordant care (Aim 2)** will be measured in terms of the frequency with which PLwD receive care that is concordant vs discordant with their documented treatment preferences and GOC, including CPR/mechanical ventilation, hospitalization, treatments for infections, artificial feeding/hydration, and hospice. Goals and preferences will be based on review of specific orders ("do not resuscitate"), advance care planning notes recording GOC discussions, or portable DNR or POLST forms, and compared to subsequent hospitalizations, use or avoidance of major treatments via CDW data extraction. This measure assesses goal concordance in the longitudinal data similar to other studies.
- **Acceptability, Appropriateness, and Feasibility (Aim 3)** will be measured in repeated surveys as part of a 12-item scale which includes 4 items to assess the acceptability of a clinical intervention, including the approval, welcome, appeal, and likeability of the intervention on a 5-point ordinal scale (Cronbach's α=0.85 and Pearson correlation coefficient= 0.80), 4 items assessing the fit, suitability,

applicability, and match of the intervention to the clinical care on a 5-point ordinal scale (Cronbach's α=0.91 and Pearson correlation coefficient= 0.73); and 4 items that assess the degree to which an intervention is implementable, possible, doable, and easy to use, on a 5-point scale (Cronbach's α=0.89 and Pearson correlation coefficient= 0.88).

- **Adoption (Aim 3)** will be measured as the frequency with which training is used, including the proportion of intervention clinics and primary care team members who agreed to and completed the training.
- **Fidelity (Aim 3)** will be measured by primary care team members' scores on post-intervention quizzes, participation in clinic-level and primary care team member-level ACP audit-and-feedback, refresher sessions and in-services, as well as periodic coaching from the research term.

8.2 SAFETY ASSESSMENTS

8.3 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

8.3.1 DEFINITION OF ADVERSE EVENTS

This study is "no more than minimal risk". This decision is based on the nature of the study and intervention as well as the subject population. This protocol uses the definition of adverse event from 21 CFR 312.32 (a): Any untoward or unfavorable medical occurrence in a human study participant, including any abnormal sign (e.g. abnormal exam or laboratory finding), symptom or disease temporally associated with the participants' involvement in the research, whether or not considered related to participation in the research.

Primary care team member participants will be provided with the research team's contact information and be able to provide feedback or contact us with any concerns at any time. We will track the numbers of outreach, contacts, and concerns we receive.

8.3.2 DEFINITION OF SERIOUS ADVERSE EVENTS

Overview. While we do not expect a potential for harm to participants as a result of the proposed AD ACP Toolkit, we will monitor unanticipated problems, potential adverse events associated with study intervention, and potential adverse events associated with subject enrollment and data collection.

- Unanticipated and incidental findings. Any incident, experience, or outcome that is unexpected (in terms of nature, severity, or frequency) given the research procedures and the characteristics of the population; related or possibly related to participation in the research; and suggesting that the research places subjects or others at a greater risk of harm (physical, psychological, economic, social) than was previously known or recognized, will be monitored.
- Potential adverse events associated with the study intervention. We do not foresee any potential adverse events associated with study intervention.

8.3.3 CLASSIFICATION OF AN ADVERSE EVENT

8.3.3.1 SEVERITY OF EVENT

For adverse events (AEs) not included in the protocol defined grading system, the following guidelines will be used to describe severity.

- **Mild** – Events require minimal or no treatment and do not interfere with the participant's daily activities.
- **Moderate** – Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.
- **Severe** – Events interrupt a participant's usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating. Of note, the term "severe" does not necessarily equate to "serious".]

8.3.3.2 RELATIONSHIP TO STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

The potential event relationship to the study intervention and/or participation is assessed by the site investigator. A comprehensive scale in common use to categorize an event is:

- Definitely Related: The adverse event is clearly related to the investigational agent/procedure – i.e., an event that follows a reasonable temporal sequence from administration of the study intervention, follows a known or expected response pattern to the suspected intervention, that is confirmed by improvement on stopping and reappearance of the event on repeated exposure and that could not be reasonably explained by the known characteristics of the subject's clinical state.
- Possibly Related: An adverse event that follows a reasonable temporal sequence from administration of the study intervention follows a known or expected response pattern to the suspected intervention, but that could readily have been produced by a number of other factors.
- Not Related: The adverse event is clearly not related to the investigational agent/procedure - i.e., another cause of the event is most plausible; and/or a clinically plausible temporal sequence is inconsistent with the onset of the event and the study intervention and/or a causal relationship is considered biologically implausible.

