Official Title:	A Multisite Cluster RCT of the Dementia Symptom Management at Home Program
NCT Number:	NCT03255967
Study Number:	17-00810
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Tool Revision History:

Version Number	Version Date	Summary of Revisions Made
1.0	30 JUNE 2017	Original version
1.1	29 SEPT 2017	Change behavioral tool from HABC to the NPI-Q; make clear the endpoint of the NPI-Q is individual symptoms, not composite, add DSMB Chair, Cognition screening instrument changed from HABC-M to QDRS, QDRS inadvertently left out of section 7.1 on initial protocol; Clinicaltrials.gov number added
1.2	27 NOV 2017	Changes based on DSMB review of protocol: Remove "Demonstration of efficacy" as a means to warrant termination or suspension; Include delirium screening instrument (3D-CAM); change: PIs will follow "Standard Clinical Practice" in responding to AE and SAE by referring to patient/caregiver primary care provider. Clarified how contamination and fidelity monitoring will be performed. Add 3D-CAM to the PWD-Dyad Survey Instruments; Change name from VNAHG of New Jersey to VNAHG.
1.3	16 AUG 2018	Add the DSM-H Clinician Survey to recruitment materials. Make clear the clinician referrals are submitted through survey link operated by REDCap. Change the screening schedule so that the research coordinator administers the Quick Dementia Rating Scale over the phone with the caregiver to determine if the PWD meets eligibility before scheduling the initial home visit.
1.4	5 OCT 2018	Remove Allegiance Home Health as the implementation site for Florida Atlantic University. Change "PAINAD or BPI" to include both instruments in assessing PWD for pain regardless of the PWD's QDRS score. Change Elixhauser comorbidity measure to Charlson comorbidity; Remove caregiver and home health care utilization from visit two.
1.5	22 JAN 2019	Edits were made to better clarify subject recruitment, consent and retention processes. Based on DSMB recommendations for maintaining subject retention, subjects will not be terminated from the study if they are unable to complete the intermediate visits. In addition, subjects will not be required during the intermediate visits to be interviewed at the same time. Language to clarify the time point for visit one has been changed from 2-3 days to 3 days. Changes to rate of subject compensation has been clarified to cover subjects who miss intermediate visits.
1.6	5 JULY 2019	Changes to the recruitment process have been recorded in line with DSMB recommendations. Clinicians will no longer be the point of referral. All referrals will be submitted by designated agency staff in line with PHI regulations. Method of referral per agency site has been described therein. Changes to the first call scripts have been edited and updated. DSM-H research study information cards with research team contacts have been included in the recruitment process. Minor formatting edits included.
1.7	31.JAN 2020	Added recruitment method for sites: CNS and FIRSTAT. The updated process will include a designated agency point of contact who will generate a daily potential patient referral report in line with PHI regulations of newly admitted persons with dementia aged 65+ who live in a private residence. The report will be made accessible designated research team for the purpose of referral submissions. In addition, edits to better clarify reporting process of adverse events has also been included. Updated Dr. Galvin's contact information.
1.8	3.JUNE 2020	The protocol has been modified to change the modality of subject visits to virtual from in-person. To achieve this, Inclusion criteria additions: internet capabilities; caregiver 8+hrs of care management per week; edit retention strategies to replace "magnet" with email visit schedule; change the need for subjects to be together for virtual visits 2-4; add QDRS score

		of ≤12 to determine which PWD assessments will be administered; edit informed consent process to reflect remote consenting through REDCap; change 3D-CAM to FAM-CAM; adds COVID-19 related questions; add electronic gift cards as method of subject compensation; clarification provided on method of data collection; change criteria for subject disenrollment
1.9	12.July 2021	The protocol has been modified to include a waiver of documentation of consent on behalf of subjects who are unable to electronically sign the informed consent document due to technical issues. Additional clarity has also been added on how subjects will receive gift card compensation electronically. The REDCap project site has been used to communicate with subjects in the form of visit reminders, providing copies of informed consent, and also as a means to verify with the subject how they wish to receive their gift card (mail/electronically). For subjects wishing to have compensation sent electronically, a notification is sent via REDCAP to the subject with the gift card's claim numbers. A record of the notification is also saved in the website file repository as a record of distribution.

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A MULTISITE CLUSTER RCT OF THE DEMENTIA SYMPTOM MANAGEMENT AT HOME PROGRAM

A phase 3 single randomized, multi-site evidence-based practice quality improvement program controlled trial targeting persons with dementia-caregiver dyads. **Principal Investigator (Lead Site):**	*Abraham Aizer Brody, PhD, RN, GNP-BC, FPCN* *NYU Rory Meyers College of Nursing* *433 First Avenue, Room 504* *New York, NY 10010* *212-992-7341* *Ab.Brody@nyu.edu*
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NYULMC Study Number:	*s17-00810*
Funding Sponsor:	*National Institutes of Health/National Institute on Aging* *PO: Kristina A McLinden, PhD* *7201 Wisconsin Avenue, Suite 3E500* *Bethesda, MD 20892-9205* *301-827-2563*
ClinicalTrials.gov Number	NCT03255967

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Amended:07-12-21

Statement of Compliance

This study will be conducted in accordance with the Code of Federal Regulations on the Protection of Human Subjects (45 CFR Part 46), 21 CFR Parts 50, 56, 312, and 812 as applicable, any other applicable US government research regulations, and institutional research policies and procedures. The International Conference on Harmonisation ("ICH") Guideline for Good Clinical Practice ("GCP") (sometimes referred to as "ICH-GCP" or "E6") as well as the National Clinical Effectiveness Committee Standards for Clinical Practice will be applied only to the extent that it is compatible with FDA and DHHS regulations. The Principal Investigator will assure that no deviation from, or changes to the protocol will take place without prior agreement from the sponsor and documented approval from the Institutional Review Board (IRB), except where necessary to eliminate an immediate hazard(s) to the trial participants. All personnel involved in the conduct of this study have completed Human Subjects Protection Training.

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List of Abbreviations

ADRD	Alzheimer's Disease and Related Disorders
AE	Adverse Event/Adverse Experience
BPSD	Behavioral and Psychological Symptoms of Dementia
CFR	Code of Federal Regulations
CG	Caregiver
CRF	Case Report Form
DHHS	Department of Health and Human Services
DSM-H	Dementia Symptom Management at Home Program
DSMB	Data and Safety Monitoring Board
FFR	Federal Financial Report
FWA	Federalwide Assurance
GCP	Good Clinical Practice
HHC	Home Healthcare
HIPAA	Health Insurance Portability and Accountability Act
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
IRB	Institutional Review Board
MOP	Manual of Procedures
N	Number (typically refers to participants)
NIA	National Institute on Aging
NIH	National Institutes of Health
OHRP	Office for Human Research Protections
NPI-Q	Neuropsychiatric Inventory Questionnaire
OHSR	Office of Human Subjects Research
PI	Principal Investigator
PWD	Persons With Dementia
QA	Quality Assurance
QC	Quality Control
QDRS	Quick Dementia Rating Scale
QOL	Quality of Life
SAE	Serious Adverse Event/Serious Adverse Experience
SCP	Standard Clinical Practice
SOP	Standard Operating Procedure
US	United States

Protocol Summary

Title	***A Multisite cluster RCT of the dementia symptom management at home program***
Brief Summary	Alzheimer's Disease and Related Disorders (dementia) poses a significant challenge to our public health. While many persons with dementia are cared for by friends and family in the community with the assistance of home healthcare, most home healthcare clinicians and agencies are ill prepared to care for this population and therefore have difficulty assisting patients and caregivers in maintaining quality of life leading to adverse patient outcomes, increased caregiver stress and burnout, and healthcare utilization. This study will therefore utilize a cluster randomized controlled design at 3 study sites to examine the ability of a multi-component evidence-based practice primary palliative care quality improvement program for home healthcare registered nurses, occupational therapists and physical therapists to improve the quality of life and reduce healthcare utilization for persons with dementia and their informal caregiver.
Phase	*3*
Objectives	1) Measure the effects of the DSM-H on quality of life (primary) and pain and BPSD severity (secondary) in the PWD. 2) Assess the effects of the DSM-H on quality of life (primary), and physical and mental health (secondary) in the informal caregiver of the PWD. 3) Assess the effects of the DSM-H on healthcare utilization in the PWD. Primary outcomes are ER visits and hospital admission rates. Secondary outcomes are outpatient visits and primary care provider contacts.
Methodology	*Multi-site cluster randomized controlled trial of a quality improvement program*
Endpoint	*Primary Endpoints: PWD and caregiver QOL. Number of PWD ER visits and inpatient admissions* *Secondary Endpoints: PWD Pain and severity of individual BPSD, antipsychotic and analgesic use. PWD outpatient visits and primary care provider contacts. Caregiver burden, depression, functional health and well-being.*
Study Duration	*3.75 years*
Participant Duration	*60 days*

