H-33720 Aggression Prevention Training for Caregivers of Persons with Dementia (APT)

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Initial Submit Date: 12/12/2013
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Section Aa: Title & PI

A1. Main Title

AGGRESSION PREVENTION TRAINING (APT) FOR CAREGIVERS -- NON VA PROTOCOL

A2. Principal Investigator

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A3a. Financial Conflict of Interest

Does any member of study personnel (Investigator (including investigator's spouse and/or dependent children)) that are involved in the design, conduct, or reporting of the research have a Significant Financial Interest (SFI) that would reasonably appear to be affected by the research for which funding is sought and/or associated with an entity/business that would reasonably appear to be affected by the research?

No

Section Ab: General Information

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A5. Funding Source:

Organization: NATIONAL INSTITUTE OF NURSING RSCH (NINR)

A6a. Institution(s) where work will be performed:

BCM: Baylor College of Medicine
Kelsey Seybold

A6b. Research conducted outside of the United States:

Country:
Facility/Institution:
Contact/Investigator:
Phone Number:

If documentation of assurances has not been sent to the Office of Research, please explain:

A7. Research Category:

A8. Therapeutic Intent

Does this trial have therapeutic intent?
Yes

A9. ClinicalTrails.gov Registration

Does this protocol/trial require registration on ClinicalTrials.gov due to it: meeting the definition of an Applicable Clinical Trial, being required under the terms and conditions of an award, or being proposed to be published in ICMJE journals?
No, this clinical is not a clinical trial, or does not meet the definition of an Applicable Clinical Trial, or does not need to be registered under the terms and conditions of an award, or is not a clinical trial with results intended to be reported in an journal belonging to the ICMJE. Registration is not required.

Section B: Exempt Request

B. Exempt From IRB Review

Not Applicable

Section C: Background Information

Optimal care and outcomes for persons with dementia (PWD) depend on family caregivers primarily responsible for care coordination and daily care. Behavioral or psychological disturbances are exhibited by 80% of PWD, including 40% who are aggressive. Growing evidence has addressed psychological disturbances of PWD and their caregivers once behavioral problems arise, but examination of prevention of such problems is lacking. Aggressive behaviors are perhaps the most problematic because they lead to increased institutionalization, injuries, caregiver burden and use of antipsychotic medications. Innovative approaches are urgently needed to replace the treatment of aggression with tranquilizing medications because of their associated morbidity and mortality in PWD. We have developed an innovative, behavioral caregiver intervention that aims to prevent development of aggression in at-risk PWD, guided by empirical evidence regarding mutable risk factors for aggression. Our team¿s prior work has identified patient pain and depression, and caregiver/PWD relationship quality as strong predictors of aggression.

Broadening Aggression Prevention Training (APT) to Be More Representative of Target Populations: The veteran sample in our current project is significantly different from the non-VA-using population in several important ways that compel us to test the intervention outside the VA. Almost all (97%) of our currently recruited dyads (n=130) are male Veterans with dementia, with women comprising 95% of the caregiver sample. Our sample is comparable to those of previous studies,

which report that 95% of veterans in the older-adult age group who use the VA are men (caregivers 95% women), poorer, more psychologically and physically ill than age-matched non-VA users and embedded in an integrated system of care. In contrast, in the non-VA-using population, women comprise 2/3 of PWD, 30% of unpaid caregivers are men, and most PWD receive their care through nonintegrated systems (ie, Medicare Fee For Service). This gender difference is potentially significant because of greater prevalence of depression in women and evidence of women experiencing pain in different ways and at higher rates than men.

Broadening APT Entry Criteria: The APT study in the VA has powerfully demonstrated to us just how difficult pain identification is for most caregivers and how critical it is to educate caregivers about the interconnections between pain, depression, pleasant activity, and communication skills. This sister protocol was the Preventing Aggression in Veteran's with Dementia study H-27841. Most of our enrolled caregivers have been able to recognize and understand the connection between the PWD¿s behavior, pain, and pain-related features only after several APT sessions in which the caregiver has had the opportunity to apply the APT information to his/her own situation with careful guidance from the therapist. These observations are, concordant with empirical evidence that even trained clinicians under-identify pain in PWD. In sum, there is good reason to suspect that caregivers may recognize the PWD is in distress but not recognize pain as the cause of the distress. Yet our inclusion criteria for the VA study require that the PWD be identified as having clinically significant pain. The challenge, then, is how to identify and enroll PWD into this preventive intervention if the caregivers who respond to our inclusion screening have not recognized the PWD has pain. We believe the solution is to broaden the inclusion criteria to include the pain-related features of depression and communication difficulties. Moreover, broadening our inclusion criteria will enable us to reach more PWD who are in distress and have potential to develop aggression. Therefore, we propose in the current study to broaden study inclusion criteria to include either: a) clinically significant pain, and/or b) clinically significant pain-related features/aggression risk factors (ie, depression or poor quality of caregiver/PWD relationship).

Executive Function (EF) and Self-Neglect (SN): Individuals who SN often suffer from dementia, depression, and pain, all associated with ED. Additionally, SN is associated with impaired social networks and refusal of care. Prior research indicates that, when self-neglecters refuse interventions of unpaid caregivers, there is progressive decline in personal, functional and environmental domains. Secondary Aims have been added to further understand the relationship of ED with psychosocial outcomes and refusal of care. Although the APT intervention is primarily directed to the caregiver, participation of the PWD in weekly homework is critical. Better understanding the relationship of these variables will help to inform later analyses. The CLOX Drawing Test will be administered to a subset of 100 consecutively enrolled subjects at baseline. It is a two part test (CLOX 1 and CLOX 2) to measure EF and global cognition. CLOX 1 is a more direct measure of EF. CLOX 1 consists of instructing the subject to draw a clock and insert the time of 1:45 using hands and numbers in a clock. Scores range from 0 to 15. A score of 10 or below on CLOX 1 indicates executive impairment. The CLOX has high inter-rater reliability estimates (CLOX 1, Pearson¿s r = 0.94, CLOX 2, Pearson¿s r = 0.93; both $p < 0.001$). The CLOX also has a high internal consistency (Cronbach¿s alpha = 0.82). After adjusting for age and education level, the Executive Interview and Mini-Mental Status Examination strongly predicted CLOX 1 scores [$F(4,82) = 50.7$, $p < 0.001$; $R2 = 0.71$]. Refusal of care will be measured by clinician assessment at each weekly session with the following two questions: ¿¿How many weeks did the PWD participate in weekly sessions with the therapist?¿ and ¿How many weeks did the PWD participate in assigned homework?¿ Responses to each question range from 0-7 and will be summed and divided by the total number of sessions the caregiver participated in to determine the PWD¿s rate of engagement in the intervention.

