Priorities Aligned Deprescribing for Persons Living with Dementia and their Caregivers

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Protocol Title:

Priorities Aligned Deprescribing for Persons Living with Dementia and their Caregivers

Study Summary:

The proposed pilot randomized control trial (RCT) will randomize 60 caregiver and people living with dementia (PlwD) dyads to patient priorities care (PPC) versus usual care. PPC consists of (1) an encounter with a facilitator who will identify health priorities (outcome goals and care preferences) from the dyads, and (2) follow-up with their geriatrics clinic provider to decide upon changes in their care that align with their identified priorities. Usual care will consist of a geriatrics clinic visit with PlwD and their caregivers, in which the dyads will be encouraged by an unblinded study coordinator to ask about reducing medication burden. We will record dyad – facilitator encounters and analyze processes, communication, and negotiation that results in the identification of blended health priorities placed in the electronic health record (EHR). We will conduct cognitive task analysis interviews with each clinician following completed follow-up visits with participant dyads. The cognitive task analysis will review clinicians' sense-making of the identified health priorities and their pre-encounter plans to change medications based on observed malalignment. We will probe clinicians about how triadic discussions of the alignment of medications with priorities affected their eventual treatment decisions. We will conduct a 3-month follow-up (chart review and telephone call) to document all medication changes from baseline and identify any adverse drug withdrawal events (ADWEs) and their clinical sequelae.

Study Team Roster

Principal Investigator: Aanand Naik, MD

[redacted]

Co-Investigator: Holly Holmes, MD

[redacted]

Co-Investigator: Rafael Samper-Ternent, MD PhD

[redacted]

Co-Investigator: Dana Giza, MD

[redacted]

Co-Investigator: Jennifer Arney, PhD

[redacted]

Co-Investigator: Sylvia Jannete Hysong, PhD

[redacted]

Research Associate Jack Banks, PhD

[redacted]

Research Associate: Justun B Holder, MHA

[redacted]

Research Associate: Suha Soni, MBBS

[redacted]

1. Study Aims

There are three specific aims associated with this study:

Specific Aim 1: Conduct a pilot randomized clinical trial with 60 PlwD and caregiver dyads and their clinicians comparing PPC and UC to identify differences in post-encounter medication changes, treatment burden (TBQ), and shared decision making (OPACIC).

Specific Aim 2: For PPC participants, we will conduct cognitive-task-analyses with primary providers to understand their sense-making and communication approaches related to deprescribing decisions in relation to the identified health priorities.

Specific Aim 3: Conduct a 3-month, post-encounter televisit to identify and categorize ADWEs.

2. Background and Rationale

2.1 Background

Burden of multimorbidity and polypharmacy for persons living with dementia (PlwD) and their caregivers. By 2030, over 170 million adults will live with the complexity of multiple chronic conditions (MCC), functional limitations, and their resulting polypharmacy and treatment burden. MCCs increase risks of adverse outcomes from polypharmacy that outweigh disease-specific outcomes that clinical practice guidelines (CPG) target. These risks compound with comorbid dementia. PlwD average 8 daily medications compared to 3 for persons without dementia. PlwD have high polypharmacy burden from anticholinergic and psychotropic medications. CPGs fail to focus on outcomes most important to older adults (independence, function, and social relationships). Finally, PlwD, their caregivers and clinicians endure the workload of managing multiple medications, and may wish to decrease this burden. The situation demands a shift that reduces polypharmacy, and focuses medication use on what matters most.

Deprescribing is an approach to reduce polypharmacy for PlwD. Deprescribing interventions reduce polypharmacy through a process that considers individual functional status, life expectancy, and goals and preferences for care. However, *deprescribing studies for PlwD have a narrow scope*. Most studies target long-term care settings or advanced dementia at the end of life. Other studies focused on specific classes of drugs, such as benzodiazepines or antipsychotics, known to be harmful. Few studies place deprescribing within ambulatory care contexts for patients with mild to moderate dementia. A recent study with PlwD and MCCs emphasized aligning deprescribing with broader goals of care, and considering tradeoffs in managing chronic care symptoms and avoiding inappropriate care.