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Population	***Dyad Population*** *Total Sample: 345 Dyads (345 PWD + 345 caregivers)* *Sample at NYU Site (VNAHG): 207* *Sample at University of Utah Site (CNS; Central Utah): 86* *Sample at University of Miami Site (FirstStat; Southern Florida): 52* *Sample Description: PWD and their informal caregiver dyads. PWD must be 65 or older and informal caregiver 18 or over; English or Spanish speaking; Informal caregiver is defined as spending at least 8 hours per week and had an established prior relationship (family, friend, neighbor).*
Study Sites	*NYU (lead): 0 clusters* *VNAHG: 12 clusters* *University of Utah: 5 clusters* *University of Miami: 3 clusters*
Number of participants	*Dyads: 345 across all sites (see population)*
Description of Study Procedure	*The DSM-H is a multi-component quality improvement program that consists of clinician training, patient- and family-centered assessment instruments, patient-caregiver dyadic centered care plans, a BPSD assessment and treatment algorithm, and caregiver teaching sheets. This study will examine outcomes of this quality improvement program.*
Reference Therapy	*Usual Care*
Key Procedures	*None*
Statistical Analysis	*Time trend analysis using repeated measure multivariate mixed effects linear models (PROC MCM in SAS) for all non-utilization outcomes. Utilization outcomes will be analyzed through logistic regression for odds of hospitalization or ER visit and Poisson Count regression for total number of hospitalizations and ER visits. Both will use random effects to measure for clustering.*

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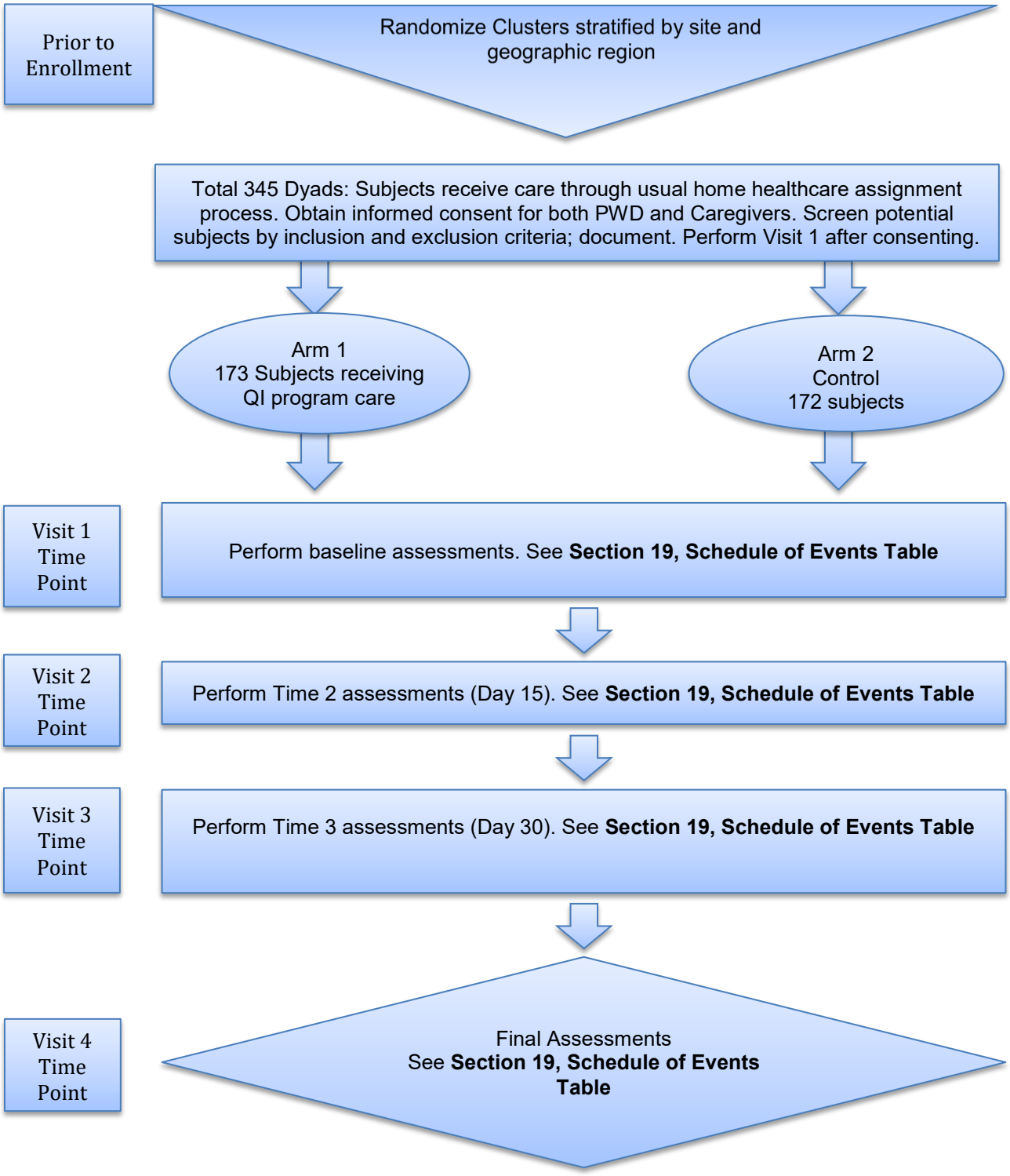
Schematic of Study Design



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2 Introduction, Background Information and Scientific Rationale

2.1 Background Information and Relevant Literature

The population of people older than 65 in the United States is expected to almost double by 2030[1]. As age is a significant risk factor, this will lead to a significant increase in patients with various causes of dementia including Alzheimer's disease and related disorders (ADRD; including Lewy body dementia, frontotemporal degeneration, and vascular contribution to cognitive impairment and dementia)[2]. The Institute of Medicine 2008 report sounded the alarm regarding the lack of properly trained clinicians in geriatrics in general[3] yet 8 years later the healthcare system is no closer to building a workforce to provide high quality care for PWD as highlighted in the National Plan to Address Alzheimer's[4]. The increase in the population of older adults is expected to overwhelm the healthcare system; the supply of hospital and long term care beds is not expected to be able to keep pace with the demand[5]. Thus, these complex patients, many with ADRD, will be forced to return to the community in sicker condition than currently seen, after shorter lengths of stay in the hospital, placing a great strain on HHC agencies as they will be expected to take on care for many of these patients. While an estimated 36% of HHC patients currently have ADRD[6], many HHC providers lack even basic training in their care due to a dearth of validated programs and the disseminated nature of the workforce makes developing these programs more complex. Clinicians also have a negative view, and do not recognize that substantial evidence exists showing differences in their care needs.[7-15, 16-19]

2.1.1 **Pain in ADRD**

Though no estimates have been recorded of the incidence of pain in the community dwelling PWD, the estimated incidence rate in older adults of over 50%[20] due to high prevalence of painful conditions. However, pain is often not treated or undertreated[21-23] and HHC clinicians have been found to be ill prepared

to provide adequate pain management to both cognitively intact and impaired patients[24,25]. Furthermore, PWD are less likely to report pain and receive less pain medication[26]. Elderly patients are also significantly less likely to discuss or label pain sensation, and more likely to be stoic in the face of pain, regardless of cognitive ability[23]. While guidelines for the treatment of pain in PWD exist[27], they are often inappropriately treated, even when identified as having pain[21]. Poor recognition and management of pain is associated with delirium, agitation, falls, decreased function, and increased hospitalization and mortality [28-31].

2.1.2 Behavioral and Psychosocial Symptoms in ADRD

BPSDs are one of the most common and distressing symptoms in the PWD, occurring in over 40% of cases[32]. BPSDs include agitation, depression, delusions, hallucinations, mania, personality changes and aggression. BPSDs are associated with weight loss[33], functional disability[34], caregiver burden and burnout[35], nursing home admission[36], and progression of dementia[37]. While multiple interventions are available for the treatment of BPSD[38,39], they are often not appropriately used and certain common pharmacologic interventions in particular can cause harmful side effects. Few studies have examined the assessment and treatment of BPSD in the HHC setting. However, multiple studies have examined the effect of BPSD in ADRD in the home, particularly as it relates to caregivers, finding that interventions can decrease BPSD and improve function, QOL, and caregiver well-being[40]. Other studies have found BPSD plays a significant role in caregiver burden and burnout[41,42], significantly increase the cost of care[43] and familial economic burden[44].

2.1.3 Interrelation of Pain and BPSDs in ADRD

The interrelation of pain and BPSDs in ADRD can have large effects on illness burden and QOL, and many patients do not present with just a single symptom. Thus it is important to study their interrelatedness.[45,46] This is certainly true of pain, depression (one of the major BPSD) and agitation (another BPSD), where research has found they interact with each other, creating an additive effect when measuring their presence and/or severity.[47-49] For instance, the presence of chronic pain in the elderly is known to induce or worsen symptoms of depression and agitation; and depression co-existing with pain is known to worsen the intensity of pain and complicate treatment[50-52]. When all three of these are present, patient function is substantially decreased[53,54].

2.1.4 Caregiving

Informal caregivers, including family, friends, neighbors and other acquaintances provide 83% of the care to PWD living in the community[55], representing 15.9 million people providing 18.1 billion hours of care[56]. Despite this striking preponderance, a recent report from the National Academies of Sciences Engineering and Medicine (previously the IOM) finds that caregivers are largely marginalized and ignored as part of the healthcare system, and not provided the training or assistance they need in order to successfully care for their charge[57]. The primary tasks informal caregivers provide PWD assistance with include activities of daily living (ADLs) and instrumental ADLs, medication management and administration, adherence to treatment regimens, interfacing with the medical team, managing BPSDs, finding support services, and managing and hiring paid caregivers[56]. These tasks are known to cause informal caregivers stress, burden and burnout, and worsen their physical and mental health, including 2-3 times greater risk of developing depressive symptoms (40%). Furthermore, the biologic variable of sex plays an important role in informal caregiving, as caregiving is performed significantly more by female individuals (68%)[58] and they spend between 1/3 and double the time providing care than male caregivers[56]. Additionally, caregivers who are older, female, spouses, or live in the same household with the PWD experience higher rates of caregiver burden[58].