Given the minimal risk nature of this study, no related adverse events are expected or unexpected.

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

The occurrence of an adverse event (AE) or serious adverse event (SAE) may come to the attention of study personnel during study visits and interviews of a study participant presenting for medical care, or upon review by a study monitor.

Any medical or psychiatric condition that is present at the time that the participant is enrolled will be considered as baseline and not reported as an AE.

8.3.5 ADVERSE EVENT REPORTING

Adverse event reporting will be refined with input from the DSMB during its initial meeting, to address any specific concerns related to this study protocol.

Investigators will report any Unanticipated Problem Involving Risk to Subjects or Others (UPIRSO)s or AEs to the overall PI and Project Manager in a timely manner.
When a UPIRSO or AE is present, the overall PI and Project Manager will submit a report to the UNC IRB within 3 working days of receipt of this information. Generally, the report should contain the following:

- Detailed information about the event or issue, including relevant dates. The report should identify the affected subjects by their study codes and not by their names or other personal identifiers.
- An assessment of whether any subjects or others were placed at risk or suffered any harm (e.g., physical, social, financial, legal or psychological) as a result of the event.
- If the event involves noncompliance, describe the result of the root cause analysis.
- Any corrective and preventative actions, planned or already taken.
- Any other information requested by Office of Human Research Ethics (OHRE), if applicable.
- If the report cannot be completed in its entirety within the required time period, the report should describe what information is still needed and when the investigator anticipates that a follow-up report will be submitted.

Information previously unknown to the IRB that suggests new or increased risk to subjects or others (hereinafter referred to as New Safety Information) is promptly reportable to OHRE within 7 calendar days of the investigator becoming aware of the information.

- Information for which the sponsor requires reporting to the IRB, may be summarized and submitted to the IRB at continuing review.
- Protocol deviations that did not harm subject(s) or others or place subject(s) or others at increased risk must be summarized and reported to the IRB at continuing review.
- Researchers may consult with the OHRE Compliance Manager if they are uncertain about what information is reportable.

8.3.6 SERIOUS ADVERSE EVENT REPORTING

The reporting of any AE / SAE will be based on NIA and UNC IRB standards, on the severity of the AE, its level of attribution to the intervention, and whether or not it is anticipated.

- All **adverse events that are both serious** (SAE) **and unexpected** would be reported to IRB, DSMB / Safety Officer (SO), and National Institute of Aging Program Officer (NIA PO) **within 48 hours** of the study's knowledge of SAE.
- Summary of SAEs would be reported to NIA PO and to the DSMB / PO **quarterly**, unless otherwise requested by the DSMB or a Safety Officer.
- Summary of all AEs regardless of classification would be presented for each DSMB meeting at 6-month intervals

8.4 UNANTICIPATED PROBLEMS

8.4.1 DEFINITION OF UNANTICIPATED PROBLEMS

This protocol uses the definition of Unanticipated Problems as defined by the UNC Office of Human Research Ethics (OHRE).
Unanticipated Problems are defined as

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

9 STATISTICAL CONSIDERATIONS

9.1 STATISTICAL HYPOTHESES

- Primary Endpoint(s):

Aim 1. Intervention Efficacy Outcomes. To conduct a cluster RCT trial to compare the efficacy of the AD ACP Toolkit (intervention) vs usual care (control) on GOC discussions (primary outcome) in 800 PLwD, and other APC practices such as preferred surrogate, decisional capacity, and portable ACP orders (secondary outcomes) over 18 months.

Hypothesis: A greater proportion of the intervention group participants will have GOC discussion and ACP practice outcomes compared to the control group participants.

- Secondary Endpoint(s):

Aim 2. Healthcare Utilization Outcomes. To compare healthcare utilization outcomes (hospitalization/ emergency department visits, length-of-stay, hospice/ palliative care, goal-concordant care), utilizing a large health care system's clinical data warehouse for PLwD with ≥50% 5-year all-cause mortality risk in intervention vs control clinics over 18 months. We will conduct pre-specified subgroup analyses by race, ethnicity, and clinic location.

Hypothesis: Intervention group participants will have lesser rates of healthcare utilization compared to control group participants.