2.2 Rationale

Appropriate deprescribing in mild to moderate dementia requires identifying health priorities. Deprescribing is most appropriate when anchored to priorities of patients and caregivers. Health priorities consist of patients' outcome goals (the health outcome the medication is intended to promote) and care preferences (what patients and caregivers are willing or not willing to do to reach those goals). To facilitate deprescribing discussions among PlwD, their caregivers, and clinicians, a collaborative approach is needed that identifies health priorities (outcome goals and care preferences) and aligns medications recommendations with those priorities. Older adults report wanting their clinicians to know their priorities (and assume they do know them), but few describe having specific discussions about priorities. We previously demonstrated that older adults with MCC describe a consistent set of health-related priorities ('What Matters Most') that typically include: social and spiritual engagement; function and independence; life enjoyment activities and roles; and managing health that balances quality with quantity of life.

Patient Priorities Care (PPC) is an evidence-based approach to aligning care with identified health priorities. We developed PPC and found evidence that it facilitates deprescribing by identifying health priorities that are misaligned with current medications. When used in the care of PlwD and their caregivers, PPC could facilitate deprescribing. Less is known about how PPC works in the triadic context of clinician, caregiver, and PlwD. Caregivers may have concerns about stopping medications considered inappropriate, e.g., benzodiazepines, given that such meds helped to manage symptoms related to dementia. Clinicians may focus on cognitive and functional harms of meds like benzodiazepines without considering tradeoffs of stopping benzodiazepines in PlwD. Without eliciting priorities, families and caregivers of PlwD may make decisions to stop medication without communication with their clinicians. Starting, stopping, or continuing a medication are all active decisions with shared responsibility, but practical methods to facilitate such collaboration (guided by priorities) are lacking. Clinicians find difficulty addressing medication use that considers both the preferences of PlwD and caregivers, while coordinating care with other specialists and healthcare professionals given the limited evidence base and lack of guidelines in this setting. A specific, actionable approach to health priorities may facilitate deprescribing that is patient-centered and concordant among PlwD, caregivers, and clinicians. Hesitancy about deprescribing can arise from the fear of adverse reactions resulting from removal of a drug. These adverse drug withdrawal events (ADWE) can be clinically-significant resulting in hospital or emergency room visits. ADWE are often attributed to exacerbations of underlying disease after drug discontinuation, with the

number of drugs stopped being the main predictor of ADWE occurrence. In reality, most medications are successfully stopped without causing ADWE. Understanding of ADWE following deprescribing is limited, especially for PlwD. Further data on the nature and severity of ADWE surrounding deprescribing is needed to better inform safe alignment of medication changes with health priorities.

3. Study Design

The proposed pilot RCT will randomize 60 caregiver and community-dwelling PlwD dyads to PPC versus usual care. PPC consists of (1) an encounter with a facilitator who will identify priorities (outcome goals and care preferences) from the dyads and transmits them in the EHR, and (2) a follow-up encounter with their usual geriatric care provider to decide upon changes in their care that align with the identified priorities. The usual care arm will consist of a geriatric clinic visit with a geriatrician that acts as their primary care provider (PCP) by the PlwD and their caregivers, in which the dyads will be encouraged by an unblinded study coordinator to ask about reducing medication burden. For PPC participants, we will record dyad – facilitator encounters and analyze processes, communication, and negotiation that results in the identification of blended priorities placed in the EHR. We will conduct cognitive task analysis interviews with each primary care clinician following completed follow-up visits with participant dyads. The cognitive task analysis will review clinicians' sense-making of the identified health priorities and their pre-encounter plans to change medications based on observed malalignment. We will probe clinicians about how triadic discussions of the alignment of medications with priorities affected their eventual treatment decisions. We will conduct a 3-month follow-up (chart review and telephone call) to document all medication changes from baseline and identify any ADWEs and their clinical sequela.

4. Selection and Enrollment of Participants

4.1 Inclusion and Exclusion Criteria

Patients will be identified through chart review and confirmation of diagnoses with their primary clinician.

Inclusion criteria:

- Dementia listed as an active problem in the medical record, including Alzheimer's disease, vascular dementia, frontotemporal dementia, Parkinson's dementia, Lewy body disease.
- FAST score of 5 or lower (This will be established by the patient's clinician).
- 2 or more additional chronic conditions
- Takes 5 or more regular medications and

- A caregiver present during visits. Caregivers may include family members or unrelated caregivers and will be identified through chart review and confirmed by clinician, patient, and surrogate decision maker if necessary. Identified caregivers must be involved in decisions and care of PlwD and routinely attend clinic visits with patient.

Exclusion criteria:

Based on a query of the EHR, the Center for Healthy Aging currently has 411 patients with dementia taking 5 or more medications seen in the last 18 months. Excluding criteria are as follows.