2.1.5 Health Disparities in Care of the PWD

There are significant disparities in care of the PWD. First and foremost, minorities have significantly higher prevalence of ADRD[59]. One of the most cited study found that a 2-3 fold higher risk in African-Americans and Hispanics compared to non-Hispanic whites (9.1%, 7.5%, 2.9% respectively in the 65-74 age cohort with even higher disparities as age increases)[60]. In addition to the higher prevalence rates, research has found that African-American and Hispanic caregivers frequently believe cognitive impairment is a normal part of aging[61] and present for initial diagnosis with higher rates of symptoms[62]. Overall, Hispanics have been found to have higher rates of BPSDs than other groups[63]. However, both African-Americans and Hispanics have lower rates of institutionalization[64,65]. Therefore caregivers in these populations require more community-based support and training to counteract the longer duration of care.

2.1.6 **Interprofessional Education**

Brody (PI) and Galvin (Site-PI) performed a systematic review of the literature in interprofessional education in ADRD[66]. They found 17 publications of 15 studies, 8 of which examined provider knowledge and attitudes and 7 showed improvement after an educational intervention.[67-72] Three also showed some level of sustainability. Separately, 8 studies examined patient outcomes, 7 of which showed positive patient outcomes, including improved caregiver satisfaction, recognition of depression, and reductions in patient decline, BPSD, and inappropriate use of antipsychotics[67,73-78]. *While these studies found positive outcomes and improved knowledge and attitudes of clinicians, they did not all use standardized instruments, the interventions were highly variable, and none of them were performed in HHC.*

2.1.7 **Existing Relevant Interventions**

While no interventions have focused on an interprofessional intervention to improve QOL of the PWD-informal caregiver dyad utilizing HHC, several interventions have been implemented in the home, outside of the HHC service delivery structure. The most established and utilized intervention, developed by Dr. Gitlin, is the Care of Persons with Dementia in their Environment (COPE) Program. This intervention focuses on enhancing the PWD's functional capacity and improving caregiver skills in managing ADRD. It includes 10 visits by an occupational therapist along with 1 telephone contact by an advanced practice nurse[40]. The intervention is highly effective and has been implemented in the Connecticut Medicaid program[79]. The weakness of this approach is that in-person contact is solely with an occupational therapist, and only 14% of HHC visits are provided by occupational therapists[80], reducing the ability to implement more broadly in the existing HHC service delivery model. Another program the MIND at Home program developed by Samus provides care coordination services linked to an RN and geriatric psychiatrist, and ADRD education and caregiving strategies. It is currently being studied in an NIA funded R01 and CMMI demonstration project. This interprofessional program has shown considerable strength in its pilot in reducing transition from home and improving QOL[81]. However, it did not show caregiver reported improvements in BPSD and is also not delivered through HHC. One intervention specifically tailored to HHC by Bruce, the CAREPATH program, assists HHC nurses to manage depression in older adults. CAREPATH provides 7 hours of training (4 in-person, 3 via web) to nurses, finding significant improvement in depressive symptoms in persons with higher symptom expression at baseline[82]. The primary limitations of this program as it relates to this work is that it is solely geared towards depression, it focuses 7 hours solely on depression, which may be more than many HHC agencies are willing to provide to a single condition, and that it did not integrate with other disciplines. Final, several successful interventions by Bakitis have been developed to perform palliative care for individuals with cancer and heart failure (ENABLE and ENABLE-CHF)[83-88]. These multi-component nurse-led psycho-educational interventions seek to support the patient and their caregiver and ENABLE has shown positive outcomes on QOL, mood, and survival though not utilization, and caregiver stress and burden, while ENABLE-CHF is currently being examined through a clinical trial. However, ENABLE and ENABLE-CHF are not performed through HHC, either utilizing tele-health, which may not be adequate for PWD given the difficulty with phone assessment in this population, or a clinic model which may be difficult to access for homebound PWD. Lessons learned from these interventions have been used in developing the DSM-H intervention.

2.2 Name and Description of the Quality Improvement Program

The DSM-H, is an evidence-based practice quality improvement program that combines training, mentorship, workflow enhancements, assessment instruments, a BPSD treatment algorithm, and caregiver teaching pamphlets for clinical staff in HHC agencies.

2.2.1 **Preclinical Data**

2.2.1.1 Under-recognition of symptoms in HC

Because symptoms such as pain and depression are significant causes of agitation in PWD, Dr. Brody undertook a study[89] that examined the recognition of symptoms in advanced illnesses in HHC. Using a 5% sample of nationwide OASIS (home health minimum data set collected on every patient) and Medicare data, he examined the rates of symptom prevalence in persons with advanced illnesses including advanced dementia post-discharge from an acute care stay. He found pain and depression in PWD were significantly under-recognized in HHC (See table 1). Using multivariate ordinal logistic regression controlling for age, race, sex, Charlson Score, and rural/urban location, he found that persons with advanced dementia were 2.5 times less likely to have had pain reported on the OASIS than the other advanced illnesses he examined. One highly methodical and well cited nationwide study found that late life pain incidence rate is 46% the month prior to death; the majority of this pain coming from arthritis; with no difference by terminal diagnosis category[90].

Table 1: Pain and Depression by Advanced Illness

	Pain At Least Daily	Depressive Symptoms
Cancer	61.8%	22.0%
CHF	51.9%	18.0%
CHF and COPD	49.7%	24.3%
COPD	53.0%	20.8%
Advanced Dementia	25.4%	10.9%

Thus the investigators would not expect significantly different rates across these disease categories, and the rates of pain in advanced dementia are likely significantly under-recognized. Similarly, using multivariate logistic regression with the same control variables, persons with advanced dementia were 1.7 times less likely to have depressive symptoms reported than persons with advanced illness, despite other studies that have found persons with dementia have similar if not higher rates of depression[91,92]. *These data support the under-recognition of pain and depression in older adults with dementia in the HHC setting.*

2.3 Clinical Data to Date

2.3.1 **Development and Implementation of the DSM-H.**

As part of Dr. Brody's National Palliative Care Research Center Career Development Award, Dr. Brody and Dr. Galvin (Mentor) developed the DSM-H. The development utilized the NIH ORBIT Model for Behavioral Intervention Development[93] and later on the Structural Model for Caregiving Stress[94]. The DSM-H focuses on assisting skilled HHC clinicians to identify and managing behavioral symptoms associated with dementia, and work as a team with the primary care provider and informal caregiver. In this initial trial, two registered nurse, physical therapist, and occupational therapist educators (6 total educators) at the study site were trained as "champions" and received 14 hours of in-person, case based interprofessional instruction over two days in dementia care; the remaining 209 RNs, PTs, and OTs received 4.5 hours of modular, on-line interactive learning training. Champions served as resources for other clinicians and helped ensure smooth implementation and completion of the program. In addition to the education, participants were provided with resources and workflow changes including previously validated assessment tools for assessing and managing symptoms in PWD, and care plans based on evidence based practice for PWD. As a measure of program evaluation, Drs. Brody and Galvin developed the Dementia Symptoms Knowledge and Attitudes Survey to be utilized as a pre- and post-test. The survey incorporates three well-validated instruments for assessing clinician knowledge and attitudes regarding pain[95], depression[96] and agitation[97] in PWD, with an investigator-derived set of four questions about confidence in treating each of these symptoms in PWD. The survey had an excellent internal consistency in HHC clinicians (Cronbach

alpha=.94) and took an average of 15 minutes to complete. In our sample of 209 clinicians, we found significant improvements in knowledge, attitudes and care confidence in treating PWD following program completion that varied by specialty. Overall, clinicians showed the most improvement in knowledge (20.9%) and confidence (27.1%) in managing BPSD from baseline with additional gains in knowledge (14.8%) and confidence (36.1%) in managing depression and knowledge (5.9%) and confidence (26.5%) in managing pain (p<.0001)[25]. Additionally, on the post-test evaluation, 97% of RNs and 100% of PTs and OTs stated the education was highly applicable to their work setting and helped them care for patients. ***Therefore, the DSM-H is an evidence-based practice integrated multi-component intervention that has shown improved clinician knowledge, attitudes and confidence in treating PWD.***

2.3.2 Pilot testing

Based on feedback from this initial trial of the DSM-H, Dr. Brody refined the clinical education programs to reduce pharmacology content and increase content on recognition of dementia and non-pharmacologic management and working with caregivers. Drs. Brody and Galvin performed a site controlled trial of the DSM-H at 2 divisions of a large HHC agency and retrospectively collected OASIS and chart data for PWD on admission and at the first 60-day re-certification or discharge from HHC. Overall, during the study period 158 PWD were seen by the control site and 174 by the intervention site. Overall, patients were older, primarily spoke English or Spanish, were either Medicare or dual Medicare/Medicaid insured, and were admitted either from home or the acute care setting (See Appendix A). There were fewer black/African American participants in the control, the only clinically significant difference (34.2% vs 51.7%; p=.0002). Overall, we found in multivariate analysis that recognition of pain, depression, and behavioral symptoms, were all clinically and statistically significantly higher in the intervention group, and there were significantly increased odds of analgesics use (OR=2.01; p<.05) and decreased odds of antipsychotic use (OR-0.53; p<.05) in the intervention cohort[98]. ***These results show the DSM-H has the potential to be improve patient care and the QOL of PWD receiving HHC.***

2.4 Rationale

While significant focus has been placed on implementing solutions for use in the acute care, nursing home, and primary care settings, few studies have focused on improving symptom management and caregiving training for PWD through HHC. Drs. Brody and Galvin have adapted interprofessional, evidence-based practices, from other settings to HHC, creating the DSM-H. The DSM-H has been piloted with over 600 HHC clinicians[25,98]. It is a multi-component performance improvement program that consists of clinician training, patient- and family-centered assessment instruments, patient-caregiver dyadic centered care plans, a BPSD assessment and treatment algorithm, and caregiver teaching sheets. The pilot studies have shown improved clinician knowledge, confidence and attitudes, and pain and BPSD recognition and management. We therefore seek to test the efficacy of the DSM-H in a behavioral phase III cluster randomized controlled trial.