Aim 3. Implementation Outcomes. We will assess implementation outcomes and explore multilevel barriers and facilitators to explain variations in those outcomes. We will use both quantitative methods to assess outcomes (acceptability, appropriateness, feasibility, adoption, and fidelity) as well as qualitative methods. Guided by the Consolidated Framework for Implementation Research (CFIR), we will collect qualitative interview data to explore barriers and facilitators to achieving those outcomes at each of the 10 intervention clinics.

As this aim is exploratory in nature, we have no explicit hypotheses at the time of this protocol initiation, and analyses will be data driven.

9.2 SAMPLE SIZE DETERMINATION

The sample size calculation is based on detecting a meaningful effect for our primary outcome, GOC discussions, in an intention-to-treat analysis. Based on our pilot study, we anticipate the difference in GOC decision-making discussion will be 15% (control) vs. 30% (intervention), resulting in the sample size n=approximately 240 (n=approximately 120 in each group) for 80% power and 5% type-I error rate. However, the sample size will be inflated by the design effect, defined by (1+ ρ*(m-1)), where m is the average number of patients sampled per clinic and ρ is the intra-class correlation coefficient (ICC). When sampling 40 PLwD patients per clinic for a total n=800 using a design effect of 3.34, we have a sufficient sample size to detect the clinically meaningful absolute difference of 15% when the ICC is 0.06 or less. A similar study, though in the UK for older adults in primary care and using different measures than our primary outcomes, had an ICC less than 0.05.[3] Given the inability to derive an ICC from our pilot data due to limited cluster sizes, we use an ICC of 0.06 in computations as most of the reported ICCs were <0.05 which makes the above assumption of ICC=0.06 conservative.

In the event that providers from all intervention clinics do not complete training above the 70% threshold within a 9-month period, we will take steps to ensure at least a subsequent per-protocol analysis can be performed with sufficient statistical power. For example, if only 8 of the 10 intervention clinics end up meeting the 70% trained threshold, we will consider a post hoc analysis excluding the data from the two clinics in which providers were not trained above the 70% threshold. In such an event, we will increase the number of charts reviewed per clinic to compensate for loss of statistical power. Specifically, using a design effect of 4.30, we will review 56 charts from each clinic. Number of charts per clinic will be recomputed based on the actual number of fully trained clinics at the beginning of the trial period.

For **Aim 3**, the sample size in qualitative studies is determined using an iterative process. We will purposively recruit all participants for the repeat-measures, mixed-method surveys and interview participants believed to be most informative based on their role. Based on the literature and our own prior studies, 60 participants are typically sufficient to reach thematic saturation given the different types of team members (i.e., further groups are unlikely to yield new findings). This sample should be sufficient for implementation evaluation.

9.3 POPULATIONS FOR ANALYSES

For our primary outcome, we will perform an intention to treat analysis of the primary care team members and the randomly chosen 800 people living with dementia in our intervention versus control sites.

We will also have a secondary cohort of people living with dementia with greater than 50% mortality risk at those sites for the analysis of our AIM 2. For the outcomes obtained via CDW extraction, analysis will use data from all patients meeting inclusion/exclusion criteria in the participating clinics with greater than 50% mortality risk.

Per-protocol analysis will exclude data from the intervention sites where <70% of providers are fully trained.

Finally, we will have a cohort of primary care team member participants in the intervention who will be the population for analysis in AIM 3.

9.4 STATISTICAL ANALYSES

9.4.1 GENERAL APPROACH

For descriptive analyses, we will examine the distributions of all major variables. Missing data should be minimal since the data collection is based on chart review. Categorical variables will be collapsed into meaningful groups. Poorly distributed continuous variables may be transformed, categorized, or analyzed using non-parametric tests. The validity of randomization will be tested by comparing intervention and control participants on baseline measurements. Any variables significantly differently distributed between intervention and control will be included as additional covariates in sensitivity analyses. We will not change the primary analysis to preserve its a priori nature. Primary analyses will be performed as randomized based on intention-to-treat, followed by secondary per-protocol analyses excluding intervention clinics with a provider training completion rate <70%. An additional exploratory per-protocol analysis will be conducted with intervention arm patient data restricted to only those cared for by fully trained providers. We anticipate the dropout problem will be minimal because older adults tend to change primary care clinics only when necessary. Though patients may die or move in a year, their medical charts may be reviewed before they leave the system. Therefore, the sample size will remain n=800 after data collection. All statistical tests will be two-sided with an overall 0.05 significance level pre-specified for analyses. The aim-by-aim analysis strategy is proposed as follows.