- FAST score of 6 or more (This will be established by the patient's clinician).
- Significant hearing, vision, or advanced cognitive impairment that limits ability to participate in PPC encounters,
- Caregiver is unwilling or able to participate in visits, or
- Deemed ineligible by their PCP.

4.2 Enrollment Procedure

Each of the four clinic primary care providers will provide their written informed consent (each have already agreed to take part). Using EPIC, a list of eligible patients who receive care from each of the clinicians will be extracted. Each of the clinicians will indicate if they feel any of the identified participants are not in a position to take part in the study.

We will mail a letter from each clinic provider informing eligible patient and caregivers about the study and provide a tip sheet about reducing medications. An RC (EP, JH or GP) will then contact each of the eligible participants via telephone at least 72 hours after mailing the packet to provide further details and attempt to enroll, conduct a baseline assessment and consent the patient and caregiver by phone. After receiving their verbal consent, the RC will perform baseline data collection. Upon completion of each element of the baseline assessment, the RC will mail a $25 gift card as a thank you to the dyad for participation.

Convenience sampling will determine if participants fall into the Usual Care (UC) or Patient Priorities Care (PPC) arm of the study. Following examination of each of the clinician's upcoming clinical appointment schedules, the first 8 participants who are enrolled in the study will not be scheduled for a PPC facilitator appointment and attend their usual clinic provider appointment i.e. UC. After completion of these 8 appointments, the 4 clinicians will collectively receive PPC training.

The next 8 participants to have appointments following PPC training will be assigned to the PPC arm. The RC will schedule these participants for an upcoming visit with a facilitator to be followed within 14 days by a clinic with a clinic provider visit. A phone visit with the coordinator will be scheduled for 3 months after the clinic provider encounter to conduct follow-up data collection.
People with dementia generally require high levels of care, most of which is provided by informal or family caregivers. Within this study, we wish to recruit dyads of patients and caregivers, rather than individual patients, as participants in order to reflect the more accurate reality of dementia management.

In Specific Aims 1 and 3, caregivers will aid with medication reconciliation and completion of survey tools which will be performed by a research coordinator (RC) via telephone, if the patient is not in a position to do so themselves.

A FAST score of 5 or lower is required for a person living with dementia to be included in this study, indicating that those with moderate to severe dementia will not be eligible for inclusion. We wish for patient participants to be capable of participating with a degree of autonomy in their phone calls with the RC, PPC appointments (if in the PPC arm), usual geriatrics appointments, and three-month follow-ups. However, we would also like their caregiver to be present during these conversations and contribute their insights and knowledge as they see fit.

5. Study Interventions

The proposed study uses innovative social science methods to adapt the PPC approach to the care of adults living with dementia. The underlying conceptual basis for PPC is derived from social and cognitive psychology models of values-based goals and goal-setting. We previously demonstrated that collaborative goal-setting among patients and clinicians can improve chronic illness outcomes. We adapted social intuitionist models to the context of medical decision making for adults with MCC. In this adaptation, health-related values provide a behavioral/motivational foundation for health outcome goals and care preferences. These related lines of research resulted in the PPC conceptual model (Figure 1). The current study furthers this innovative line of inquiry by adapting PPC to the context of triadic decision making among PlwD, their caregivers and clinicians. We will use thematic analysis to understand the identified outcome goals, and care preferences of caregivers and PlwD, the extent of concordance among priorities, and how the final priorities documented in the EHR reflect blended versus unitary (primarily caregiver vs. PlwD) priorities consensus.

We use cognitive task analysis in Specific Aim 2. Cognitive task analysis provides detailed information regarding tasks that require substantial cognitive activity (decision-making, problem solving, etc.) to make sense and arrive at decisions. Cognitive task analysis involves processing stages of knowledge perception, cognition and analysis, and sense-making. In Specific Aim 2, we will elicit clinicians' perceptions of the identified priorities including their own sense of outcome goals and care preferences. We will describe clinicians' assessments of the degree of alignment & efficacy of prescribed meds with the identified priorities. We will ask clinicians to define what aspects of care are aligned and misaligned with the identified priorities with specific probing about planned efforts to reduce or deprescribe specific medications. The analysis across clinicians will allow us to develop a model of sense-making and planned action around deprescribing that is driven by misalignment with identified priorities.

We will advance the evidence-base for deprescribing by characterizing the prevalence and severity of ADWE that arise from our priorities-informed medication changes. We will describe triadic deliberations related to these ADWE-deprescribing instances to understand if the likelihood of such events are discussed. This analysis will also determine whether pharmacist and/or decision support tools are needed to better inform the deprescribing activity.