2.5 Potential Risks & Benefits

2.5.1 Known Potential Risks

The performance improvement program itself is inherently not risky (**minimal risk**) as it is an implementation of evidence-based practices. The primary risk to patients and caregivers in this study is the emotional nature of the questions from study data collection, which is solely an immediate risk. While the measures being used are all evidence based and thoroughly tested, they cover issues such as increased severity of dementia, depression, agitation, burden and quality of life that could create emotional problems. This will be minimized by implementing a thorough training plan and manual for the research assistant performing the assessments, laying out responses that should be provided to sensitive questions, ensuring that the assessment instruments are uniformly administered, and methods and contact numbers for referrals in case of any emotional disturbance related to the research. We are

currently performing a study using these instruments and have a set training for research assistants administering these instruments. Additionally, other peer reviewed studies have not reported any adverse reactions to these instruments, so we see this risk as minimal. Additionally, we will perform an informed consent with both the caregiver and PWD if able, or patient surrogate if unable, so that they have full awareness of the purpose of the project, potential types of questions, and the voluntary nature of the study. The second risk is loss of confidentiality. We minimize the risk by maintaining the data in a secured fashion (see section 11). This vulnerable population is included as the focus of the research is in improving the quality of care they receive.

As the potential risks are minimal and there are potential direct benefits to subjects in the performance improvement cohort, including improved PWD and caregiver QOL and symptom management, and reduced utilization, the potential benefits of this study far outweigh the minimal risks to this study. The value in this study is that if efficacy is found, the intervention can be created into a product that is disseminated to some of the over 12,000 active HHC agencies in the country to improve the quality of care in these settings and QOL for hundreds of thousands of PWD-informal caregiver dyads.

2.5.2 Known Potential Benefits

Potential benefits to patients in the intervention includes improved quality of care and quality of life, including reduction in pain and BPSD, and reduced healthcare utilization, which could lead to lower out of pocket costs. For caregivers receiving care from care teams who are part of the performance improvement program, potential benefits include reduced depression, burden, and improved physical and mental health. These hypothesized benefits are based on our preliminary data found in section 2.3.2.

3 Objectives and Purpose

3.1 Primary Objectives

Aim 1: Measure the effects of the DSM-H on quality of life and symptom severity in the PWD.
H1: PWD cared for by a HHC team utilizing the DSM-H performance improvement program will show reduced symptoms and improved ratings of pain, BPSD, and caregiver-rated QOL at the end of the first 60-day HHC certification period compared to the control (usual care) group.

The primary outcome of Aim 1 is caregiver rated QOL. It will be measured using the Quality of Life-Alzheimer's Disease[99].

Aim 2: Assess the effects of the DSM-H on quality of life, and physical and mental health in the informal caregiver of the PWD.
H2: Informal caregivers of PWD cared for by a HHC team utilizing the DSM-H performance improvement program will show reduced ratings of burden, and depression, and improved functional health and well-being at the end of the first 60-day HHC certification period compared to the control (usual care) group.

The primary outcome of Aim 2 is informal caregiver QOL. It will be measured using the Caregiver-Targeted Quality of Life Measure[100].

Aim 3: Assess the effects of the DSM-H on healthcare utilization in the PWD.
H3: PWD cared for by a HHC team utilizing the DSM-H performance improvement program will show a reduction in emergency room visits and hospital admissions compared to the control (usual care) group, and a greater number of outpatient visits.

The primary outcomes to be measured are the number of emergency room visits and hospital admission rates of the PWD at 30 and 60 days. It will be measured through interviews with the informal caregiver using the Resource Utilization Inventory[101].

3.2 Secondary Objectives

The secondary objectives of Aim 1 are to assess the effects of the performance improvement program on pain and individual BPSDs in the PWD, and the use of antipsychotic and analgesic. They will be measured at all four time points (0, 15, 30, and 60 days). BPSD will be measured using the NPI-Q[102]. The type of pain assessment administered to the PWD will depend on their level of cognitive impairment. The level of impairment will be determined by the Quick Dementia Rating System (QDRS) score. The PWD who obtains a score of $\leq$12 will receive the Brief Pain Inventory Short Form[103] and those whose score $\geqq$12 on the QDRS will receive the PAINAD which will be used to measure pain at rest and with movement. All PWD subjects will be assessed for pain during each visit using the respective measure.

The secondary objectives of Aim 2 are to assess the effects of the performance improvement program on informal caregiver burden, depression, and functional health and well-being. The PHQ-9[104] will be used to measure caregiver depression, the Zarit Burden Interview [105] for caregiver burden and the SF-12 for caregiver health at 0 and 60 days.

The secondary objectives of Aim 3 are to assess the effects of the performance improvement program on the number of outpatient visits and contacts with the primary care provider. These will be measured through interviews at 30 and 60 days with the Resource Utilization Inventory[101].

4 Study Design and Endpoints

4.1 Description of Study Design

This study will use a blinded cluster randomized controlled trial methodology. Each HHC care team will be randomized to either partake in the DSM-H performance improvement program or provide usual care. The project director based at NYU and RAs at all sites will be blinded to prevent bias in data collection. The study statistician based at NYU will perform the randomization utilizing SAS 9.4 stratified by agency and geographic location. The study PI will relay to the agencies which teams will serve as intervention or control. The study PI and statistician will not collect study data in order to maintain the integrity of the blinding. The potential for contamination between care teams randomized to receive the DSM-H performance improvement program and those who will provide usual care is minimal due to the nature of HHC clinician workflow where minimal time is spent in the office, and different care teams do not generally congregate with each other except during highly structured staff meetings. The investigators considered randomizing by site and using other HHC agencies; however, given the lack of contamination found in prior studies of the DSM-H combined with differences in care provision at other sites/locations and the need for a large number of clusters when using this methodology, the investigators felt this method was the most likely to provide valid and reliable results. It is not possible to randomize by patient in HHC because patients are seen by care teams in a given geographic region. Patients in the performance improvement group will receive care from a care team who has received the DSM-H performance improvement program, and those in the control will receive usual care from a care team who has not received the performance improvement program. Patients at the study sites are only cared for by members of the same care team and therefore there is no potential for patients to receive a mixture of care teams.

4.2 Study Endpoints

4.2.1 Primary Study Endpoints

Given that this is a dyadic, implementation science intervention, it is not appropriate to look at a single primary endpoint. There are therefore 3 primary endpoints that will be examined in this study. For the Aim 1 primary endpoint, PWD QOL, a 0.5 SD difference between the baseline and 60 day visit would be clinically meaningful based on prior studies[40] and therefore considered a positive outcome. For the Aim 2 primary

endpoint, informal caregiver QOL, given its rate of variability and floor and ceiling effects, a 0.5 SD difference between the baseline and 60 day visit would be clinically meaningful and therefore considered a positive outcome[100]. For the Aim 3 primary endpoint, a 10% reduction in readmissions and ER visits at 60 days will be considered a clinically meaningful positive outcome. This would results in 220 fewer ER visits and 63.8 fewer admissions per 1000 patients based on prior evidence[106].

4.2.2 Secondary Study Endpoints

Aim 1 secondary endpoints include individual BPSDs, pain, antipsychotic use and analgesic use. These endpoints were chosen secondary to their relationship to QOL and caregiver QOL as noted above in sections 2.1.1 and 2.1.2 as well as their interrelationship as noted in section 2.1.3.

Aim 2 secondary endpoints include informal caregiver burden, depression, and health, which as noted in section 2.1.4.

Aim 3 secondary endpoints include outpatient visits and primary care provider contacts. These endpoints are included as BPSDs and pain are both indicators of additional concerns amongst caregivers and can increase burden due to the coordination that is required of caregivers[107].

4.2.3 Exploratory Endpoints

In this study we will explore both sub-group analysis by gender, race/ethnicity, health literacy, and high and low symptom individuals.

5 Study Enrollment and Withdrawal for PWD-Caregiver Dyads

5.1 Inclusion Criteria

1. PWD over the age of 65
2. Admitted to one of the three HHC agencies
3. The patient and family caregiver speak English and/or Spanish.
4. The informal caregiver is ≥18 years of age and manages the PWD's care for at least 8 hours per week.
5. Patients who score ≥6 on the Quick Dementia Rating Scale (at least mild impairment).
6. PWD and the caregiver have internet connection.