Section D: Purpose and Objectives

The objectives of this proposal are to assess whether this caregiver intervention, Aggression Prevention Training for Caregivers of Persons with Dementia (APT), decreases 1) incidence of aggression, 2) aggression-related outcomes(injuries, caregiver burden, nursing-home placement, caregiver burden, positive aspects of caregiving, and behavior problems), and 3) pain and pain-related features (decreased pleasant activity frequency, poor relationship quality, and depressive symptoms).

Secondary objectives are to examine the relationships between executive dysfunction (ED) and 1) pain, 2) caregiver-patient related problems, 3) depression and 4) behavior problems and the association between ED and PWD engagement in the APT intervention.

The proposed study is a randomized, controlled trial of APT, a 6-8 session, home-based intervention. We will recruit 220 community-dwelling dyads (PWD and caregiver) that will be randomized to APT or enhanced usual primary care (EU-PC). APT uses active learning tools, including didactics, role-playing, and multimedia (eg, books and DVDs). Four core modules will address the 4 main aggression risk factors identified by our team and others: a) recognizing pain, b) treating pain pharmacologically and behaviorally, c) increasing pleasant activities to decrease depression, and d) improving the quality of the dyadic relationship through enhanced dyadic communication skills. Caregivers can select 2 to 3 additional elective sessions; the needs of the dyad guide elective selection to further enhance skills related to these core topics. EU-PC provides the patient and caregiver educational materials on pain, notifies the primary care provider of clinically significant pain, depression, and aggression in the PWD (see Reporting and Documentation Procedures attached in Section S), and provides 8 weekly supportive telephone calls to caregivers. PWD and caregiver outcomes will be collected at baseline, and at 3, 6 and 12 months. The CLOX Drawing Test will be administered at baseline to a subset of 100 subjects to measure executive function. Data analysis will include both univariate descriptive statistics and inferential statistics, including regression models, repeated-measure modeling and Cox proportional hazards models.

Section E: Protocol Risks/Subjects

E1. Risk Category

Category 1: Research not involving greater than minimum risk.

E2. Subjects

Gender:
Both

Age:
Adult (18-64 yrs), Geriatric (65+ yrs)

Ethnicity:
All Ethnicities

Primary Language:
English

Groups to be recruited will include:
Both patients and healthy, non-patient, normals

Which if any of the following vulnerable populations will be recruited as subjects?
Cognitively impaired

Vulnerable populations require special protections. How will you obtain informed consent, protect subject confidentiality, and prevent undue coercion?

Patients and caregivers will provide independent informed consent for their own participation. Although this study involves minimal risk, particular attention will be given to being sure that patients and caregivers understand that confidentiality will be maintained and that refusing to consent will not affect eligibility to receive any services or benefits from the BCM. Following the initial determination of eligibility, research assistants (RAs) will review the consent forms to ensure that potential participants understand their content. This will be done in-person at the subject's home or by telephone (procedure attached in Section S). RAs will discuss what will be asked of them if they consent to participate and whether they understand what consenting to participate involves. If there is any confusion, RAs will continue the discussion until the consent form is clarified. If patients are not able to understand and remember the content of the informed consent, assent will be obtained from the patient; and informed consent will be obtained from the caregiver.

Special training in research in subjects with Dementia Drs. Kunik and Snow and Ms. Wilson have extensive experience in training RAs in working with older adults with mental health problems. Dr. Kunik is a clinical leader within the BCM gerospychiatry service, and Dr. Snow is a leader in dementia research at the Tuscaloosa VA. Dr. Snow makes trips to Houston, on average, 5 times a year. Ms. Wilson has collaborated on many of the studies that have led to this proposal and has experience leading studies of home-based mental health interventions for older adults. They will draw on their considerable geriatric mental health training expertise and the extensive training resources of the Houston VAMC, Baylor College of Medicine, and the Houston HSR&D Center (Houston Center for Quality of Care & Utilization Studies) to train staff in several key areas as follows:

Dementia Research Training Dementia research training will include observing experienced clinical researchers such as Drs. Kunik and Snow administer the project tools, as well as supervised practice administering the tools. This component will also include strategies for doing confidential interviews in the home environment and for observing subjects for signs of stress and fatigue. Training in Ethical Aspects of Dementia Research Training in ethical aspects of dementia research will include the project coordinator and RAs reviewing and demonstrating understanding and competence in following the informed-consent procedures of the project, including how to recognize when research subjects do not exhibit decisional capacity and conducting ¿reconsent¿ procedures for subjects with decreased cognitive capacity, for example. An important component of this area will be ensuring that project personnel understand the provisions of Texas statutes regarding the mandated reporting of elderly or disabled individuals who are in a state of abuse, neglect, or exploitation (Chapter 48 of the Human Resources Code). There are 2 key resources for helping interviewers recognize possible indicators of abuse, neglect, or exploitation and understand procedures for reporting possible mistreatment. Project personnel will complete a Geriatric Medicine Self-Instruction DVD Module on Elder Mistreatment (including a test using case-based scenarios) produced by Baylor faculty through the Huffington Center on Aging, where Dr. Kunik is a faculty associate They will also review printed training resources of the Texas Department of Protective and Regulatory Services (TDPRS). TDPRS is affiliated with Baylor as a training resource, and a program supervisor has agreed to provide consultation and training to Dr. Kunik and staff on these issues. This training on informed consent and recognizing indicators of possible mistreatment will also include practice and feedback sessions with dyads of standardized patients and family caregivers.

E3. Pregnant woman/fetus

Will pregnant women and/or fetuses (as described in 45 CFR 46 Subpart B) be enrolled in the research?

No

E4. Neonates

Will neonates of uncertain viability or nonviable neonates (as described in 45 CFR 46 Subpart B) be enrolled in the research?

No

E5. Children

Will children be enrolled in the research?

No

Section F: Design/Procedure

F1. Design

Select one category that most adequately describes your research:

z.r) Randomized, Efficacy Study -- Surgical Techniques/Interventions

Discuss the research design including but not limited to such issues as: probability of group assignment, potential for subject to be randomized to placebo group, use of control subjects, etc.

50% of patients will be randomized into the EU-PC and 50% into the APT intervention. It is equally likely that a participant will be randomized into either intervention. The RA will not know when consenting the subject if they will be in the active APT intervention or in the control group (EU-PC).

Inclusion Criteria:

Patients can participate in the study if they meet the following criteria: (1) have a documented diagnosis of dementia; (2) receive care from, BCM GMA, the BCM Alzheimer Center, or Kelsey-Seybold; (3) reside outside Nursing Home;(4) live within 40 miles of the Texas Medical Center; (5) have mild-to-moderate dementia; (6) have no history of aggression in the past month; (7) have an informal caregiver directly involved with them at least 8 hours a week who sees them at least twice a week; (8) speak English; and (9) report clinically significant pain, depression, or caregiver/PWD relationship difficulties (either self-report or caregiver proxy-report).

