TITLE: ENgaging in Advance Care Planning Talks Group Visit Intervention for Cognitive Impairment (ENACT-aMCI

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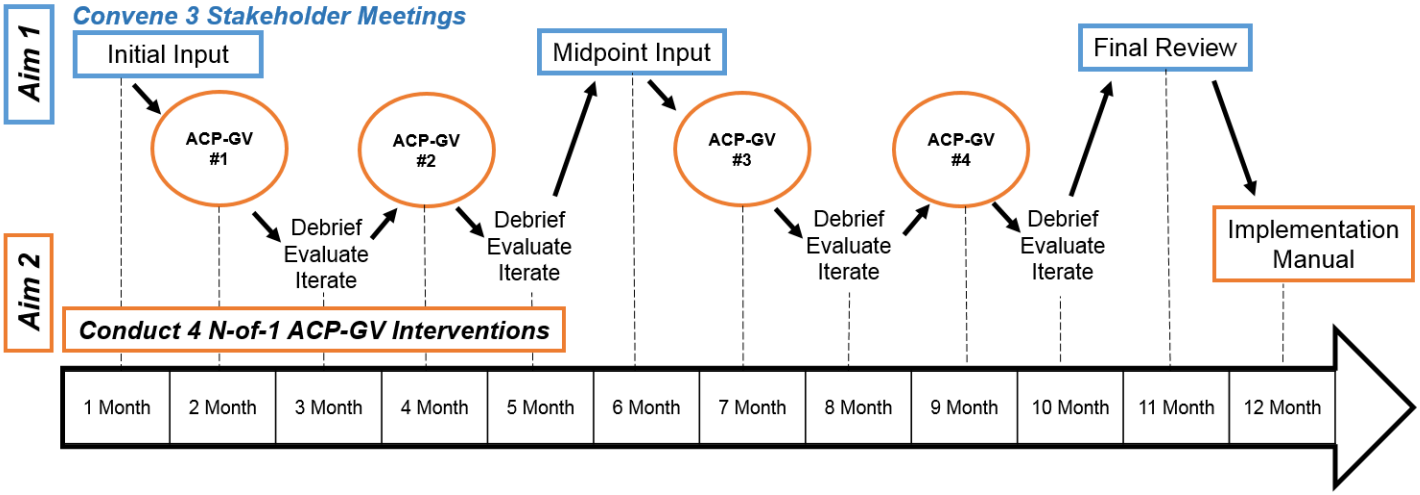
RESEARCH AND STATISTICAL ANALYSIS PLAN

This supplement will prioritize stakeholder input to adapt the ACP-GV intervention for aMCI and ADRD patient-study partner dyads, and identify mechanisms of action underlying person-centered approaches to support ACP-related decision making. This study will provide necessary feasibility data and experience conducting patient-centered ACP research among individuals affected by aMCI and ADRD to inform a future pragmatic clinical trial of ACP decision making strategies in aMCI/ADRD. **Figure 1** shows an overview of activities.



<u>Supplement Aim 1:</u> Identify appropriate ACP-GV intervention modifications for individuals with aMCI or ADRD by convening a longitudinal group of affected patient-study partner stakeholders.

Study Design: To design for patients and caregivers, promote intervention feasibility, and return findings to participants, we will convene five aMCI patients and their study partners for three focus group-style meetings over one year to suggest and review ACP-GV adaptations. In line with stakeholder engagement methods from the parent K76 study, we will solicit individual and group-level input to identify suggestions for adapting the ACP-GV intervention so that it is appropriate for individuals affected by aMCI/ADRD, has defined intervention components (i.e. ACP decision tools, facilitation techniques, structural design aspects), and focuses on clinically meaningful ACP outcomes. The Aim 1 activities will address the following questions:

<u>Question 1a:</u> What evidence-based ACP decision tools should be used in the adapted ACP-GV?

<u>Question 1b:</u> How should facilitation or other structural design aspects of the ACP-GV be adapted?

<u>Question 1c:</u> What are meaningful aMCI/ADRD patient and caregiver outcomes related to ACP in the context of the ACP-GV (e.g., patient readiness for ACP, caregiver preparedness, ACP documentation)?

Study Setting and Participants: Participants with suspected aMCI and their study partners will be recruited from Dr. Bettcher's studies and open recruitment from the University of Colorado. We will specifically recruit both men and women, ages 65 and older, and purposefully invite individuals from diverse self-reported racial/ethnic backgrounds to maximize potential for generalizability.