5.2 Exclusion Criteria

An individual who meets any of the following criteria will be excluded from participation in this study.

1. Patients with a separate Axis 1 diagnosis other than forms of dementia, depression or anxiety.
2. PWD residing in assisted living facilities or board and care homes
3. PWD solely receiving infusion or home health aide services.

5.3 Vulnerable Subjects

This research will be performed exclusively with cognitively impaired subjects and their informal caregivers. The research is specifically focused on whether the intervention improves the quality of care and quality of life for persons with dementia and their caregivers. It is therefore necessary to work with this vulnerable population. All patients in this study will be cognitively impaired, and some may lack the capacity to consent. These patients will all be included in this study. Capacity will be assessed at baseline as described in section 5.4 below. They will not be monitored over the study period as dementia is a chronic, progressive disease there is no reasonable expectation that the PWD would have a capacity status change in such a short period of time (60 days). Should the person with dementia subject become distressed from participating in the study, they will be withdrawn from the study.

5.4 Strategies for Recruitment and Retention

A centralized referral system will be customized to each of the three HHC agency's organizational structure and workflow. Each agency will determine which staff will be designated as the point of contact (POC) to submit patient referrals to the DSM-H research team. The method of referral will differ among agencies based on each organizational workflow. Each HHC agency accepts new referrals for patient admission through an intake process prior to the patient meeting with a nurse to initiate start of care (SOC). The nurse who completes the patient's admission visit, administers an OASIS assessment and OASIS cognitive screen or administers a mini-cog test[108] for the patient's SOC report. The HHC agency's POC will review patient information obtained through intake and the SOC report. New admissions who are aged 65 years and older with a diagnosis of dementia or cognitive impairment, and who reside in a private residence will be referred to the DSM-H research study. Referral submissions will be received via REDCap, encrypted transfer, or secure email based on agency and NYU guidelines. If sent by encrypted transfer or secure email, the research coordinator or project director will upload the referral information directly into redcap, the study log.

Each agency has determined how their centralized referral system will be facilitated as noted below:

New Jersey site (VNAHG) there will be a single point of contact in their research/innovation group who will run twice-daily reports of persons with dementia newly admitted to the agency who live in a private residence. Reports are based on the nurse's SOC report submitted at the end of the day.

Utah site (CNS) there will be a single point of contact within the agency who will generate a daily report of persons with dementia newly admitted to the agency who live in a private residence. The report will be based on the nurse's SOC report and made available to designated study staff or care team office referral specialist for referral submission.

Florida site (FIRSTAT) there will be a single point of contact within the agency who will generate a daily report of persons with dementia newly admitted to the agency who live in a private residence. The report will be based on the nurse's SOC report and made available to designated study staff or care team office referral specialist for referral submission.

Persons with dementia who are newly admitted into each HHC agency will be included in an "opt-out" referral process. Admission packets, provided to those who have been identified as meeting DSM-H inclusion criteria, will include a DSM-H research study information card. The DSM-H info-card provides an overview of the research study, the duration of participation, contact information for the research coordinators, as well as, ways in which the patient and caregiver can opt out from being contacted.

In follow up to the patient referrals received by each agency, the research team will contact the patient and/or caregiver to introduce them to the research study and to screen the referral for subject eligibility. To determine if the PWD's level of cognitive impairment meets eligibility for inclusion, the QDRS is administered to the caregiver who will rate the PWD's symptoms and behaviors. A PWD who scores $\geq$6 on the QDRS will meet eligibility for study inclusion as this score indicates mild impairment, similar to a score of <23 on the MMSE. The research team will also inquire about whether the caregiver makes decisions on behalf of the PWD, or if there is a legally authorized representative who acts on the PWD's behalf. If the PWD has a LAR, then that representative's contact information will be obtained and the LAR will be included in the consent process. A virtual visit is scheduled for both the PWD and caregiver within 3 business days of the PWD's admission date so that additional information about the study can be provided and informed consent can be conducted. Weekend days and U.S. recognized business holidays are not counted as a business day. The PWD must have the capacity to consent in order to sign their consent form.

Capacity to consent will be determined using a standardized 3-question approach[109] performed by the research assistant or project director. These individuals will receive training from the PI and Site PI in the form of two simulations prior to being allowed to consent using this procedure. In these simulations, one will have capacity and the other will not. They must correctly assess both simulations prior to being allowed

to perform the consent process. This standardized approach has been shown to be valid for use by research assistants with PWD. The three questions that will be asked after reviewing the study consent form are: 1) What is the purpose of the study, 2) What are the risks, and 3) What are the benefits. If the initial response is vague or suggests misunderstanding, the interviewer re-explains or clarifies the question without redisclosing information about the study. The interviewer scores the answer to each question as as either 0 (incapable) 1 (questionable) or 2 (capable). Definitions of these are as follows: *"2-point score reflects clear understanding of the disclosed material, a 0-point score reflects definite misunderstanding of the disclosed material, and a 1-point score reflects either partial but less than fully adequate understanding or, if this persists even after prompting for clarification, an uncertain level of participant understanding."* The score is then totaled and a score of less than 3 is considered to not have capacity. This method has a high level of sensitivity and specificity and is more accurate than using other methods including the mini-mental status exam (MMSE).

This standardized process is accurate and objective. There is limited conflict of interest in having the study personnel perform this assessment as opposed to an independent assessor as the study could still recruit dyads through surrogate consent should a subject not have capacity, and the patient flow at the participating HHC agencies far exceeds the needs of this study thus limiting pressure to enroll on the part of the study staff.

In instances where a PWD does not have the capacity to consent, their enrollment will be contingent upon consent being provided by either their LAR or a legal surrogate as determined by their state of residence. Further, once consent on the behalf of the PWD has been acquired, the PWD will be asked to assent verbally and if able, by signature. If the PWD provides verbal assent but is unable to provide their signature due to disability (cognitive/physical), the researcher will note on the assent form that the PWD provided verbal assent but was unable to sign.

The legal surrogate will be verified by either the HHC agency or through written documentation. Should they not have written documentation of being an appointed surrogate, the law of the state of residence will determine the priority order for determining the surrogate, which is as follows:

Florida: spouse, adult child, parent, adult sibling, close friend
New Jersey: spouse, adult child, parent, sibling, close friend
Utah: spouse, adult child, parent, sibling, grandchild, grandparent, individual who is healthcare proxy

Because PWD in HHC are primarily homebound, tend to receive HHC for at least 60 days, with follow-up is provided through scheduled home visits, we do not anticipate significant retention problems. Additionally, the study burden is minimal, requiring approximately an hour per dyad at baseline and 60-days, and 20 minutes at the 15 and 30 days. Study staff will obtain detailed contact information for the PWD, caregiver, and where applicable proxy, will schedule the follow-up visits at the initial visit, email or text the visit schedule to the caregiver (based on caregiver preference; no PHI or PII included, see templates), and call 4 days and 1 day prior to each follow-up appointment to confirm and/or reschedule.

The greatest risks to retention are re-hospitalization and institutionalization, either for short-term post-acute rehabilitation after a re-hospitalization or long-term institutionalization for ADRD. Subjects are not required to attend the intermediate and final visits together. Efforts to accommodate the subjects' schedules will be considered in data collection. Phone interviews with the PWD and caregiver to collect participant survey data will occur for all time points. If both subjects are unavailable to complete an intermediate visit, the visit will be recorded as missed. To maintain subject retention, subjects will be terminated from the study only if the caregiver, as respondent, does not complete visit four.

Dyads will be enrolled starting in month 6 of year 1 and continuing through month 9 of year 4 (3 years, 3 months). Follow-up will continue through Month 2 of year 5. The investigators therefore anticipate recruiting 9 new dyads per month at all sites throughout the 4 years, with 5-6 through the VNA Health Group, 2-3 at the University of Utah and 1-2 at University of Miami.

Given that this research study is of short duration (60 days) there is no reasonable expectation that there to be a change in capacity during the time period of the study and will therefore not monitor for capacity beyond the initial visit.

5.5 Duration of Study Participation

This study will last at most 65 days from recruitment to completion. The total duration is intended to be 60 days, however, for the interim study visits (visits 2 and 3) we will allow the visit +/- 3 days to allow for PWD-caregiver schedule, and at visit 4, up to +5 days leeway.

5.6 Total Number of Participants and Sites

Recruitment will end when approximately 345 dyads (345 PWD and 345 caregivers) are enrolled. It is expected that approximately 345 dyads will be enrolled in order to produce 300 evaluable dyads.

Sample at VNAHG Site: 207 dyads (207 PWD, 207 caregivers) enrolled, with expectation of 180 complete dyad cases (180 PWD, 180 caregivers).
Sample at University of Utah Site: 86 dyads enrolled (86 PWD, 86 caregivers) with expectation of 75 complete dyad cases (75 PWD, 75 caregivers).

Sample at University of Miami Site: 52 dyads enrolled (52 PWD, 52 caregivers) with expectation of 45 complete dyad cases (45 PWD, 45 caregivers).

5.7 Participant Withdrawal or Termination

5.7.1 Reasons for Withdrawal or Termination

The primary potential cause for withdrawal from the study is if either member of the dyad choses to withdraw from the study at any point.