Exclusion Criteria:

Patients with advanced dementia will be excluded by 2 criteria: a) score of greater than 6 on the Functional Assessment Staging (FAST) scale; or b) inability to complete by phone the Memory Impairment Screen--Telephone Version (MIS-T) or Philadelphia Geriatric Pain Intensity Scale. PWD will also be excluded if they have been aggressive in the past month; we will administer the aggression subscale of the Cohen-Mansfield Agitation Inventory (CMAI).

F2. Procedure

Our patient identification and recruitment procedures are based on our prior studies of PWD. The key initial criterion for study eligibility for patients is having a dementia diagnosis. The research team will partner with participating sites through 3 recruitment mechanisms to identify PWD: (1) direct provider referral (2) patient self-referral and (3) partial HIPAA-waiver-approved, database-generated lists of patients meeting geographical and selected ICD-9 codes from the 046, 290, 291, 292, 294, 331 and 333 series (or corresponding ICD-10 codes).

PWD identified through direct or database methods will receive a letter from the research team written at 6th-grade reading level to inform the PWD and caregiver that study staff will contact them the following week, unless they request not to be contacted by calling a toll-free number. PWD and caregivers will also be sent a Pain Thermometer as well as the response choices for the other study assessments/scales. A telephone script will be used to obtain verbal consent to administer the initial protocol screening, which will assess the presence of an eligible caregiver; clinically significant pain, depression or PWD/caregiver relationship difficulties; dementia of mild-moderate severity; absence of aggression; and willingness of PWD and caregiver to participate. Participant written informed consent for eligible and willing PWD and caregivers will be obtained in person or by mail immediately after the initial telephone screening appointment. A trained research assistant (RA) will administer the 15-minute telephone screen and informed consent to the caregiver and PWD. Following assent, caregivers will be asked a series of questions to assess level of PWD cognitive and functional impairment (FAST caregiver interview); presence of an eligible caregiver; and history of aggression, clinically significant pain or pain-related features, such as depression or caregiver/patient relationship problems. Prior to the RA¿s initiating the telephone screen, he/she will briefly describe the study and its voluntary nature to caregivers and PWD and obtain caregiver and patient verbal assent. PWD will be asked to complete the Mental Impairment Screen, telephone version (MIS-T) to collect further data regarding cognitive impairment and will also answer questions about their current level of pain, depression, and relationship with caregiver. PWD will be included if they screen positive for either: a) pain, b) depression, or c) caregiver/PWD relationship problems. We will screen for perceptions of pain using 2 measurement strategies. We will assess caregiver perceptions of the PWD¿s clinically significant pain with a screening question we have used previously: ¿During the past 4 weeks, did your [loved one/care recipient] often have physical pain, body aches, and/or discomfort?¿ The PWDs¿ perceptions of their own pain will be measured using 2 questions from the Philadelphia Geriatric Pain Intensity Scale, which assess pain intensity at time of assessment and over the past week. Both items use a response scale of 0 (no pain) to 5 (unbearable pain), presented as a thermometer graphic with verbal descriptors arranged

from ¿no pain/no interference¿ near the bulb to ¿unbearable pain/a great deal of interference¿ at the top. These items have demonstrated adequate internal consistency and test-retest reliability in PWD. The PWD will be considered to have clinically significant pain if either a) the caregiver answers affirmatively to the pain-screening question, or b) the PWD rates his or her pain at the level of 2 or higher on either the Philadelphia Geriatric Pain Intensity Scale current or past week pain ratings. PWD will also be included if they or their caregiver answers affirmatively to the Geriatric Depression Scale-1, ¿Do you or your loved one often feel downhearted and blue?,¿ which has a sensitivity and specificity of 71% and 74%, respectively.75 Finally, PWD will also be included if they or their caregiver answers affirmatively to the 1-question relationship screen used in our Partners in Dementia Care study, ¿Do you have concerns about tension or strain in the relationship between you and your caregiver/person you care for?¿

A home-based intervention was chosen for the following reasons. It may be difficult for some patients to travel to the study-site due to dementia-related cognitive/behavioral and physical factors, and other physical factors (such as pain). In addition, work schedules and the demands of caregiving may make travel to to the study-site difficult for the caregiver. In order to reduce this potential barrier and increase generalizability, all study visits will be conducted in the patient's home or via telephone. In addition, it is felt that the home-environment will be more conducive to active participation and learning for both patients and caregivers.

It is necessary to conduct the screening phone call prior to written informed consent for the following reasons: 1) It would be impracticable to conduct home visits to obtain written informed consent for all potentially eligible subjects prior to screening due to limited study resources. 2) We feel it is overly burdensome to ask to visit a patient's home without first assessing eligibility.

We plan to use the information collected on the screening telephone call as research data for the following reasons: 1) We will use the information gathered to determine the reasons potential subjects did not want to participate in the study or did not qualify for the study, to aid in the design of future research targeting this population. 2) Some of the questions asked at screening are also needed to characterize participants that enroll in the study. To reduce study burden, we will not repeat these questions after written informed consent is obtained.

Participants who screen eligible during the telephone assessment and sign consent documents will proceed to baseline. Eligible participants will be randomly assigned to intervention groups (APT or EU-PC) immediately following baseline evaluation based on random numbers generated in SAS PROC PLAN.

Assessments. Assessments will be done at baseline and 3, 6, and 12 months and will consist of a measure of demographic information and validated instruments. They will be administered by independent evaluators (IEs) blinded to random assignment .The CLOX Drawing Test (see Section S) will be administered in-person at baseline to a subset of 100 consecutively enrolled subjects; it should take less than ten minutes to complete. Prior to the assessment, instructions will be given to each subject in terms of what the measure is testing (i.e. ¿I will be assessing your ability to draw a clock¿). The remainder of the assessments will be administered by telephone. An unblinded RA will notify the PCP or referring MD of patients who have been identified as having clinically significant pain, depression, or aggression at baseline or on any of the follow-up calls (see Documentation and Reporting Guidelines attached in Section S).