9.4.2 ANALYSIS OF THE PRIMARY ENDPOINT(S)

Aim 1 Intervention Efficacy Outcomes. We will compare the proportions with a GOC discussion between control and intervention primary care team members by clinic. Because patients in the same clinic may have correlated outcomes, we will use a generalized estimating equations (GEE) model with a binomial distribution, logit link function, intervention arm as the main independent variable of interest and an

exchangeable working correlation structure to account for a site (clinic) effect. Possible confounders will be included as additional independent variables in the regression model to adjust the difference between intervention and control in follow-up sensitivity analyses. Odds ratio (OR) for intervention arm and its statistical significance at α=0.05 level will serve as a formal test of the primary efficacy hypotheses. The secondary outcomes include discussions of surrogate decision-makers, capacity assessment, dementia prognosis, and completion of portable DNR or POLST. A similar analytic strategy will be employed for the secondary efficacy outcomes.

9.4.3 ANALYSIS OF THE SECONDARY ENDPOINT(S)

Aim 2 Healthcare Utilization Outcomes. We will compare healthcare utilization between intervention and control clinics. The healthcare utilization, including hospitalizations/emergency department visits, length-of-stay, hospice/palliative care referral, and goal-concordant care, will be collected from the entire cohort of PLwD patients identified by the CDW in the 18-month intervention period. We expect to collect healthcare utilization outcomes from up to 2,660 PLwD in the 20 clinics based on current clinic census data, who will meet criteria for inclusion based on 5-year mortality risk scores. Hospitalizations and emergency department visits will be treated as count data. We will fit a series of GEE models with each count outcome as the dependent variable, a negative binomial distribution, a log link function, natural logarithm of observed follow-up time as an offset, intervention arm as the independent variable of interest, and an exchangeable working correlation structure to account for clustering by clinic. The incident rate ratio (IRR) for intervention arm and its statistical significance at α=0.05 will serve as formal tests of hypotheses. Length-of-stay is a highly skewed time-to-event variable. We will use a shared frailty model to test the intervention effect with a proportional hazards component while accounting for clustering due to clinic with a shared frailty parameter. Hospice/palliative care and goal-concordant care will be treated as binary variables and will follow the same analytic plan as Aim 1.

Aim 3 Implementation Outcomes. For the qualitative CONSORT outcomes, an iterative analytic approach to the implementation interviews will be used, such that after conducting interviews, transcripts will be reviewed and suggested changes to the interviews will be made and a revised guidebook presented to the remaining participants. In this way, codes will be iteratively refined as data are collected. Two coders will use a qualitative software management tool (e.g., ATLAS.ti) to develop codes based on a codebook grounded in the CFIR construct guidance on the CFIR and general interview guide principles. Codes will then be created inductively for emergent themes. The coders will be overseen by Drs. Kistler and Leeman, in collaboration with the team, who will discuss initial and emerging codes and create a final codebook. Once reliability ≥ 80% is achieved, the coders will independently code the remaining transcripts. Summary tables of findings with example quotes will be developed. The qualitative analysis drawn from the interviews will follow standard techniques, including transcription of all interviews, independent dual coding, and discussion and resolution of coding inconsistencies. A master list of codes will be formulated by consensus and the team will collaboratively group codes into themes to elucidate barriers and facilitators to the use and content of the intervention and ACP for PLwD. Coding discrepancies will be discussed with the group and resolved by consensus.

We will use linear mixed models for implementation outcomes that can be treated as continuous variables, time point as the fixed effects of interest; any participant characteristics of interest as a fixed-effect covariates in sensitivity analyses; a participant random effect to account for the correlation between multiple time points within the same person; and an exchangeable correlation structure to account for clustering due to clinic.

9.4.4 SAFETY ANALYSES

N/A

9.4.5 BASELINE DESCRIPTIVE STATISTICS

We will collect basic clinic information at the point of recruitment. We will also collect baseline ACP data in the intervention and control groups. We will reassess descriptive statistics at the start and end of the implementation time period.

9.4.6 PLANNED INTERIM ANALYSES

No interim analyses are planned for efficacy, safety or futility except routine adverse event reports to the DSMB stratified by intervention arm.

9.4.7 SUB-GROUP ANALYSES

No confirmatory subgroup analyses are planned. Subgroup analyses will be conducted with an exploratory philosophy with hypothesis generation as the goal.