Participants are free to withdraw from participation in the study at any time upon request. An investigator may terminate participation in the study if:

- The participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation
- The study team is unable to maintain or appropriately reschedule study appointments.

5.7.2 Handling of Participant Withdrawals or Termination

Given the minimal risk nature of this study, individuals who chose to withdraw from the study will not continue to be followed in any form. We have factored in a 15% study non-completion rate and anticipate recruiting 345 dyads to meet the 300 dyads required study participants. Subjects will not be disenrolled based on data related issues. If subjects are unable to attend intermediate visits (Visit 2 and/or 3), those visits will be counted as missed. If the caregiver does not complete visit four, both subjects will be terminated from the study.

5.8 Premature Termination or Suspension of Study

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to the principle investigator, the NIA program officer, and the DSMB. If the study is prematurely terminated or suspended, the PI will promptly inform the IRB and will provide the reason(s) for the termination or suspension.
Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants

- Insufficient compliance to protocol requirements
- Data that are not sufficiently complete and/or evaluable
- Determination of futility
- DSMB or NIH halts study for any other reasons not listed above.

Study may resume once concerns about safety, protocol compliance, data quality are addressed and satisfy the NIH, IRB and DSMB.

6 Study Quality Improvement Program

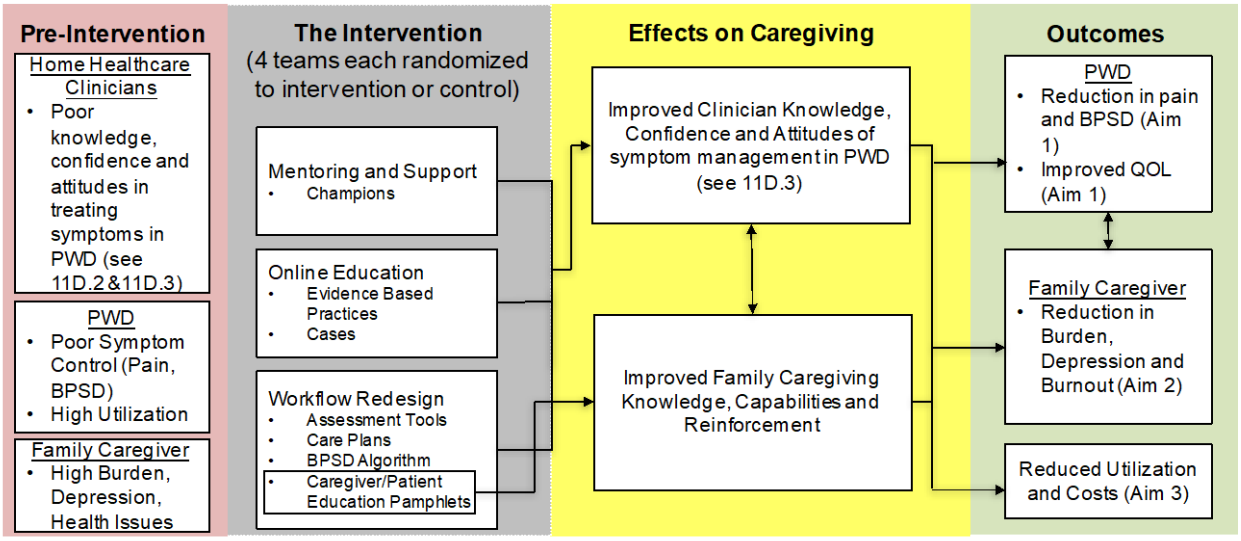
6.1 Study Behavioral or Social Quality Improvement Program

The DSM-H is a quality improvement program that has been tested in several HHC agencies in New York. It is a multi-modal quality improvement program for improving the quality of care provided to PWD-informal caregiver dyads through HHC. All training was initially created through participatory research with an interprofessional team of clinicians, and then refined through feedback from clinicians who completed the training. It has been culturally tailored for use in diverse settings and tested with multiple minority communities in New York, including multiple Hispanic groups and African-Americans and Caribbean blacks. Components of the intervention are described in detail below and in Figure 2 (see below). The DSM-H quality improvement program presented in this section is not in and of itself a study intervention. We are solely in this study measuring the outcomes of the quality improvement program, however include the components of the program here so it is easier to understand the research protocol around the study of outcomes.

6.1.1 **Champions training**

Champions training consists of two full days of interactive in-person didactic content, case studies, and role-playing simulation cases. There are three core components of the champion training, the Leadership Training Program, training on care of the PWD and their caregiver, and communication both within the team and with the PWD-caregiver dyad in a patient-centered fashion. The leadership content is modeled after the Hartford Institute for Geriatric Nursing's highly successful NICHE program leadership training program, which provides implementation training on geriatric principles for acute care hospitals and has been implemented in over 700 hospitals nationwide and internationally[110]. The leadership training portion also includes performance improvement and methods for ensuring implementation in their agency and serve as the change leaders in their agency. ADRD specific content mirrors non-champion training (see below) in more depth, and includes assessing patients for ADRD, assessing and managing pain and BPSD in PWD using the safest, least restrictive, non-pharmacologic and pharmacologic treatments, caring for individuals who are either resistant or unable to complete care due to ADRD, working with caregivers who work with PWD. It also covers additional topics in palliative care of ADRD including goals of care discussions, utilization of advanced directives, and transitioning to hospice. The third component, dyadic person-centered team based care is based on three well validated programs, AHRQ TeamSTEPPS[111] and SBAR[112] for healthcare team communication and the Antecedent-Behavior-Consequence method of problem solving[113] to help clinicians work with caregivers to identify and solve the most problematic behaviors. Champions are designated from each discipline by each agency participating and serve as facilitators, resources/mentors and ensures quality improvement program fidelity in implementation throughout the study.

Figure 2: DSM-H Components and Effects on the PWD and Caregiver



PWD-Person With Dementia; BPSD-Behavioral and Psychological Symptoms of Dementia; QOL-Quality of Life

6.1.2 Non-champion clinician training

Non-champion clinician training (registered nurses, physical therapists, occupational therapists) will undergo five hours of online interactive learning modules which are each one hour in length and will be available over two months. This is done based on our prior experience to ensure completion of the modules without over-burdening staff or requiring them to take a lower patient workload, which could have significant fiscal impact on the agency and thus reduce the likelihood of involvement. The content of the modules largely mimics the larger champion course but in less detail, focusing more on assessment/recognition of conditions. The five 1-hour modules are: **1.** Defining and distinguishing types of ADRD, assessing patients for ADRD; Basic non-pharmacologic and pharmacologic treatments for decline in PWD; Working with PWD to complete care tasks (e.g. registered nurse care, physical or occupational therapy care, instructing caregivers); **2.** Assessing PWD for pain; non-pharmacologic and pharmacologic strategies for treating pain in the PWD; **3.** Understanding, assessing and recognizing BPSD; **4.** Non-pharmacologic and pharmacologic treatments for managing BPSD; **5.** Dyadic person-centered team based care concepts derived from AHRQ TeamSTEPPS, SBAR, and Antecedent-Behavior Consequence method of problem solving.

6.1.3 Validated Instruments

Validated assessment instruments are integrated into the workflow of HHC clinicians who are part of the teams receiving the DSM-H performance improvement program to allow for better assessment of cognition, pain, and BPSD and are validated in both English and Spanish. These tools are reviewed in the education of both champions and non-champions. Instruments included are the mini-cog[108] for cognition, NPI-Q[102] for BPSD, the Cornell Scale for Depression in Dementia[114] in moderate/severe dementia, the Geriatric Depression Scale-Short Form[115] in mild dementia for depression, the PAINAD[116] and BPI for pain assessment in moderate/severe dementia, and the caregiver strain index[117]. These instruments are not part of research and are for clinical use by the HHC agency clinicians as they see fit in their clinical judgement.

6.1.4 Interprofessional care plans

Interprofessional care plans that guide overall care for PWD, with modules specific to pain and BPSD, are available to clinicians in the performance improvement care teams. These care plans provide algorithms to guide clinicians when dealing with specific issues in older adults and are consistent with the information taught in the online and champion education programs. For instance, in PWD with sleep disturbance, care plans describe evidence based practices around implementing appropriate sleep hygiene and habits, stimulating patients during the day through activities, and environmental changes to improve sleep quality. Each plan is associated with tailored caregiver and/or patient education pamphlets that are written in both English and Spanish (generalized Latin American Spanish) that can be reviewed on site electronically and then mailed or brought to the next visit.

6.1.5 Administration of Quality Improvement Program

The administration will be delivered by the HHC team as part of their practice in the community. The number of sessions may be variable as HHC teams see patients a variable number of times depending on the condition they are seeing the patient for and operational needs of the HHC agency.

6.1.6 Procedures for Training Quality Improvement Teams and Monitoring Fidelity

Because there are multiple care teams receiving the performance improvement program, and we need to understand how well the program is implemented in order to assess the research outcomes, we will measure fidelity of implementation (e.g. clinician exposure to the performance improvement program) as well as differences across control and performance improvement teams through assessing registered nurse, physical and occupational therapist knowledge, attitudes and confidence using Drs. Brody and Galvin's previously validated dementia symptom knowledge and attitudes survey at baseline, 6 months, and annually thereafter[25], comparing differences across intervention and control teams for contamination, and through measuring the number of care plans initiated, caregiver teaching sheets provided to caregivers, and assessment instruments used at each site and in each care team throughout the trial.