The APT Intervention. APT is designed to reduce incidence of aggressive behavior in PWD with pain and/or pain-related features, who are at increased risk of aggression. It targets several areas of patient life that are known causes of aggression: pain, mood problems such as depression; lack of engagement in pleasurable activities; and difficulty in PWD/caregiver communication that may interfere with recognition of pain and negatively influence relationship quality. The intervention focuses most heavily on improving identification and management of pain through caregiver education and skill training. It also uses behavioral activation to increase pleasant events, known to be an important part of managing and preventing pain and treating depression. Finally, by providing training to improve communication skills, we expect to improve the quality of the PWD/caregiver relationship, improve the caregiver¿s ability to effectively engage the PWD in the intervention, and enhance the caregiver¿s ability to advocate to the clinical provider on behalf of the PWD. Caregivers will receive 6 to 8 sessions of weekly treatment ***(see Section S PAVeD caregiver workbook and clinician workbook attachements for more information). Sessions lasting up to 45 minutes will be conducted in the PWD's home by licensed providers with behavioral health expertise. APT consists of 4 ¿core¿ sessions covering identification and management of pain, improvement of PWD-caregiver communication skills, and behavioral activation through increased pleasant activity planning. Two to 3 elective sessions build on core skills in these 3 areas, chosen with the PWD and/or caregiver through an assessment of collaborative goal setting during the first session. The intervention will be primarily geared toward the caregiver; but each session also provides opportunities for optional PWD involvement, depending on his/her dementia severity and willingness. Sessions will include didactics, skill-building, discussion, and role-playing (see Section S PAVeD caregiver workbook and PAVeD clinician manual attachments). Participants will also be provided a copy of Pain Management for Older Adults: A Self-help Guide as an additional resource for optional reading on topics covered in the intervention. All physicians with enrolled participants in either arm will receive CME modules pertaining to assessing and treating pain in older adults; this will increase their sensitivity toward and knowledge about pain identification. The Exit Interview attached in section S will be administered to all caregivers enrolled in the intervention group as soon as possible after their last home session to gather feedback on the intervention.

Enhanced Usual Primary Care. EU-PC participants will receive feedback on their level of pain and depression, a booklet from the National Institute on Aging on memory problems, the book, Pain Management for Older Adults: A Self-help Guide, and a letter encouraging them to discuss additional treatment options with their providers. Caregivers receiving EU-PC will also receive 8 weekly 15-minute calls to query symptom severity, ascertain needs for immediate psychiatric care, and provide minimal support. If caregivers report pain or other physical or psychological symptoms in the PWD, they will be

encouraged to address them with their primary care providers.

APT and Usual Care Interventionists. A minimum of 2 RAs with a license in nursing, social work, psychology, or counseling will provide the APT intervention and EU-PC. Each RA will be assigned both APT and EU-PC patients. Treatment diffusion will be monitored by ongoing treatment integrity ratings. All providers will receive training with emphasis on providing care for PWD and their caregivers. Training will include best practices for delivering educational interventions, skills training, and behavioral activation. Providers will not be restricted based on discipline but will be expected to have a background in mental health and interest in older adults. Providers will be blind to baseline data collected during IE telephone assessments.

APT and EU-PC intervention sessions and telephone assessments at baseline, 3, 6, and 12 months will be audio-recorded without PHI for quality assurance purposes. See data analysis section for information on security of audio-recordings.

If detected during APT or EU-PC intervention sessions or during telephone assessments at baseline, 3, 6, and 12 months, clinically significant pain, aggression, and depression symptoms will be reported to the PCP or referring MD according to the Documentation and Reporting guidelines attached in Section S. If the participant's PCP is not with Baylor College of Medicine or Kelsey-Seybold, he or she will be asked to complete a Release of Information Form giving permission for us to communicate this information to the PCP.

Section G: Sample Size/Data Analysis

G1. Sample Size

How many subjects (or specimens, or charts) will be used in this study?

Local: 4250 Worldwide: 4250

Please indicate why you chose the sample size proposed:

In our prior and currently funded grants, we recruit patients using methods similar to those described in this proposal to identify PWD with clinically significant pain. To determine the number of patients available for this study, we asked our clinical partners to provide the number of PWD, using dementia ICD-IX codes and restricting to patients within 40 miles not living in a long-term care facility. We identified 1273 patients. Based on our prior studies, an estimated 60% of patients will meet the criterion for clinically significant pain, resulting in 764 existing eligible patients; broadening inclusion criteria to include pain-related features will result in even more eligible patients. On the basis of our prior recruitment data, we predict excluding approximately 30% of patients due to severe dementia, history of aggression, or lack of eligible caregiver. Thus, we estimate that 535 will meet all selection criteria. In our current APT study, we have had a consent rate of 80-90%. To conservatively estimate, an 80% consent rate results in 428 patients.

One-hundred consecutively enrolled subjects will be asked to do the CLOX Drawing Test at baseline to achieve our secondary objectives. This will give adequate power to detect significant differences of small to medium magnitude in outcomes between those with and without executive function (ED). Given an N of 100 and an alpha of 0.05, there is 97% power to detect a medium effect (F2 = 0.15) and 80% power to detect an effect size for ED (over and above two covariates) as small as F2 = 0.08.

Expected Recruitment Efforts and Minimization of Attrition. In our current VA Study and prior studies, we were able to enroll 6-8 dyads per month. In the VA study and others that we completed with PWD and their caregivers, attrition is about 10%; therefore, we plan to recruit 220 dyads, 6 patients per month over 37 months. We expect we will need to contact approximately 300 dyads using our partial HIPPA Waiver in order to enroll 220 dyads in the study.

We have listed a sample size of 1500 above. This number is an estimate of the number of patient names/contact information we will receive from our partners (Baylor Geriatrics, Baylor Neurology, and Kelsey-Seybold) using our two recruitment methods: 1) database queries using our partial HIPPA Waiver and 2) direct provider referral. Many of these will turn out not to be eligible as described in the first paragraph of this section. See Sections J2 and F for details of our recruitment and screening methods.

Amendment 4/7/16: As of the end of March 2016, the percentage of patients referred from our clinical partners that have been enrolled in the study (assigned to APT or EU-PC) is less than expected (about 7%). Therefore, we are requesting to increase the number of patient names we will receive from our partners over the course of the recruitment period from 1500 to 2500. We still plan to randomize only 220 subjects.

Amendment 3/1/17: With pior IRB approval, we increased our sample size to 4000. This is the number of database and direct referrals we anticipated we would need in order to enroll 220 subjects based on the percent of referrals enrolled over the course of the study (less than 7%).

Amendment 8/18/17: With IRB approval, we will enroll and extra 10 subjects to replace someof our drop-outs. In order to do this we expect to need another 250 referrals (database and direct) from our clinical partners. Therefore the sample size above has been increased to 4250.

G2. Data Analysis

Provide a description of your plan for data analysis. State the types of comparisons you plan (e.g. comparison of means, comparison of proportions, regressions, analysis of variance). Which is the PRIMARY comparison/analysis? How will the analyses proposed relate to the primary purposes of your study?

General Considerations. Direct computer-assisted data entry will be used during telephone interviews. Computer-assisted data entry decreases data-entry errors by restricting entry values to the expected range for each field. Under the supervision of Dr. Kunik, the RA will design the data-entry form and work with the programmer to check for appropriateness of variable definitions, numeric and character fields and variable names in the data form. These data can then be uploaded into the UNIX computing system at the Houston VA Center of Excellence Computing Center. Statistical Analysis Software (SAS Version 9.2, Cary, NC) will be used to conduct the data analysis. All data collected in this study will remain confidential and be reported only in the form of aggregate statistics.