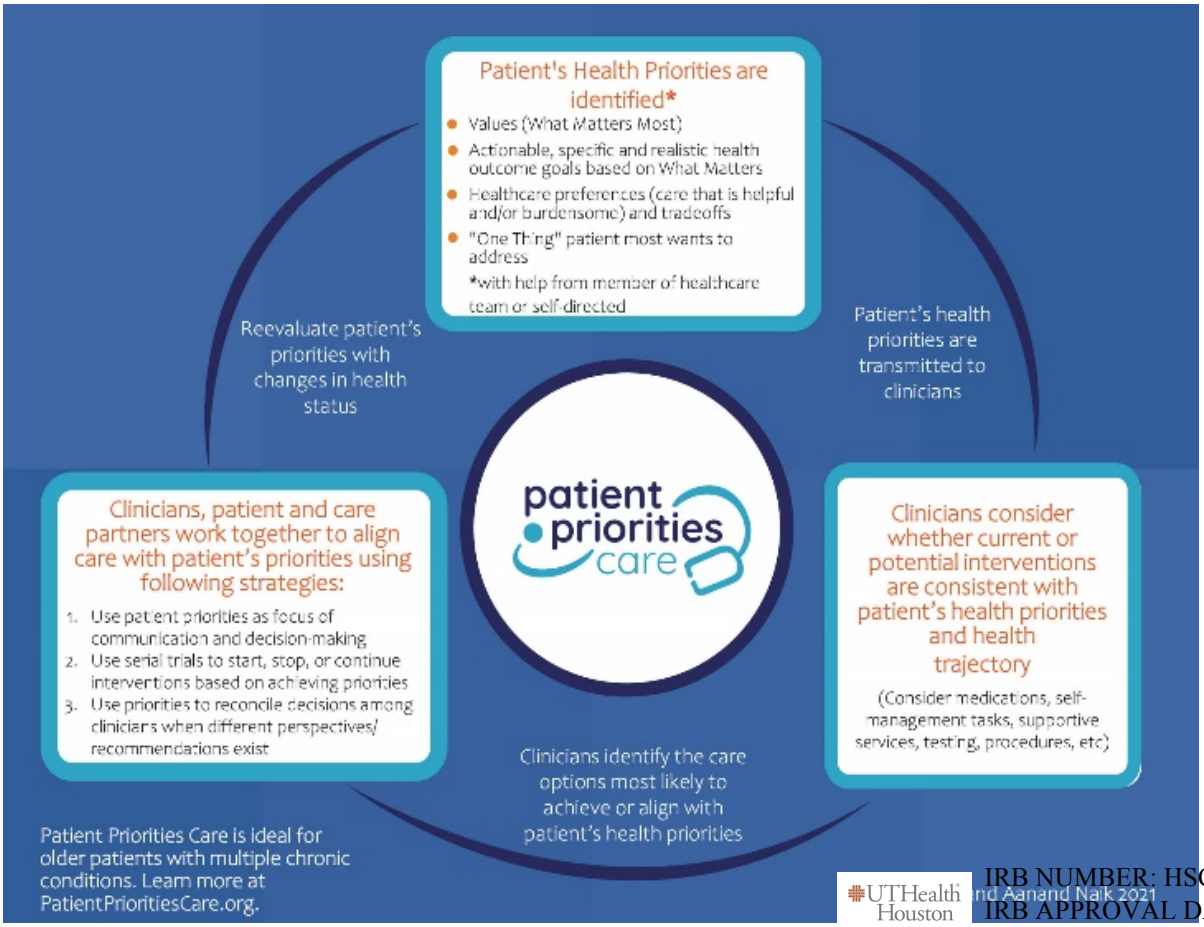


Figure 1 - Summary of PPC process.