9.4.8 TABULATION OF INDIVIDUAL PARTICIPANT DATA

No individual data will be listed by measure and time point.

9.4.9 EXPLORATORY ANALYSES

Aim 3 is an exploratory aim as noted above.

10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

10.1.1 INFORMED CONSENT PROCESS

10.1.1.1 CONSENT/ASSENT AND OTHER INFORMATIONAL DOCUMENTS PROVIDED TO PARTICIPANTS

Consent forms describing in detail the post-training implementation interview will be provided to the primary care team member participant and verbal consent will be completed prior to starting the interview. Informed consent for participation in the training, pre- and post-training surveys, and

participation in coaching calls will not be required as the research poses no more than minimal risk to the participants.

10.1.1.2 CONSENT PROCEDURES AND DOCUMENTATION

For Aims 1 and 2, we plan for the medical director at all participating clinics to provide a letter of support for the study. Informed consent for participation in the training, pre- and post-training surveys, and participation in coaching calls will not be required as the research poses no more than minimal risk to the participants. Prior to the training, we will review the training and study purpose and expected time commitment. We will have primary care team participants complete post-intervention interviews in Aim 3. The consent forms for the interviews will include wording indicating that the participant may choose not to answer questions or may end the interview or his/her participation at any time. A participant also will be encouraged to speak to a research team member if he/she has any questions or concerns.

Given the reliance on the electronic health record for our outcomes, we are not consenting individual patients/PLwD as the information we will collect is the typical information found in medical records, as was done in our pilot study.

10.1.2 STUDY DISCONTINUATION AND CLOSURE

This study will be closed after completion of target enrollment, and study procedures discontinued after follow-up data collection, and planned data analyses with appropriate presentation, publication, and data sharing.

10.1.3 CONFIDENTIALITY AND PRIVACY

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, the safety and oversight monitor(s), and the sponsor(s) and funding agency. This confidentiality is extended to the data being collected as part of this study. Data that could be used to identify a specific study participant will be held in strict confidence within the research team. No personally-identifiable information from the study will be released to any unauthorized third party without prior written approval of the sponsor/funding agency.

All research activities will be conducted in as private a setting as possible. All information will be kept in strict confidence and coded with subject identification numbers. Survey data will be entered directly into the REDCap survey site and require password-protected and encrypted computers for access. While we will primarily use verbal consent for participants, if we have paper files – including interview consent forms—we will store them in a folder kept on the research coordinator or in a locked location while in the field and later stored in a locked filing cabinet in a locked office. If necessary, lists linking subject identification numbers to names will be maintained in a separate, secure file, and will be destroyed after all data are verified. All research at UNC is conducted in accordance with Federal regulations related to human subject research and with (**Health Insurance Portability and Accountability Act)** HIPAA-related requirements. All individuals conducting research receive required human subjects training and certification prior to the initiation of study activities. To safeguard subject confidentiality, subjects will be identified by number rather than by name in data collection instruments.

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

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

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored at locations approved for this purpose by the University of Pittsburgh, including an access-restricted network server (with daily backups managed by the Department of Medicine/institutional network operations center) and Microsoft OneDrive cloud storage. Data stored will not include the participant's contact or identifying information. Rather, individual participants and their research data will be identified by a unique study identification number. The study data entry and study management systems used by clinical sites and by University of Pittsburgh research staff will be secured and password protected. At the end of the study, all study databases will be archived at the University of Pittsburgh for the duration of required period of currently 7 years.

Measures Taken to Ensure Confidentiality of Data Shared per the NIH Data Sharing Policies

It is NIH policy that the results and accomplishments of the activities that it funds should be made available to the public (see *https://grants.nih.gov/policy/sharing.htm*). The PI will ensure all mechanisms used to share data will include proper plans and safeguards for the protection of privacy, confidentiality, and security for data dissemination and reuse (e.g., all data will be thoroughly de-identified and will not be traceable to a specific study participant). Plans for archiving and long-term preservation of the data will be implemented, as appropriate.