Data analysis will include both univariate descriptive statistics and formal hypothesis testing. The distribution of continuous variables will be presented as summary statistics, such as means and standard deviations. Categorical variables will be presented as frequency tables.

Attrition Rates and Missing Data. Our anticipated participation rate for this study is expected to be similar to that of our prior work. For patients who are eligible but elect not to participate, we will document reasons for nonparticipation and determine trends by age, gender, or race/ethnic classification that may lead to a potential bias in our findings. We will attempt to minimize missing data through careful design of data-collection procedures. There were very little missing data in our prior work with telephone assessments. We will review missing data to determine whether missing items can be logically completed. If missing items cannot be logically completed, we will use appropriate multiple imputation techniques (S+ MissingData [S-PLUS Version 6]) for loglinear, Gaussian, and conditional Gaussian models) to test the sensitivity of our results to biases introduced by the missing items.

In general, the primary source of missing data will be through participant attrition. We anticipate a low attrition rate (10%) based on our prior work. As described below, we will use analytic techniques (eg, hierarchical linear models) that are robust to violation of missing-data assumptions (ie, ¿missing completely at random¿). To reduce the possibility of bias in missing data, where possible, we will incorporate information from secondary sources for participants with missing data from attrition to try to ascertain whether they differ in important ways from other study participants. We will use X2 tests to determine whether there are differences in attrition between the 2 study arms. Prior to testing hypotheses, we will compare baseline demographic and clinical variables in APT and EU-PC with X2 and independent sample t-tests. Variables with p values < .25 in these univariate tests will be included as covariates in all subsequent multivariate models107 or as propensity scores.

Primary Hypothesis: APT will result in lower 1-year incidence of aggression than EU-PC. We will use negative binomial regression models to estimate the difference between our intervention and the control group in the rate of aggressive behavior at the 1-year follow-up period. For participants who drop out of the study, their time until study attrition will be used as their exposure period. Statistical significance will be determined using the X2 statistic associated with the parameter estimate for group membership. Baseline demographic and clinical variables that differ between groups in univariate tests will be included as covariates or propensity scores.

Secondary Hypotheses 1: APT will result in greater reduction in aggression-related outcomes (nursing home placement, caregiver burden, positive aspects of caregiving, and behavior problems) over the 1-year assessment period than EU-PC. We will separately identify between-group (APT vs. EU-PC) differences in change over the 1-year follow-up period for injuries to PWD or others, caregiver burden, and nursing home placement, using a hierarchical linear modeling approach to repeated-measure modeling. These mixed models will maximize participant data by allowing us to account for various lengths of follow-up for each participant, as well as for missing observations (other than attrition). Conditional models will contain fixed terms for the intercept, treatment group (APT or EU-PC), time period (baseline; 3, 6, or 12 months), treatment group by time period interaction, and any previously identified variables that differ between treatment groups. Modeled random effects will include between-patient variation in baseline scores (i.e., the intercept where baseline assessments are scored 0) and variation in the slopes over time. In other words, we will model and attempt to explain variance between treatment groups for both baseline outcomes and overall change over time in outcomes. Given the 4 time points, the focus will initially be on linear patterns of change, although we will evaluate the relative fit of a quadratic or cubic pattern of change, using the likelihood ratio test. These analyses will allow us to examine the immediate impact of treatment, as well as retention, improvement, or decay in outcomes across the 12-month follow-up period.

Reduction in risk of nursing-home admission will be evaluated using a Cox proportional hazards model to test for between-treatment group differences. Similar to the approach we used for Hypothesis 1 to test for differences in onset of aggression, we will first estimate the unadjusted differences between groups, followed by estimates incorporating all identified covariates.

Secondary Hypothesis 2: APT will result in greater decreases in pain severity and pain-related features (low pleasant-activity levels, poor quality of caregiver-PWD relationship and depressive symptoms) than EU-PC over the 1-year follow-up period. These analyses will be conducted using the same approaches described for secondary Hypothesis 1.

Secondary Hypotheses 3: PWD who screen positive for ED will report significantly higher rates of pain (Philadelphia Geriatric Pain Intensity Scale), caregiver-patient related problems (Mutuality Scale), depression (30-item Geriatric Depression Scale) and behavior problems (Revised Memory and Behavior Checklist). Differences between those with and without ED in 1) pain, 2) mutuality, 3) depression, and 4) behavior problems will be evaluated with a series of multiple

linear regression models. Four models will be conducted, one for each outcome, with ED as the primary predictor and gender and caregiver relationship as covariates.

Secondary Hypotheses 4: PWD who screen positive for ED will have significantly lower engagement in intervention than PWD who do not screen positive for ED. An additional linear regression model will be conducted to test for differences between those with and without ED in engagement (Aim 2).

Data on Intervention Process and Quality Assurance. Data will be collected by RAs and IEs, who will be trained in completing all questionnaires (see human subjects section for training information). Study personnel will instruct participants how to accurately respond to each questionnaire and will ensure data quality by reviewing each document for response errors and omissions. For telephone-based assessments, an assessment guide will be provided to increase reliability and validity of responses. All IEs will be blinded to participant randomization and will remind participants not to reveal any information about study interventions during assessment interviews. Study providers will not be involved in outcome data-collection and will be blind to IE assessments. Under the supervision of the PI, all IEs will be trained to administer questionnaires in a standardized manner. IEs will undergo rigorous training and calibration for all study measures. Fidelity Review The first two APT cases assigned to each clinician will be closely supervised and rated for adherence to the protocol and clinican competency by a clinician investigator; if needed, close supervision will continue for additional cases until ratings of 6 or higher (¿good¿ on a 0-8 scale) are achieved. A random 10% of the APT sessions will be monitored by Dr. Jessica Calleo. If clinician adherence or competence falls below 6 for 2 consecutive tapes: ¿ Provider will receive additional supervision ¿ Supervisor will listen to all sessions until the appropriate rating is achieved for 2 consecutive sessions ¿ If provider is unable to attain integrity rating within a reasonable period of time, supervisor will decide on best course of action (eg. additional training, etc.) The first two EUPC cases assigned to each clinician will also be closely supervised and rated by a clinician investigator for adherence to the protocol. Close supervision will continue for additional cases as needed. A random 10% of the EUPC sessions will be monitored by Dr. Sheila Richey. Lynn Snow will conduct a similar review of baseline and follow-up (3, 6, and 12 month) telephone assessments by the IE for quality assurance.

Additional measures of treatment fidelity will describe the extent to which participants understand and use the skills during and after the intervention. First, during each session, providers will assess caregivers¿ level of understanding, using targeted questions at key points (see Appendix). These questions will be used as checkpoints to determine whether to proceed to the next session or provide additional teaching. A second measure will assess between-session use of skills. At the beginning of each session, providers will record the caregiver¿s level of participation in skills training by documenting the number of home practice assignments completed. Finally, providers will inquire about caregivers¿ interactions with health providers and document the caregiver¿s reported use of specific provider-patient communication techniques taught in the first session.