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6. Study Procedures

6.1 Data Collection and Management:

Specific Aim 1: The number of medications will be determined from the medication list in the EHR and medication reconciliation will be performed over the phone. We also plan on collecting medication and care changes from patient's chart on EPIC. The RC will extract the number and types of chronic conditions determined from the problem list, which will be used to calculate the Deyo comorbidity score. Baseline data includes socio-demographic factors (age, sex, race/ethnicity, educational level, living arrangement, and marital status), and subjective social status. Patients will complete the TBQ at baseline and after the clinic provider visit. The TBQ measures perceptions of burdensomeness of overall care and treatment burden (*e.g.*, medication taking, self-monitoring, visits to the provider, tests, tasks to access and coordinate care) imposed by healthcare as assessed with 15 items; possible range, 0-150; Cronbach α = 0.90; higher scores indicate greater perceived burden). RC will collect all survey and chart review data using REDCap (Research Electronic Data Capture – project- redcap.org). We have previously developed and used these rigorous data collection, tracking, and retrieval system procedures. Upon completion of each element of the baseline assessment, an RC will mail a $25 gift card as a thank you to the dyad for participation. An RC will collect outcome data (at 3-month follow-up) on the full sample of patients by telephone. Data will be collected and stored in REDCap using the same procedures. Upon completion of each element of the 3 month follow up assessment, the RC will mail a second $25 gift card as a thank-you to the dyad for their participation.

Primary outcome measures are (1) number and type of medication changes, and (2) changes in patient-reported TBQ. We will measure medication changes using a structured chart review tool using our validated process to guide uniform abstraction and classification to a) document specific changes in medications (i.e., discontinuation, addition, dose reduction, and substitution), b) attribute changes to alignment with priorities, and c) identify documentation of any avoided medications. We have previously validated this chart review process and used it in two recent studies. Secondary outcomes measures are shared decision making and facilitator-dyad conversation analysis to understand how PlwD and caregivers arrive at blended priorities. We will measure patients' perceptions of whether health care decisions were collaborative and focused on their goals using the Older Patient Assessment of Chronic Illness Care (OPACIC) score (11 items; range, 1-5; Cronbach α = 0.87; higher scores indicate better perceived chronic disease care). PPC only: We will collect audio recordings of all 25 facilitator-dyad conversations to identify health priorities. Dr. Arney, an experienced qualitative sociologist, will use qualitative analysis to code

transcripts to determine how patient and caregiver: (a) values and outcome goals were identified, (b) care preferences were discussed, (c) how participants blended their differences versus chose a unitary (PlwD vs caregiver) goal or preference to document in the EHR, and (d) how dyad participants understood the importance of eliciting and reconciling both participants' priorities.

Specific Aim 2:

We will schedule interviews to be held via videoconference (e.g., Zoom, Webex) with study clinicians after each completes 3-4 PlwD-caregiver dyad encounters. To reach the PPC target (n=25), we plan to conduct interviews (covering 6-8 patient-caregiver encounters) with each study clinician. We anticipate conducting two hours of interviews per clinician divided over 2-3 sessions. Interviews will occur within one month of completing dyad encounters (see Appendix for interview guide). Interviews will last 45-60 minutes, conducted by Dr. Hysong (Co-I)—an industrial/organizational psychologist with cognitive-task-analysis expertise and a secondary note-taker (JB) will capture responses, important quotations, and make field notes as interviews occur. Interviews will be recorded and autocaptioned to create an automated transcript. We will analyze interviews and develop themes about clinician metacognition regarding (mis)alignment of current care.

Cognitive-Task-Analysis Interview guide domains. We will ask each clinician to walk a naïve user through the following cognitive processing domains: a) How they review and interpret the identified health priorities template? b) Interpretation of whose priorities are described (patient, caregiver, blended) and the relevance of that judgment. c) How currently prescribed medications align with the identified gaps (i.e., clear misalignment of care preferences, poor attainment of outcome goals, potential tradeoffs between meds and priorities, and clear gaps with unaddressed priorities)? d) Planned strategies for approaching PlwD/caregiver dyad regarding potential medication changes. Appendix 1 provides a full script for the interview guide including probes and the steps of our think aloud protocol. This protocol asks the subject to verbalize any mental processes and information considered during planning, sense-making, and task performance – in essence 'thinking aloud' as the cognitive tasks is performed.[40] In addition, we will review medication changes that occurred post-encounter (as documented in EHR) and ask the clinician to describe: a) which PPC decision strategies [as described in Figure 1] s/he used during the clinical encounter, b) specific challenges, questions, or concerns that arose from the conversation, c) how any tradeoffs were addressed and resolved, and d) how final decisions regarding medication changes were resolved.

Specific Aim 3:

At three months post-encounter, an unblinded RC will contact patients and their caregivers. Full medication reconciliation will be conducted and the medication list will be compared to the post-encounter list after the PPC intervention. PlwD and their caregivers will be asked about symptoms, side effects, or adverse events

(urgent or emergency department visits and hospitalizations) that they think may be attributable to a medication or to stopping of a medication. If there are potential events, the RC will follow a structured questionnaire to determine the likelihood of an ADWE or an adverse drug reaction (ADR). Upon completion of each element of the 3 month follow up assessment, the RC will mail a second $25 gift card as a thank-you to the dyad for their participation.