Certificate of Confidentiality

To further protect the privacy of study participants, the Secretary of Health and Human Services (HHS) has issued a Certificate of Confidentiality (CoC) to all researchers engaged in biomedical, behavioral, clinical or other human subjects research funded wholly or in part by the federal government. Recipients of NIH funding for human subjects research are required to protect identifiable research information from forced disclosure per the terms of the NIH Policy (see *https://humansubjects.nih.gov/coc/index*). As set forth in 45 CFIR Part 75.303(a) and (National Institutes of Health Grants Policy Statement) NIHGPS Chapter 8.3, recipients conducting NIH-supported research covered by this Policy are required to establish and maintain effective internal controls (e.g., policies and procedures) that provide reasonable assurance that the award is managed in compliance with Federal statutes, regulations, and the terms and conditions of award. It is the NIH policy that investigators and others who have access to research records will not disclose identifying information except when the participant consents or in certain instances when federal, state, or local law or regulation requires disclosure. NIH expects investigators to inform research participants of the protections and the limits to protections provided by a Certificate issued by this Policy.

10.1.4 FUTURE USE OF STORED SPECIMENS AND DATA

Data collected for this study will be analyzed and stored at University of Pittsburgh (see 10.1.3). After the study is completed, the de-identified, archived data will be available for use by other researchers including those outside of the study according to the study data sharing policy. Permission to transmit data to University of Pittsburgh will be included in the informed consent form for interviews.

10.1.5 KEY ROLES AND STUDY GOVERNANCE

The research team will be led by Dr. Christine E. Kister at the University of Pittsburgh and Dr. Laura C. Hanson at UNC and managed by project managers at each institution. Drs. Kistler and Hanson and the project managers will provide administrative leadership and study coordination to ensure timely completion of research tasks and consistency with protocol standards. University of Pittsburgh will be the administrative home and will support all data analysis. Data analysis will be led by the study biostatistician, Subashan Perera, PhD.

10.1.6 SAFETY OVERSIGHT

All study protocols and amendments, consent forms, and other study materials will undergo review by the Institutional review Board at the University of North Carolina at Chapel Hill prior to initiating research and will be subject to Annual and other required reviews. This trial will utilize a single IRB based at UNC.

In addition to study monitoring and oversight by Dr. Kistler and the Project Managers, safety oversight will be under the direction of a Data and Safety Monitoring Board (DSMB) composed of individuals with the appropriate expertise relevant to the proposed trial. Members of the DSMB will be independent from the study conduct and free of conflict of interest. The DSMB will meet at least semiannually to assess safety and implementation data from each arm of the study. The DSMB will operate under the rules of an approved charter that will be written and reviewed at the organizational meeting of the DSMB. At this time, each data element that the DSMB needs to assess will be clearly defined. The DSMB will provide its input to National Institute on Aging.

10.1.7 CLINICAL MONITORING

N/A. Given the minimal risk of the trial, independent audits will not be conducted.

10.1.8 QUALITY ASSURANCE AND QUALITY CONTROL

The project managers and research assistants will perform internal quality management of study conduct, data collection, documentation and completion. All sites will follow a common quality management plan.

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

Informed consent --- Study staff will review both the documentation of the consenting process as well as a percentage of the completed consent documents. This review will evaluate compliance with GCP,

accuracy, and completeness. Feedback will be provided to the study team to ensure proper consenting procedures are followed.

Source documents and the electronic data --- Data will be captured and entered directly into the study database. To ensure accuracy, site staff will compare a representative sample of source data against the database, targeting key data points in that review.

Intervention Fidelity — Consistent delivery of the study interventions will be monitored throughout the intervention phase of the study. Procedures for ensuring fidelity of intervention delivery are described in **Section 6.2.1, Interventionist Training and Tracking**.

Protocol Deviations – The study team will review protocol deviations on an ongoing basis and will implement corrective actions when the quantity or nature of deviations are deemed to be at a level of concern.

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

10.1.9 DATA HANDLING AND RECORD KEEPING

10.1.9.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

Data collection will be the responsibility of the clinical trial staff at the site under the supervision of the site investigator. The investigator will be responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

All source documents will be completed in a neat, legible manner to ensure accurate interpretation of data. Electronic medical record data will be accessed and entered directly into electronic Case Report Forms (CRFs) in a secure web application online survey database. The data system includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate. Clinical data will be entered directly from the source documents. At no time will personal identifying information be stored on portable laptop computer devices.

10.1.9.2 STUDY RECORDS RETENTION

Study documents will be retained for a minimum of 3 years after all study activities have been completed and will comply with all NIH and NIA data retention standards.