<u>Inclusion criteria</u> for the diagnosis of aMCI will be based on the National Institute on Aging and Alzheimer's Association workgroup *clinical* criteria for MCI[21], but will depart from the core clinical criteria in that we will focus specifically on individuals with early memory impairment. The rationale for this decision is that our goal is to enrich our aMCI cohort for likely AD pathology and minimize the likelihood of a non-degenerative primary etiology. Study criteria will thus include the following clinical determinations: a) cognitive complaint that reflects a decline in cognition; b) objective neuropsychological impairment in one or more domains, including memory, using comprehensive criteria by Jak (i.e., cutoff of 1 SD below normative data on two memory tests)[22]; c) preservation of independence in functional activities; and d) not meeting criteria for a dementia. <u>Exclusion criteria</u> will be: major psychiatric disorder (e.g., schizophrenia, bipolar disorder, major depression within past two years); neurological or autoimmune conditions affecting cognition (e.g., Parkinson's disease, epilepsy, multiple sclerosis, head trauma with loss of consciousness > than 30 min; large vessel infarct); systemic

medical illnesses (e.g., cancer, renal failure); substance abuse or dependence (DSM-V criteria); and current depression (defined as Geriatric Depression Scale [GDS][23] score > 15).

To maximize recruitment of aMCI subjects, we will also institute the following plan: 1) In addition to the parent projects, we will recruit from the Memory Disorders Clinic, the University of Colorado Hospital, and Seniors Clinic, which have collectively evaluated more than 1,200 aMCI and ADRD patients in the past two years. 2) We will work with the Department of Neurology's recruitment specialist to streamline the recruitment pipeline. Dr. Bettcher's projects utilize a multi-step approach to screen participants, including a 10-minute phone screen and an in-person visit to the Rocky Mountain Alzheimer's Disease Center. The phone screen addresses basic demographics and history, and also serves to identify/confirm a participant study partner. Potential participants who pass this screen undergo an in-person cognitive evaluation and a mood assessment. Participants with suspected aMCI will undergo an additional screening of memory using a list-learning task, story recall, and visual recall (i.e., Story Recall, Visual Reproduction). All potential participants are reviewed by Dr. Bettcher to ensure that inclusion criteria are met.

Longitudinal Stakeholder Group Sessions: The stakeholder group will meet three times, aligned with Aim 2 activities as follows: at the beginning of the study, after two cycles of the ACP-GV intervention, and after completion of four cycles of ACP-GV intervention rapid-prototyping process. To promote participation, a brief description of the ACP-GV intervention and key discussion questions will be mailed prior to each meeting. At each meeting, we will review the overall purpose of achieving robust stakeholder input and introduce the ACP-related decision making topics for discussion. The group will share ideas, engage in a discussion about the suggested adaptations, and personally use ACP decision tools to make recommendations for use. At all three meetings, participants will discuss person-centered support for ACP decision making in the context of cognitive impairment, including suggestions for evidence-based ACP decision tools, appropriate adaptations to the ACP-GV intervention, and meaningful outcomes for individuals affected by aMCI/ADRD over short-term (months) and longer term (years) periods. Potential outcomes include patient readiness for ACP, caregiver preparedness, and ACP documentation. At the end of each meeting, we will summarize the ideas for the participants, and we will incorporate input into the ACP-GV rapid-cycle prototyping process. The mid-point and final meetings will include detailed feedback and discussion of ACP-GV intervention experiences so that stakeholders can make new or updated suggestions to promote the feasibility of ACP decision making in the ACP-GV intervention. The final meeting will also function as a form of "member checking" to assure that we have reached consensus on the final ACP-GV adaptation, including ability for stakeholders to review and revise the on-line Advance Care Planning Group Visit Implementation Manual.

Data Collection: All groups and interviews will be conducted at a convenient location for participants. A qualitative research assistant will create detailed field notes. All sessions (~1.5 hours each) will be audiotaped and transcribed. After each meeting, Dr. Bettcher, a qualitative research analyst, and I will de-brief and utilize iterative, inductive and deductive analytical strategies including field notes and memoing; qualitative content methods of analysis; consultative and reflexive team analysis[24,25] of the meeting transcriptions to identify suggested ACP decision tools (**Q1a**), appropriate facilitator or structural design adaptations (**Q1b)**, and meaningful patient and study partner/caregiver outcomes (**Q1c**). Detailed logs of analysis and interpretation, transcripts, and coding will be maintained to ensure transparency. ATLAS.ti will be used for data management.

Qualitative Analysis: Data analysis occurs longitudinally and begins at the time of the first focus group meeting as participants generate ideas and provide concrete suggestions for intervention adaptation. The words participants use, their beliefs, needs and preferences will be described. The qualitative research analyst and I will initially code individually and then meet to discuss codes, establish inter-code reliability, and create an initial code list. The code list will be revisited and revised with each subsequent focus group meeting. Text within and between codes will be compared to develop themes. We will use observer triangulation (using the interdisciplinary team), participant triangulation (comparing patient and study partner perspectives) and member checking (eliciting feedback while returning results at the final meeting) to increase validity.