Primary outcome measures are the number, likelihood, and severity of ADWEs and ADRs. The outcomes will be determined by the RC using the Naranjo scale or the Adverse Drug Withdrawal Event Scale. Secondary outcomes are the perceived alignment of medication changes with patient priorities based on our structured chart review tool. The TBQ and the OAPCIC will be repeated.

Table 1 - Procedures, data collection and measures.

Timeframe		Procedure	PPC	UC	Data Collection/Measure
Baseline data collection		*Unblinded coordinator will collect by phone after consent but prior to randomization*. We previously collected measures by phone.	X	X	1) Comprehensive medication list 2) Treatment Burden Questionnaire (TBQ) scale 3) Older Patient Assessment of Chronic Illness Care (OPACIC) scale
Intervention Period	**PPC Intervention Dyads Only:** Priorities identification w/facilitator	Unblinded coordinator schedules visit with participant dyad and PPC facilitator to a structured encounter to identify health priorities	X		1) Audiorecording of patient and caregiver discussion of individual values, health outcome goals, and care preferences and process of reaching consensus health priorities document 2) EHR documentation of blended health priorities arising from encounter (outcome goals, and care preferences)
	All Participating Dyads: Clinic encounter with primary care provider	*Unblinded coordinator will schedule all participants* for a clinic provider visit.	X	X	1) Documentation in EHR of changes in medications resulting from encounter with patient/caregiver 2) Cognitive Task analysis interviews with clinicians about all 25 PPC related encounters with participant dyads (field notes, recordings, other documentation)
		For PPC participants, clinicians will focus on priorities aligned medication changes.	X		
		For usual care, participants are instructed to ask clinicians about burdensome medications or questions about medications.		X	

Three-month follow-up data collection	*All participants will have a follow up telephone call with a research coordinator.* Research coordinator reviews chart to document med changes, conducts follow-up questionnaire and ADWE assessment, including any clinical sequela	X	X	1) Any documented linkage of changes in medications to patient priorities (goals or preferences) in the EHR record 2) Repeat TBQ and OPACIC scales 3) Any documentation about medication related adverse events, burdens of medications, or concerns about withdrawal related side-effects. 4) Structured chart review to document potential clinical significance of ADWEs and other medication related events

7. Safety Assessments

We will obtain approval from the UT-Health Institutional Review Board prior to beginning work. The study team has extensive experience leading IRB-approved projects. We will leverage this experience in the protection of human subjects for the proposed study. All data will be collected specifically for research purposes.

We will first obtain written informed consent from the clinic primary care providers (all have already agreed to participate). For patient and dyad recruitment, we will use data extracted from UTPhysicians registry to identify potentially eligible patients and their caregivers from the panels of enrolled clinicians. Consenting will be done over the phone by the research coordinator before randomization. The investigator will explain the research study to the person with dementia and the family caregiver and answer any questions that may arise. A verbal explanation will be provided in terms suited to the participant's comprehension of the purposes, procedures, and potential risks of the study and of their rights as research participants. Participants will be informed that participation is voluntary and that they may withdraw from the study at any time, without prejudice, and that the quality of their medical care will not be adversely affected if they decline to participate in this study. Participants will have the opportunity to ask questions prior to consenting. The participants will be given a copy of the ICF so that they may discuss the study with their family or surrogates or think about it prior to agreeing to participate. The informed consent process will be conducted and documented in the source document (including the date), before the participant undergoes any study-specific procedures. For participants with dementia, PCP will be asked about decision capacity. If they are deemed unable to consent, verbal assent will be obtained and consent will be provided by the caregiver. Copy of the signed ICF will be provided to the caregiver. The compensation for taking part in the study i.e. two x $25 gift cards for completion

of every assessment at baseline and three month follow up will also be explained to each dyad by an RC when the dyad is enrolled on the telephone. Our 4 clinician participants will each receive $400 per hour of cognitive task analysis interviews they complete with Dr. Hysong.