As the survey is primarily being collected for research purposes and not quality improvement purposes, we will consent clinicians who participate in the completion of the knowledge surveys. Completion of the training and clinical performance however will be seen as an operational, quality improvement requirement of the agencies, similar to Drs. Brody and Galvin's prior successfully IRB approved studies. Champions will hold a monthly conference call with the investigators and spend 4 additional hours each month performing performance improvement through PDSA methodology and Audit and Feedback and will receive guidance by the investigators to ensure adequate implementation, and are provided training in this during champions training. Additionally, as is standard practice with complex performance improvement programs[118] we will hold annual site visits and include process-based interviews with managers and executive leadership to elicit suggested improvements, whether there have been any changes in usual care during the time, or any concerns that have not been previously addressed. Finally, we will collect OASIS data, which is a standardized nationwide clinical data set entered usually by the RN in HHC to examine difference between documentation and our gold standard assessments, as well as for performance improvement on a quarterly basis.

6.1.6.1 Clinician Procedures for Fidelity Monitoring

6.1.6.1.1 Sample population and justification of Clinician Fidelity Monitoring

We will include all registered nurses, physical therapists, and occupational therapists serving in the performance improvement or control teams who are providing direct care to patients in the field. Given the professions included, we expect the population to be overwhelmingly female and white. We have received staffing information from the agencies involved and subjected to turnover, expect that the overall population will be 85% female, 64% Caucasian non-Hispanic, 14% black non-Hispanic, 21% Caucasian Hispanic, and 1% Asian. A total of 300 clinicians will be recruited and perform fidelity monitoring through an online survey at the NYU study site.

6.1.6.1.2 Recruitment and retention strategies of Clinician Fidelity Monitoring

6.1.6.1.2.1 Recruitment Strategy of Clinician Fidelity Monitoring

The PI and/or site-PI will perform an introduction to the study and its purpose to all eligible clinicians at a site visit at a regularly scheduled staff meeting to explain the purpose of the trial. This will be followed by an all-staff email regarding the study from the agency CEO or delegate. We will also receive a list of eligible staff from the HHC agency. We will send several emails requesting participation in the study. For those individuals who do not respond to email, we will also perform a recruitment phone call to their agency cell phone. We will seek a waiver of documentation of consent and provide a statement at the beginning of the Qualtrics survey using a standardized statement approved by the NYU School of Medical IRB at onset of collection of fidelity surveys.

6.1.6.1.2.2 Retention Strategy of Clinician Fidelity Monitoring

For clinicians on performance improvement care teams, we will offer CEUs for completion of the surveys and online training. For those in control teams, we will offer upon completion of the study access to the online modules for their own training, as well as CEUs upon completion. In our past studies we have shown high recruitment and retention rates (92-100%) using these methods.

6.1.6.1.2.3 Criteria for inclusion/exclusion of Clinician Fidelity Monitoring

All English speaking registered nurses, physical therapists and occupational therapists employed or contracted by the agency who are part of an intervention or control care team and greater than 18 years of age will be eligible. This includes both bedside clinicians as well as the managers, team leads, and educators who support them.

6.1.6.1.2.4 Risks to Clinician in Fidelity Monitoring

There is minimal risk to the healthcare staff. The greatest risk is the loss of confidentiality. We will not share individual data to supervisors. We will not be providing individualized data back to the agencies on care team performance and will only use it for internal research team monitoring of fidelity. Champions at the agencies are trained as part of the champions training to perform their own performance improvement identification and management based on chart audits, OASIS data, and feedback from agency staff. No staff will have job actions performed secondary to fidelity monitoring by the researchers.

6.1.6.1.2.5 Data Collection and Security for Clinician Fidelity Monitoring

All fidelity measurement data will be collected using Qualtrics, which is hosted by NYU Data Services. In order to access Qualtrics, you must use your NYU campus login credential and starting September 1, 2017, multifactor authentication, to access through a secure portal. Once data is collected and being prepared for analysis, it will be downloaded into a NYU Box folder owned by the PI that will only be accessible to the appropriate study personnel. NYU Box is controlled by NYU and only accessible through NYU campus login credentials with multifactor authentication. It is HIPAA compliant and approved by NYU for maintaining sensitive information. Data will be collected through the Qualtrics survey by the clinician either on a personal or agency owned device. Data collected by Qualtrics is secure and encrypted.

6.1.6.1.2.6 Potential Benefits for Clinician Fidelity Monitoring

There are no inherent benefits associated with performing the DSKA as part of participation in this study.

6.1.6.1.2.7 Source of Materials for Fidelity Review

The DSKA will be collected at baseline, six months, and annually thereafter. It takes approximately 20 minutes to complete. It includes baseline demographics (first survey only for an individual) and 79 likert style items regarding their knowledge, confidence and attitudes towards pain, depression and behavioral symptom assessment and management in persons with dementia. We have administered, and clinicians have completed the DSKA hundreds of times in the past four years in intervention and control settings and

it has a Cronbach Alpha of .94. An additional source material includes chart data from subjects at the agencies compared to our gold standard assessments.

6.1.6.1.2.8 Importance of Knowledge to be Gained in Fidelity Monitoring

This will help the investigators to understand the fidelity of implementation of the quality improvement program as well as whether there are environmental changes across the agency.

6.1.6.1.2.9 Withdrawal or Termination of Clinicians in Fidelity Monitoring

Clinicians may choose to withdraw from the study at any point. They will be terminated from the study only if they leave the agency. We will continue to maintain enrollment even if clinicians miss a survey at a given time point and anticipate that not all clinicians will complete at all time points.

6.1.7 Assessment of Subject Adherence with Study Quality Improvement Program

Subjects will not be monitored for any specific adherence to care interventions suggested by HHC team members as this is a service delivery, evidence based practice intervention.

7 Study Procedures and Schedule

7.1 Study Procedures/Evaluations

7.1.1 Study Specific Procedures

All data will be collected virtually via telephone and through internet capabilities. The following questionnaires will be collected by the research team as part of research assessment of efficacy of the intervention as it relates to the aims for both performance improvement and control subjects:

- Quick Dementia Rating Scale (QDRS): Is a 10-item tool that measures cognitive impairment based on the severity of dementia.
- Neuropsychiatric Inventory Questionnaire (NPI-Q): Is a 13-item tool that measures caregiver perceptions of dementia BPSD presence and severity.
- Quality of Life in Alzheimer's Disease (QOL-AD): Is a 13-item tool that measures caregiver perceptions of quality of life in the PWD
- PAINAD: Is a pain assessment tool for use in persons with moderate to severe dementia who cannot provide reliable report.
- Brief Pain Inventory Short Form (BPI) is a 9-item tool that measures pain location, severity and intensity.
- FAM-CAM: Is an 11-item tool that is an informant-based assessment of delirium.
- Medication Record and use: We will create a list of medications the PWD is taking as well as the frequency of administration of any PRN medications taken, including any OTC or herbal supplements. The primary reason for collecting this data is to examine analgesic and antipsychotic use.
- Caregiver Targeted Quality of Life Tool (CGQOL): Is an 80-item tool with 10 domains for measuring the quality of life of the caregiver of the PWD.
- Public Health Questionnaire 9 (PHQ-9): Is a 9-item tool that measures depressive symptoms.
- Zarit Burden Inventory: Is a 22-item tool that measures caregiver burden.
- SF-12: The SF-12 is a 12-item tool that measures functional health and well-being.
- ADLs and IADLS: Are 12 items that measure functional status as part of the QOL-AD.
- Charlson Comorbidity Index: Is a reliable and valid comorbidity assessment tool.
- The Short Assessment of Health Literacy (SAHL): Is an 18-item test designed to examine health literacy levels
- Other non-instrumented questions that will be asked include sociodemographics (DOB, sex, highest education level attained, race, ethnicity, primary language, religion, marital status, household members, number type and frequency of unpaid and pain caregivers, and primary care provider name and contact for both PWD and caregiver.

- Information obtained from the chart includes: Number of visits by the home healthcare staff by type, comorbidities.
- Resource Utilization Inventory: Is a 13-item tool to measure healthcare resource utilization.
- HHCAHPS: Is a 32-item standardized patient satisfaction survey. While home healthcare agencies attempt to collect this on all patients, they are not always successfully able to do so and we will therefore measure independently to avoid missing data.
- Investigator derived questions asking if their caregiving practices have shifted due to the COVID-19 pandemic. The COVID-19 related questions are included in the subject dyad instruments.

7.1.2 Standard of Care Study Procedures

Individuals who are in the control group will receive usual care as provided by the HHC agency.

7.2 Study Schedule

7.2.1 Screening

Screening is initiated during the initial call and completed prior to subjects being introduced to the informed consent process.