Section H: Potential Risks/Discomforts

H1. Potential Risks/Discomforts

Describe and assess any potential risks/discomforts; (physical, psychological, social, legal, or other) and assess the likelihood and seriousness of such risks:

The potential risks foreseen generally relate to psychological discomfort that may be associated with the assessment and/or treatment process of the study. Participants may experience mild distress related to answering personal questions and/or mental fatigue from responding to multiple questions at one time. In addition, there is a limited risk of loss of privacy due to the nature of the questions. The intervention and usual care groups of this study are not expected to create any significant risk for participants. Participants will be informed about available alternative treatments including the use of additional medical treatment (where possible), and/or no treatment. In summary, the therapeutic risks are viewed as minimal as are the research risks.

H2. Data and safety monitoring plan

Do the study activities impart greater than minimal risk to subjects?

No

H3. Coordination of information among sites for multi-site research

Is the BCM Principal Investigator acting as the SPONSOR-INVESTIGATOR for this multi-site research?

No or Not Applicable

Is BCM the COORDINATING CENTER for this multi-site research?

No or Not Applicable

Section I: Potential Benefits

Describe potential benefit(s) to be gained by the individual subject as a result of participating in the planned work.

Subjects may benefit from being better able to manage their pain. They may also be less likely to become aggressive.

Caregivers will learn how to better manage pain and distress and will learn to better communicate with persons with dementia. Although this is particularly true in the intervention group, those in the control group will also receive substantial educational information. Primary care providers will learn of patients¿ pain and depression level and therefore may be better to manage these symptoms. Given that the risks from the intervention and research assessments are minimal, we gauge the risk-benefit profile to be positive.

Describe potential benefit(s) to society of the planned work.

The current treatment of persons with dementia and aggression continues to be antipsychotic medications, which have limited efficacy and substantial adverse consequences. If this intervention is efficacious, it will provide an urgently needed alternative to current treatment. In addition, the paradigm of prevention in mental health is of growing importance. Since the risks of this proposal are minimal, the balance of risks to potential knowledge gained is very favorable.

Do anticipated benefits outweigh potential risks? Discuss the risk-to-benefit ratio.

Given that the risks of this largely educational intervention are minimal, the risk to benefit ration is positive. Patients may benefit from better management of their pain and less development of aggression, caregivers may benefit from gaining knowledge on how to better manage their care recipients who have dementia, and providers may benefit from learning more about how to address pain in persons with dementia

Section J: Consent Procedures

J1. Waiver of Consent

Will any portion of this research require a waiver of consent and authorization?

Yes

Please describe the portion of the research for which a waiver is required. (Example: chart review to determine subject eligibility)

The research team will partner with participating sites to identify PWD through partial HIPAA-waiver-approved, database-generated lists of patients meeting geographical and selected ICD-9 diagnostic codes from the 046, 290, 291, 292, 294, 331 and 333 series (or corresponding ICD-10 codes). We have tried directly recruiting patients through newsletters, fliers, and through primary care doctor referral on numerous occasions without success. Initial access to the PHI is necessary to identify potentially eligible patients. Given our strict eligibility criteria, it would be impossible to recruit our targeted sample of patients w/out first limiting recruitment to dementia patients who could then be approached to evaluate for pain/pain-related symptoms.

Explain why the research and the use or disclosure of protected health information involves no more than minimal risk (including privacy risks) to the individuals.

All PHI will be kept secure and not shared. Only the study team will be able to see research records, questionnaires, and other identifying information. All information will be stored in a locked file cabinet in a locked storage room at the MEDVAMC. We will store information collected on a secure computer server behind the MEDVAMC firewall. This means that the information will be in a computer that no one outside the VA/ BCM can get into. A number will be assigned to each patient and caregiver, which will be kept separate from all identifying information, except for a password-protected master list stored on a secure server behind the MEDVAMC firewall.

Explain why the waiver will not adversely affect the privacy rights and the welfare of the research subjects.

PHI will be combined with information from other people in the study. We will write about the combined information and not about any person individually. We will not share any records unless the law requires us to. PHI will not be reused or disclosed to or shared with any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the PHI would be permitted under the privacy rule.

Explain why the research could not practicably be conducted without the waiver and could not practicably be conducted without access to and use of the protected health information.

The research could not practicably be conducted without the waiver without access to and use of PHI because the scientific validity would be compromised if the investigators did not have access to the database. In order for the results of the study to be valid, the PI needs to be sure that the participants are appropriately selected for the study. In past studies, we have tried to recruit through other means such as through healthcare providers or advertisements, but these have not worked in this population of older adults with dementia and their caregivers. We have not been able to recruit enough subjects, and those subjects that we did recruit were not representative of the general population of persons with dementia and their caregivers. Recruiting through these traditional methods has resulted in recruiting psychologically, cognitively, and physically healthier patients (and caregivers); those that are less likely to benefit from the intervention.

Describe how an adequate plan exists in order to protect identifiers from improper use and disclosure.

PHI will not be reused or disclosed to or shared with any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the PHI would be permitted under the Privacy Rule.

Describe how an adequate plan exists in order to destroy identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law.

Per VA policy, all research data collected, including identifiers, for this research study will be destroyed six years from the date the research study is closed.

Describe how adequate written assurances exist in order to ensure that the PHI will not be reused or disclosed to (shared with) any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the PHI would be permitted under the Privacy Rule.

This Waiver of Consent is for obtaining database lists of patients diagnosed with dementia and their contact information. Subjects who are found to be interested and eligible will be asked to sign a written consent form that contains a statement that PHI will not be reused of disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the PHI would be permitted under the Privacy Rule.

Information from health records such as diagnoses, progress notes, medications, lab or radiology findings, etc.

Yes

Specific information concerning alcohol abuse:

No

Specific information concerning drug abuse:

No

Specific information concerning sickle cell anemia:

No

Specific information concerning HIV:

No

Specific information concerning psychiatry notes:

No

Demographic information (name, D.O.B., age, gender, race, etc.):

Yes

Full Social Security #:

No

Partial Social Security # (Last four digits):

No

Billing or financial records:

No

Photographs, videotapes, and/or audiotapes of you:

No

Other:

Yes, as described:
medical record numbers

Will additional pertinent information be provided to subjects after participation?

No

If No, explain why providing subjects additional pertinent information after participation is not appropriate.

This is an educational intervention and patients and caregivers will be receiving substantial information during the study. Providing additional information after the study is not likely to be useful to them.

J1a. Waiver of requirement for written documentation of Consent

Will this research require a waiver of the requirement for written documentation of informed consent?