To ensure protection against potential risks, this study will be approved by the UT Health and Institutional Review Board. For Aims 1 and 2, interviews will be designed to minimize potential discomforts with sharing healthcare information. Interviewers will be trained to recognize and address signs of discomfort among study participants. The following precautions will be taken in both phases of the study to address possible apprehension with disclosing health care related information. Study participants for all study aims will be assured that:

i. Participation is voluntary;
ii. They do not have to answer any questions with which they are uncomfortable;
iii. They can discontinue study participation at any time; and
iv. Participation will in no way affect the care that patients receive at the VA or the employment status of primary care staff.
v. In addition, we will implement extensive measures to protect against the risk of loss of confidentiality. The following precautions will be taken for participants in all phases of the study to minimize a potential risk of breach of confidentiality.

For Aim 3, the proposed study has minimal therapeutic risks, but because it does involve a treatment intervention (i.e., physical interaction with study patients) with a group of multi-morbid older adults, data collection regarding complications or adverse events related to treatment will be monitored. Participating clinicians will be required to report on the hospitalization or death of any patient older than 65. Each such event will be reported to the Project Manager who will document and track the resolution progress at each local site. The Project Manager will notify the study co-PIs. The Project Manager and the PIs will follow IRB requirements for unanticipated event reporting, and safety reporting.

8. Statistical Considerations

8.1 Qualitative and Qualitative Rationale

Specific Aim 1: Quantitative Analysis

The quantitative analyses are intended to assess feasibility (ensure procedures result in adequate recruitment, measure completeness of post-encounter data collection and missing data) and generate effect size data for differences in changes in medications, ADWEs and adverse medication effects, and group differences in TBQ and OPACIC scores. Changes in medication and care will be analyzed from patient's chart on EPIC ensuring that we capture changes due to PPC versus usual care. We will use these effect size estimates and calculations of intraclass correlation coefficients to determine our power and sample size estimates for a subsequent larger effectiveness clinical trial of PPC for persons living with dementia and their caregivers.

Specific Aims 1 and 2: Qualitative Analysis

For qualitative analyses in aim 1 we will recruit 25 participant dyads randomized to PPC arm. These interviews will be nested within 4 primary care providers. Analyses will be stratified by dementia severity (mild versus moderate) which will have previously determined through FAST scoring. We anticipate 10-15 dyads at least for each strata. Given our prior qualitative studies of PPC interventions, this sample is sufficient to reach thematic saturation of our targeted interview guide questions.

For aim 2, we will recruit all the available primary care providers (likely N=4-5 providers) with each provider caring for 4-6 patient dyads enrolled in the study accounting for 4-6 cognitive process per provider with 25 total interviews. This overall sample size and per provider strata will be sufficient to reach thematic saturation for our cognitive task analysis based on our prior work.

8.2 Data Analysis Plan

Specific Aim 1:

We will compare baseline demographic and clinical characteristics for the PPC and UC participants using independent samples t tests (for interval variables) and $\chi 2$ tests (for categorical variables). Primary and secondary outcome analyses at post-intervention will be intention-to-treat. For analysis of between group treatment changes, we will perform either multiple logistic regression or use generalized linear mixed effects models (using PROC GLIMMIX). For other outcomes, Analysis of Covariance will be employed to examine treatment differences in structured outcomes post-intervention. Models will include treatment group (i.e., PPC vs. UC) as a predictor and respective baseline scores for the outcome, age, and Deyo comorbidity score. Additionally, we will conduct chart reviews to check for differences in care and medication based on treatment group. We will calculate treatment group effect sizes with 95% confidence intervals post-intervention. To help inform multilevel modeling in a larger clinical trial, we will calculate intraclass correlation

coefficients (ICCs) for outcomes to determine the degree of total variance explained by variance between clinicians. These ICC estimates will inform the power calculations for a larger clinical trial.

Specific Aim 2:

To balance efficiency with scientific rigor, we will use qualitative analyses adapted rapid qualitative analysis to analyze our interviews and identify patterns in how clinicians interpret alignment of current medications with identified health priorities and negotiate treatment changes. The research team will create a coding matrix template to capture the cognitive processing domains for each interviewee. After each interview, Dr. Hysong will summarize responses into the coding matrix template. A second analyst (Dr. Arney or Dr. Naik) will independently review the matrix, listen to the audio recordings, and build upon the primary analyst's notes and categorizations when appropriate. The two analysts will meet after both have analyzed each interview to reconcile discrepancies; any impasse will be resolved by a third analyst. Using the reconciled template, the research team will meet to construct a written mental model for guiding the process of priorities interpretation and alignment with current care, and refinements to PPC decisional strategies for approaching patient/caregiver dyads for negotiating treatment changes in the context of PlwD.