Design Considerations and Feasibility

Dr. Bettcher and I will work closely with my content mentors, including Dr. Jacqueline Jones, qualitative expert, to maximize strategies for focus group participation by individuals with cognitive impairment. We will integrate best practices for meeting the needs of aMCI individuals and their care partners, such as: 1) using clear graphics, 2) offering take-home materials, and 3) following up by phone to address emerging questions. We will offer brief interviews by phone or in-person after each meeting to provide opportunities for participants to share additional input. We chose three meetings, instead of five meetings which could convene the stakeholders after each n-of-1 cycle, to maximize participation by reducing potential participant burden.

Supplement Aim 2: Conduct a single arm feasibility study of the ACP-GV with suggested adaptations from aMCI and ADRD patient-study partner dyads.

Study design: We will conduct four cycles of n-of-1 ACP-GV interventions involving four patient-caregiver dyads per group (32 total participants). Each cycle will use pre-post multi-method evaluation, human-centered design principles, and rapid-cycle prototyping to address the following ACP-GV intervention questions:

Question 2a: Is it feasible to recruit aMCI or ADRD patient-partner dyads to the adapted ACP-GV and collect the participant-reported meaningful outcomes (i.e. acceptability, appropriateness, beneficial or helpful)?

Question 2b: In the context of the ACP-GV intervention, what are mechanisms of action for person-centered approaches for ACP-related decision making in aMCI or ADRD?

Design Considerations: This study is a feasibility study, rather than a clinical trial, because the key focus is on rapidly evaluating the feasibility of design adaptations that are solicited through human-centered design principles. Although some individuals whom we perceived to have cognitive impairment have previously participated in an ACP-GV prototype, it is important to formally understand the mechanisms of action and acceptability from the participants' perspectives of this model of care. We have chosen a rapid-cycle prototyping approach with planned, structured involvement of stakeholder input (aligned with Aim 1), to maximize the opportunity to develop a feasible intervention within a one-year time period. The rapid-cycle prototyping enables us to attempt and evaluate significant adaptations relatively quickly.

Study setting and population: I will recruit 16 older adults (≥ age 65) affected by aMCI or early ADRD and 16 associated study partners from Dr. Bettcher's existing research studies and other University of Colorado Hospital settings as described in Aim 1. The inclusion and exclusion criteria, recruitment process, and informed consent process are the same as for Aim 1, and are described in the Human Subjects form.

Intervention Development: The current ACP-GV intervention consists of up to 12 patients meeting in two 2-hour sessions, one month apart (**Table 1**). In this supplement Aim 2, we will conduct four n-of-1 ACP-GV interventions with planned adaptations. To generate ideas for adaptations, we (researchers and patient/study partner stakeholders) will use rapid-prototyping methods guided by The Bootleg toolkit from the Institute of Design at Stanford.[26] This free, on-line, state-of-the-art resource outlines a human-centered design process and describe dozens of specific methods to support design thinking work. Each n-of-1 ACP-GV intervention will be guided by detailed suggestions from the aMCI/ADRD stakeholders, including potential changes to the Facilitator Guide and specific facilitation prompts and discussion topics, planned use of ACP decision tools, modified or new handouts, and specific resources to meet the needs of individuals with aMCI/ADRD. Each n-of-1 ACP-GV intervention will be approximately every two to three months, based on the evaluation, analysis, stakeholder focus groups, planning detailed changes to the next cycle, and recruitment of study participants.

Outcomes: We will evaluate feasibility of participation including recruitment and retention of patient-study partner dyads, participant acceptability, and feasibility of measuring patient- and caregiver-reported outcomes (as selected in Supplement Aim 1) for each n-of-1 ACP-GV intervention cycle. We will also assess patient-level baseline and 3-month ACP outcomes using validated instruments from the parent K76 award (i.e., primary outcome: advance directive completion, secondary outcomes: self-efficacy, readiness, ACP discussions).[27] To understand potential impact of the ACP-GV intervention on cognitive or mood-related outcomes, we will assess As with the parent K76 study, I will collect qualitative data on implementation process measures, including interviews with patients and study partners, to understand the ACP-GV intervention from multiple perspectives.

Data Collection and Analysis: Data will be stored in a secure REDCap database.[28] For feasibility (**Q2a**), we will track recruitment and participation rates, including reasons for not participating. We will track the length of time and completeness of responses for the participant-reported outcomes, as well as level of assistance provided by a research assistant (i.e. reading questions aloud; repeating questions; filling out responses). To address the question of mechanisms of action for person-centered approaches to ACP-related decision making (**Q2b**), each n-of-1 ACP-GV intervention session will be audio and video recorded, transcribed, observed by a research assistant who will create field notes, assessed for intervention fidelity using the Fidelity Checklist with the planned adaptations, and formally de-briefed by the facilitator team to capture "what worked and what did not work." Additionally, follow up interviews will be conducted with more than half of the participants (20 patients or study partners) after completing the session. The qualitative analysis will be conducted following the methods outlined in Supplement Aim 1 to address the questions of feasibility, participant acceptability, and mechanisms of action for ACP-related decision making in individuals with aMCI/ADRD.