Yes

Explain how the research involves no more than minimal risk to the participants, and the specifics demonstrating that the research does not involve procedures for which written consent is normally required outside of the research context.

A home-based intervention was chosen for this study for several reasons. It may be difficult for some patients to travel to the study-site due to dementia-related cognitive/behavioral and physical factors, and other physical factors (such as pain). In addition, work schedules and the demands of caregiving may make travel to to the study-site difficult for the caregiver. In order to reduce this potential barrier and increase generalizability, all study visits will be conducted in the patient's home or via telephone. In addition, it is felt that the home-environment will be more conducive to active participation and learning

for both patients and caregivers.

Subjects will first be screened for eligibility by telephone using a telephone script (attached in Section S). Verbal consent to conduct the telephone screening and use the information collected as part of the research will be obtained before any other questions are asked. A trained research assistant (RA) will administer the 15-minute telephone screen to the caregiver and PWD. Caregivers will be asked a series of questions to assess level of PWD cognitive and functional impairment (FAST caregiver interview); presence of an eligible caregiver; and history of aggression, clinically significant pain or pain-related features, such as depression or caregiver/patient relationship problems. PWD will be asked to complete the Mental Impairment Screen, telephone version (MIS-T) to collect further data regarding cognitive impairment and will also answer questions about their current level of pain, depression, and relationship with caregiver. These questions are minimally invasive and would not require written informed consent outside of a research setting.

We feel it is necessary to conduct the screening phone call prior to written informed consent for the following reasons:

1) It would be impracticable to conduct home visits to obtain written informed consent for all potentially eligible subjects prior to screening due to limited study resources.

2) We feel it would be overly burdensome to ask to visit a patient's home without first assessing eligibility.

We plan to use the information collected on the screening telephone call as research data for the following reasons: 1) We will use the information gathered to determine the reasons potential subjects did not want to participate in the study or did not qualify for the study, to aid in the design of future research targeting this population.

2) Some of the questions asked at screening are also needed to characterize participants that enroll in the study. To reduce study burden, we will not repeat these questions after written informed consent is obtained.

If a subject is found to be eligible based on telephone screening, a trained RA will visit the subject's home to obtain written informed consent as soon as possible.

J2. Consent Procedures

Who will recruit subjects for this study?

PI
PI's staff

Describe how research population will be identified, recruitment procedures, any waiting period between informing the prospective participant and obtaining consent, steps taken to minimize the possibility of coercion or undue influence and consent procedures in detail.

Our patient identification and recruitment procedures are based on our prior studies of PWD. The key initial criterion for study eligibility for patients is having a dementia diagnosis. The research team will partner with participating sites through 3 recruitment mechanisms to identify PWD: (1) direct provider referral and (2) participant self-referral, (3) partial HIPAA-waiver-approved, database-generated lists of patients meeting geographical and selected ICD-9 codes from the 046, 290, 291, 292, 294, 331 and 333 series (or corresponding ICD-10 codes). We have tried directly recruiting patients through newsletters, fliers, and through primary care doctor referral on numerous occasions without success. Initial access to the PHI is necessary to identify potentially eligible patients. Given our strict eligibility criteria, it would be impossible to recruit our targeted sample of patients w/out first limiting recruitment to dementia patients who could then be approached to evaluate for pain/pain-related symptoms. A waiver of consent for database review for subject identification is attached in section S. Dr. Valory Pavlik in BCM Neurology and Dr. Susan P. Williams in BCM Geriatrics, along with Dr. Michael Newmark at Kelsey-Seybold, will be sharing the names, addresses, and phone numbers of their patients who meet the basic eligibility study criteria with Dr. Mark Kunik and his study staff. All data will be sent to the coordinating center (VA) for storage. Data will be stored on VA servers located at the Michael E. Debakey VA Medical Center and in locked filing cabinets in a locked filing room located at HSR&D Center of Excellence Nabisco Building 2450 Holcombe Blvd., Suite 01Y Houston, TX 77021, Storage Room 121. See Section K for further explanation of Confidentiality.

PWD identified through direct or database methods will receive a letter from the research team written at 6th-grade reading level to inform the PWD and caregiver that study staff will contact them the following week, unless they request not to be contacted by calling a toll-free number. PWD and caregivers will also be mailed response cards and the Philadelphia Geriatric Pain Intensity Scale. PWD who do not opt-out, but are not reached by phone may receive a second opt-out letter after contact information is re-verified with the referring provider.

We will attend the clinics of our clinical partners if needed to explain the study in person to any patients referred. We will collect the names and contact information of patients who are interested and schedule them for telephone screening.

Fact Sheets and flyers will be posted at dementia-specific adult day care centers in the Houston area. The flyers will specify that the PWD must be a patient of one of our clinical partners (see flyer attached in Section S). Patients and their caregivers can contact study staff to schedule a telephone screening.These fact sheets and flyers will also be distributed at community events such as the annual Alzheimer's Update at the Museum of Natural Science.

Periodically, Susan Reed, a nurse practitioner with Kelsey-Seybold Department of Neurology, or other qualified personnel will give a 45 minute talk on Coping with Dementia at the main Kelsey-Seybold Clinic at Holcombe Blvd. The Kelsey

Research Foundation will invite active patients of Kelsey-Seybold Clinics who have been diagnosed with dementia and their caregivers to the talk. The IRB approved APT Study Fact Sheet and Flyer will be available at the talk, and study staff will be on hand to answer questions about the study. A private room will be reserved for patients who wish to screen for the study after the talk. Patients may also schedule a telephone screening for a later date.

Due to space limitations, see additional text attached in Section S.

Are foreign language consent forms required for this protocol?
No

J3. Privacy and Intrusiveness

Will the research involve observation or intrusion in situations where the subjects would normally have an expectation of privacy?
No

J4. Children

Will children be enrolled in the research?
No

J5. Neonates

Will non-viable neonates or neonates of uncertain viability be involved in research?
No

J6. Consent Capacity - Adults who lack capacity

Will Adult subjects who lack the capacity to give informed consent be enrolled in the research?
Yes

J7. Prisoners

Will Prisoners be enrolled in the research?
No

Section K: Research Related Health Information and Confidentiality

Will research data include identifiable subject information?
Yes

Information from health records such as diagnoses, progress notes, medications, lab or radiology findings, etc.
Yes

Specific information concerning alcohol abuse:
No

Specific information concerning drug abuse:
No

Specific information concerning sickle cell anemia:
No

Specific information concerning HIV:
No

Specific information concerning psychiatry notes:
No

Demographic information (name, D.O.B., age, gender, race, etc.):
Yes

Full Social Security #:
No

Partial Social Security # (Last four digits):
No

Billing or financial records:

No

Photographs, videotapes, and/or audiotapes of you:
Yes

Other:
Yes, as described:
medical record numbers

At what institution will the physical research data be kept?
Data will be stored at the VA HSR&D Center of Excellence, Nabisco Building 2450 Holcombe Blvd., Suite 01Y Houston, TX 77021.