Specific Aim 3:

Outcome analyses post-intervention will be intention-to-treat. We will compare the incident rates of ADWEs and ADRs in the PPC vs. UC groups. Differences between the arms will be assessed under intention-to-treat principles using multilevel generalized estimated equations (GEE) models, adjusting for clinic provider. Prior studies of ADRs and ADWEs have shown relatively low event rates, and we will therefore assume a Poisson or negative binomial distribution for outcomes and will model the proportion of patients in each arm with an outcome. We will express rates of outcomes in PPC and UC arms as rate ratios with 95% confidence intervals.

9. Data Collection and Quality Assurance

9.1 Sources of Materials

Research material obtained from the participants will consist of questionnaires of participant reported data, transcriptions of interviews, and chart reviews of medications and other changes in recommended care. Participants will be assigned unique identification numbers (i.e. H001, H002, etc.) for purposes of data collection. Participant names and addresses that are linked to the unique research identification number will be placed in a separate password-protected electronic file until

it is apparent that this information is no longer needed. At that time, it will be destroyed and deleted from all files and databases. All data will be stored and archived on a double password-secured computer and in Microsoft Excel or Microsoft Word format.

9.2 Knowledge of the Policies of the Local Institutional Review Board (IRB)

The PI will be responsible for knowing the policies of the IRB (the UTHealth Committee for the Protection of Human Subjects, CPHS). The PI will adhere to CPHS policies and maintain accurate documentation of correspondence and reports (e.g. annual report). The researchers for this project have a statistician who will be responsible for all data and data security. Formal data reviews will be conducted once monthly to insure accuracy and data quality. A summary of the data reports will be included in the progress reports submitted to the funding agency.

9.3 Adverse Events (AEs) and Serious Adverse Events (SAEs) Collection and Reporting

AEs and SAEs will be brought to the immediate attention of the PI. All AEs are collected on an Adverse Event Form. All AEs experienced by the participant during the home visit will be recorded. The AE form contains a column to indicate whether the event is serious. Thus, SAEs are a subset of the reported AEs. Routine reporting of AEs will be performed monthly. All SAEs will be reported within 24 hours of the study's knowledge of the SAE to the IRB and the PI. An expedited report of an SAE will be submitted by telephone, fax, or email to the IRB within 24 hours of the event being reported to the PI. The PI will be responsible for ensuring participants' safety on a daily basis.

9.4 Content of Data and Safety Monitoring Report

The content of the data and safety monitoring report will include: Report Summary; Protocol Synopsis (Project Organizational Chart, Personnel, Brief Statement of Purpose of Trial, Projected Timetable and Schedule); Narrative/Trial Summary (Study Status, Action Items, Resolution of Action Items, Summary of Protocol Changes); Recruitment and Participant Status figures and tables; and Safety Assessments for All Participants tables and listings of adverse events and serious adverse events.

10. Participant Rights and Confidentiality

10.1 Institutional Review Board (IRB) Review

We will obtain approval from UT-Health prior to beginning work. The study team has extensive experience leading dual-site IRB-approved projects. We will leverage this experience in the

protection of human subjects for the proposed study. All data will be collected specifically for research purposes.

10.2 Informed Consent Forms

We will first obtain written informed consent from the clinic primary care providers (all have already agreed to participate). For patient and dyad recruitment, we will use data extracted from UTPhysicians registry to identify potentially eligible patients from the panels of enrolled clinicians. Consenting will be done over the phone by the research coordinator before randomization. The investigator will explain the research study to the person with dementia and the family caregiver and answer any questions that may arise. A verbal explanation will be provided in terms suited to the participant's comprehension of the purposes, procedures, and potential risks of the study and of their rights as research participants. Participants will be informed that participation is voluntary and that they may withdraw from the study at any time, without prejudice, and that the quality of their medical care will not be adversely affected if they decline to participate in this study. Participants will have the opportunity to ask questions prior to consenting. The participants will be given a copy of the ICF so that they may discuss the study with their family or surrogates or think about it prior to agreeing to participate. The informed consent process will be conducted and documented in the source document (including the date), before the participant undergoes any study-specific procedures. A copy of the ICF document will be given to the participants for their records. For participants with dementia, PCP will be asked about decision capacity. If they are deemed unable to consent, verbal assent will be obtained and consent will be provided by the caregiver. Copy of the signed ICF will be provided to the caregiver.

11. Glossary

RCT: Randomized control trial

PlwD: People living with dementia

PPC: Patient priorities care

EHR: Electronic health record

ADWE: Adverse drug withdrawal event

ICF: Informed consent form