10.1.10 PROTOCOL DEVIATIONS

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

These practices are consistent with ICH GCP:

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

It will be the responsibility of the site investigator to use continuous vigilance to identify and report deviations within 7 working days of identification of the protocol deviation, or within 7 working days of the scheduled protocol-required activity. All deviations will be addressed in study source documents, reported to the National Institute on Aging Program Official and University of North Carolina at Chapel Hill IRB. Protocol deviations will be sent to the reviewing Institutional Review Board (IRB) per their policies. The site investigator will be responsible for knowing and adhering to the reviewing IRB requirements. Further details about the handling of protocol deviations will be included in the MOP.

10.1.11 PUBLICATION AND DATA SHARING POLICY

This study will be conducted in accordance with the following publication and data sharing policies and regulations:

National Institutes of Health (NIH) Public Access Policy, which ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central upon acceptance for publication.

This study will comply with the NIH Data Sharing Policy and Policy on the Dissemination of NIH-Funded Clinical Trial Information and the Clinical Trials Registration and Results Information Submission rule. As such, this trial will be registered at ClinicalTrials.gov, and results information from this trial will be submitted to ClinicalTrials.gov. In addition, every attempt will be made to publish results in peer-reviewed journals. Data from this study may be requested from other researchers for 7 years after the completion of the primary endpoint by the biostatistician, Dr. Subashan Perera. Considerations for ensuring confidentiality of these shared data are described in Section 10.1.3.

10.1.12 CONFLICT OF INTEREST POLICY

The independence of this study from any actual or perceived influence, such as by the pharmaceutical industry, is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the design and conduct of this trial. The study leadership in conjunction with the National Institutes on Aging has established policies and procedures for all study group members to disclose all conflicts of interest and will establish a mechanism for the management of all reported dualities of interest.

10.2 ADDITIONAL CONSIDERATIONS

None.

10.3 ABBREVIATIONS AND SPECIAL TERMS

AE	Adverse Event
ANCOVA	Analysis of Covariance
CFR	Code of Federal Regulations
CLIA	Clinical Laboratory Improvement Amendments
CMP	Clinical Monitoring Plan
COC	Certificate of Confidentiality
CONSORT	Consolidated Standards of Reporting Trials
CRF	Case Report Form
DCC	Data Coordinating Center
DHHS	Department of Health and Human Services
DSMB	Data Safety Monitoring Board
DRE	Disease-Related Event
EC	Ethics Committee
eCRF	Electronic Case Report Forms
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Amendments Act of 2007
FFR	Federal Financial Report
GCP	Good Clinical Practice
GLP	Good Laboratory Practices
GMP	Good Manufacturing Practices
GWAS	Genome-Wide Association Studies
HIPAA	Health Insurance Portability and Accountability Act
IB	Investigator's Brochure
ICH	International Council on Harmonisation
ICMJE	International Committee of Medical Journal Editors
IDE	Investigational Device Exemption
IND	Investigational New Drug Application
IRB	Institutional Review Board
ISM	Independent Safety Monitor
ITT	Intention-To-Treat
LSMEANS	Least-squares Means
MedDRA	Medical Dictionary for Regulatory Activities
MOP	Manual of Procedures
NCT	National Clinical Trial
NIH	National Institutes of Health
NIH IC	NIH Institute or Center

OHRP	Office for Human Research Protections
PI	Principal Investigator
QA	Quality Assurance
QC	Quality Control
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SMC	Safety Monitoring Committee
SOA	Schedule of Activities
SOC	System Organ Class
SOP	Standard Operating Procedure
UP	Unanticipated Problem
US	United States

10.4 PROTOCOL AMENDMENT HISTORY

*The table below is intended to capture changes of IRB-approved versions of the protocol, including a description of the change and rationale. A **Summary of Changes** table for the current amendment is located in the **Protocol Title Page**.*

Version	Date	Description of Change	Brief Rationale
1.2	1/30/26	Changes made to the definition of a trained clinic and the implementation period.	Aligns with the pragmatic nature of the trial and harmonizes the data collection time period.

11 REFERENCES

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2. Endo A, Nagatani F, Hamada C, Yoshimura I. Minimization method for balancing continuous prognostic variables between treatment and control groups using Kullback-Leibler divergence. *Contemporary clinical trials*. 2006;27(5):420-431. doi:10.1016/j.cct.2006.05.002
3. Smeeth L, Ng ES. Intraclass correlation coefficients for cluster randomized trials in primary care: data from the MRC Trial of the Assessment and Management of Older People in the Community. *Control Clin Trials*. Aug 2002;23(4):409-21. doi:10.1016/s0197-2456(02)00208-8