How will such physical research data be secured?
Data will be stored in locked filing cabinets in a locked filing room (Storage Room 121).

At what institution will the electronic research data be kept?
Michael E. Debakey VA Medical Center

Such electronic research data will be secured via BCM IT Services- provided secured network storage of electronic research data (Non-Portable devices only):
No

Such electronic research data will be secured via Other:
Yes, (describe below):
The database will be stored on a secure VA server located at the Michael E. Debakey VA Medical Center behind a locked door with access limited to IT personnel. During non-business hours, the server is behind 3 locked doors. The server is password-protected and is behind a behind a firewall. The data is backed up automatically each night. The exact location of the data is: M: Research\Kunik_M_APT_Caregiver_H-33720_H-33911.

Will there be anyone besides the PI, the study staff, the IRB and the sponsor, who will have access to identifiable research data?
Yes, identify the classes of the persons:
The subject's physician will be notified of significant pain, depression or aggression noted during the study. This is explained in the consent form.

Please describe the methods of transmission of any research data (including PHI, sensitive, and non-sensitive data) to sponsors and/or collaborators.
Any transmission of PHI to collaborators will be sent via secure email.

Will you obtain a Certificate of Confidentiality for this study?
No

Please further discuss any potential confidentiality issues related to this study.
The study protocol involves research staff meeting subjects in their homes, requiring sensitive data to leave the VA. The information will be a paper subject research record to be hand carried and remain with the research assistant or research clinician at all times. Protocol requires research assistants and clinicians to visit patients in their home for review of consent forms and to execute study intervention. The consent is a one time home visit, and the intervention is a series of home visits up to eight visits per patient. The information will be temporarily moved for each study participant from the VA to the patient's residence when visited by a research assistant or research clinician. The patient's contact information (name, telephone number and address) is required to be with the RA for purposes of direction and safety. The clinician also requires contact information for purpose of direction and safety.

All sessions will be audio recorded (both Enhanced Usual Care and Manual Intervention) by the Research Clinician using a Olympus DS-5000iD or DS-7000 and hand-carried from the participants home back to the VA at the end of each intervention session. The recorders are data encrypted and require a password to be heard. The recordings will be uploaded to the VA database and stored on the secure VA drive (M: Research\Kunik_M_APT_Caregiver_H-33720_H-33911). Once the recordings are downloaded they will be deleted from the audio recorder.

Section L: Cost/Payment

Delineate clinical procedures from research procedures. Will subject's insurance (or subject) be responsible for research related costs? If so state for which items subject's insurance (or subject) will be responsible (surgery, device, drugs, etc). If appropriate, discuss the availability of financial counseling.
Subjects will not be responsible for research related costs. The only clinical procedures will involve education of caregivers and patients.

If subjects will be paid (money, gift certificates, coupons, etc.) to participate in this research project, please note the total dollar amount (or dollar value amount) and distribution plan (one payment, pro-rated payment, paid upon completion, etc) of the payment.

Dollar Amount:

100

Distribution Plan:

Caregivers will receive $25.00 for each of the 4 assessment interviews. These recruitment methods have been previously approved by the BCM institutional review board. Patients will not be reimbursed as their involvement with research assessments is minimal.

Section M: Genetics

How would you classify your genetic study?

Discuss the potential for psychological, social, and/or physical harm subsequent to participation in this research. Please discuss, considering the following areas: risks to privacy, confidentiality, insurability, employability, immigration status, paternity status, educational opportunities, or social stigma.

Will subjects be offered any type of genetic education or counseling, and if so, who will provide the education or counseling and under what conditions will it be provided? If there is the possibility that a family's pedigree will be presented or published, please describe how you will protect family member's confidentiality?

Section N: Sample Collection

None

Section O: Drug Studies

Does the research involve the use of ANY drug* or biologic? (*A drug is defined as any substance that is used to elicit a pharmacologic or physiologic response whether it is for treatment or diagnostic purposes)

No

Does the research involve the use of ANY gene transfer agent for human gene transfer research?

No

O1. Current Drugs

Is this study placebo-controlled?

No

Will the research involve a radioactive drug?

No

Section P: Device Studies

Does this research study involve the use of ANY device?

No

Section Q. Consent Form(s)

None

Section R: Advertisements

Mode of Advertising: Other: Clinics, Day Centers, and Community Events

Exact language of Advertisement:

See Flyers and FACT Sheets attached in Section S. These will be posted at Day Centers and handed out by study-staff or BCM or Kelsey-Seybold Providers when recruiting patients out of the clinics. They will also be distributed at community events such as the BCM Update on Alzheimer's.

The following print ad will be posted in Day Center newsletters:

Baylor College of Medicine is looking for patients with dementia to participate in a clinical trial of an educational intervention designed to help their caregivers improve identification and management of their pain and distress. Investigators hope this will help prevent the onset of certain behavioral symptoms that may occur in patients with dementia. Patients may qualify if they are experiencing pain, depression, or a strained relationship with their caregivers and currently receive clinical care from Baylor Geriatrics Associates, Baylor Alzheimer¿s Disease and Memory Disorders Center, or Kelsey-Seybold Clinics. Study visits are conducted either in-home or by telephone. For more information, please contact Matthew Escamilla, BS at 713-440-4661 or Matthew.Escamilla@bcm.edu.

A 4X6 inch tent card with study information will be displayed at the clinics of our clinical partners as well as at dementia-specific day centers and community event. See proof attached in Section S.

Addendum to Section J2 Consent Procedures

A telephone script will be used to obtain verbal consent to administer the initial protocol screening, which will assess the presence of an eligible caregiver; clinically significant pain, depression or PWD/caregiver relationship difficulties; dementia of mild-moderate severity; absence of aggression; and willingness of PWD and caregiver to participate.

Participant written informed consent for eligible and willing PWD and caregivers will be obtained in person or by mail immediately after the initial telephone screening appointment. These recruitment methods have been previously approved by the BCM institutional review board. Verbal permission to use the answers to the telephone screening questions for the research will have been obtained from the PWD and caregiver prior to collection of this data. Participants will be reminded of this at the time of in-person written informed consent. No other research procedures will take place until the consent forms have been signed and subjects have received the signed copies. See Section S for "Procedures for Consent by Mail."

Particular effort will be made to recruit women and minorities via fliers (representing different genders and races) and specific recruitment through the participating clinics. We will use the expertise of other investigators and community practitioners as "cultural guides" should we identify challenges in recruitment or retention of the racial and ethnic minorities. Study administrative staff will be trained to consider and respect different attitudes, preferences, and communication styles of minorities, women, and older adults. In our prior studies, we have had 20% minority recruitment, which is similar to the prevalence of minorities in the older veteran population from which we were recruiting.