The research team will contact patients and caregivers who have “not opted out” from being contacted based on their HHC agency’s referral. The research team will inquire on their interest in learning about the study and whether they may be interested in participating prior to screening for eligibility. Screening will be initiated in the first contact to ensure that they have met the inclusion/exclusion criteria. To determine if the PWD’s level of cognitive impairment meets eligibility for inclusion, the QDRS will be administered to the caregiver who will rate the PWD’s symptoms and behaviors. Caregivers will be provided with a copy of the QDRS assessment form for their review. A research team member will complete the form with the caregiver over the phone. A score will be tallied to determine the PWD’s level of cognitive impairment. A PWD who obtains a score $\geq$6 on the QDRS will meet eligibility for study inclusion. If the screening is positive and the PWD and caregiver are interested in participating, the research team member will conduct the informed consent process. The screening, informed consent, and visit one assessments for each subject will be completed within 3 business days from the PWD’s start of care date. In circumstances where subjects who provide their consent verbally yet lack the ability to electronically sign the informed consent document due to lack of internet access or computer literacy, we will mail them a copy of the consent form to review and confirm at visit 2 their intent to continue participation in order to ensure equity in participation. Providing consent/assent has been obtained, the remainder of the virtual visit will be utilized for subject data collection. Further, the QDRS score will determine which assessments are administered to the PWD.

7.2.2 Enrollment/Baseline

The enrollment and baseline visit (if eligible and enrolled) will occur on the same day.

Enrollment/Baseline Visit
Visit 1, (Day 0/1) the following surveys will be collected during visit one. Surveys administered to the PWD are indicated by their QDRS score:

- PAINAD (if QDRS>12)
- FAM-CAM
- Brief Pain Inventory Short Form (BPI; if QDRS$\leq$12).
- Quality of Life in Alzheimer’s Disease (QOL-AD) (if QDRS $\leq$12)
- Neuropsychiatric Inventory Questionnaire (NPI-Q)
- Caregiver Targeted Quality of Life Tool (CGQOL):
- Public Health Questionnaire 9 (PHQ-9)
- Zarit Burden Inventory
- SF-12
- Charlson Comorbidity

- Katz ADLs and Lawton IADLS (through the QOL-AD)
- The Short Assessment of Health Literacy (SAHL)
- Other non-instrumented questions that will be asked include sociodemographics (DOB, sex, highest education level attained, race, ethnicity, primary language, religion, marital status, household members, number type and frequency of unpaid and pain caregivers, medication record and use, primary care provider name and contact for both PWD and caregiver.
- Information obtained from the chart includes: Number of visits by the home healthcare staff by type, comorbidities, COVID-19 questions.

7.2.3 Intermediate Visits:

7.2.4

Visit 2 (Day 15+/-3)
The following surveys will be administered for visit two:
Surveys administered to the PWD are indicated by their QDRS score:

- BPI (If QDRS<12)
- PAINAD (If QDRS >12)
- FAM-CAM
- NPI-Q
- Katz ADLs and Lawton iADLs (through the QOL-AD)
- Non-instrumented: Medication Record and Usage, AE and SAE

Visit 3 (Day 30+/-3)
The following surveys will be administered for visit three:
Surveys administered to the PWD are indicated by their QDRS score:

- PAINAD (If QDRS >12)
- FAM-CAM
- BPI (If QDRS≤12)
- NPI--Q
- Katz ADLs and Lawton iADLs (through the QOL-AD)
- Resource Utilization Inventory
- Non-instrumented: Medication Record and Usage, Resource Utilization Inventory, AE and SAE, COVID-19 questions

7.2.5 Final Study Visit

Final Study Visit (Visit 4, Day 60+5)
The following surveys will be administered for visit four:
Surveys administered to the PWD are indicated by their QDRS score:

- PAINAD (If QDRS >12)
- FAM-CAM
- BPI (If QDRS≤12).
- QOL-AD (If QDRS≤12)
- NPI-Q
- CGQOL:
- Public Health Questionnaire 9 (PHQ-9)
- Zarit Burden Inventory
- SF-12
- Charlson Comorbidity
- Resource Utilization Inventory

- HHCAHPS
- Katz ADLs and Lawton IADLS (through the QOL-AD)
- Non-instrumented: Medication Record and Usage, Resource Utilization Inventory, AE and SAE
- Information obtained from the chart includes: Number of visits by the home healthcare staff by type, comorbidities, COVID-19 questions.

7.2.6 Collection of Home Health Record

Following the final study visit, the home health agency will extract the PWD subject's health record, including OASIS documentation, symptom scores, assessment information, and administrative visit information.

7.2.7 Withdrawal/Early Termination Visit

Should individuals withdraw from the study for any reason, we will attempt to ask for the reason and ask if any SAE or AE have occurred if the PWD/caregiver are reachable. We will also if withdrawal is for non-communication with the study team we will review the HHC medical record to ascertain if there was an SAE or AE.

7.3 Concomitant Medications, Treatments, and Procedures

Not Applicable

7.4 Justification for Sensitive Procedures

There are no sensitive procedures, provocative testing or deception inherent in this study.

7.5 Prohibited Medications, Treatments, and Procedures

Not applicable

7.6 Prophylactic Medications, Treatments, and Procedures

Not applicable

7.7 Rescue Medications, Treatments, and Procedures

Not applicable

7.8 Participant Access to Study Agent at Study Closure

Not applicable. Should the individual still be receiving HHC from the intervention team at the close of the study period they will continue to receive the intervention.

8 Assessment of Safety

8.1 This study is a minimal risk study given that it is an evidence-based implementation science intervention. However, the investigators will monitor for the following safety parameters and events throughout this study. In instances where an adverse event (AE) or a serious adverse event (SAE) has been identified, the investigators will follow standard clinical practice (SCP) whereby the investigator will notify the subject's health care provider responsible for initiating and/or approving the subject's enrollment into HHC services. In situations where an AE or SAE has been determined to be related to the study and the subject has withdrawn, investigators will actively monitor in follow up. Specification of Safety Parameters

Due to the pragmatic nature of the trial, the DSMB has directed this trial to perform a highly focused AE collection process which requires following single adverse event: a PHQ-9 score worsened by greater than or equal to 5 points during the course of the study. The DSMB further requires monitoring the following severe AEs: Caregiver attempted suicide; death of caregiver; death of person with dementia a; medical event that may jeopardize the subject, including hospitalization of either the person with dementia or caregiver, suicidal ideation, elder neglect or abuse, or an environmental threat such as unsecured firearm.

In cases of the following safety parameters, the site-PI and PI shall be notified immediately, a telephone triage performed, and then SCP will be followed by notifying the subject's primary care provider to advise of the situation.

Due to the virtual nature of data collection, safety monitoring will be done to the best of abilities for:

Imminent home safety threats/hazards (e.g. hoarding/cluttering, unsecured gun).
Suspected elder abuse or neglect.

Caregiver Depression: Should caregivers have a score of ≥10 on the PHQ-9 or exhibit suicidal ideation via item 9 of the PHQ-9 or verbally outside of any instrumentation, Definition of Adverse Events (AE)

An *adverse event* (AE) is any symptom, sign, illness or experience that develops or worsens in severity during the course of the study. Intercurrent illnesses or injuries should be regarded as adverse events. Abnormal results of diagnostic procedures are considered to be adverse events if the abnormality:

- results in study withdrawal
- is associated with a serious adverse event
- is associated with clinical signs or symptoms
- leads to additional treatment or to further diagnostic tests
- is considered by the investigator to be of clinical significance

The following AEs will be monitored in this study:

Worsening of depression symptoms: Caregivers whose PHQ-9 score worsen by greater than or equal to 5 points during the course of the study

8.1.1 Definition of Serious Adverse Events (SAE)

Serious Adverse Event

Adverse events are classified as serious or non-serious. A ***serious adverse event*** is any AE that is:

- fatal
- life-threatening
- requires or prolongs hospital stay
- results in persistent or significant disability or incapacity
- a congenital anomaly or birth defect
- an important medical event

Important medical events are those that may not be immediately life threatening but are clearly of major clinical significance. They may jeopardize the subject and may require intervention to prevent one of the other serious outcomes noted above. For example, drug overdose or abuse, a seizure that did not result in in-patient hospitalization, or intensive treatment of bronchospasm in an emergency department would typically be considered serious.

All adverse events that do not meet any of the criteria for serious should be regarded as ***non-serious adverse events***.

The following SAEs will be monitored in this study:

Caregiver attempted suicide: A case in which a caregiver is noted to have attempted suicide. This information may be provided by the PWD surrogate, PWD (if only mild dementia) or other family member, friend, or caregiver when attempting to complete follow-up visits.

Death of Caregiver: A case in which a caregiver is noted to have died. This information may be provided by the PWD surrogate, PWD (if only mild dementia) or other family member, friend, or caregiver when attempting to complete follow-up visits. We will attempt to ascertain the cause of death of the caregiver

Death of PWD: A case in which the PWD has died. We will attempt to contact the caregiver and primary care provider to ascertain the cause of death.

Any SAE will be immediately reported to the site-PI and overall PI, who will follow SCP by notifying the subject's health care provider and then notifying the IRB of record and DSMB for further review.

8.1.2 Definition of Unanticipated Problems (UP)

Unanticipated Problems Involving Risk to Subjects or Others
Any incident, experience, or outcome that meets all of the following criteria:

- Unexpected in nature, severity, or frequency (i.e. not described in study-related documents such as the IRB-approved protocol or consent form, the investigators brochure, etc)
- Related or possibly related to participation in the research (i.e. possibly related means there is a reasonable possibility that the incident experience, or outcome may have been caused by the procedures involved in the research)
- Suggests that the research places subjects or others at greater risk of harm (including physical, psychological, economic, or social harm).

This definition could include an unanticipated serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, the intervention, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects (21 CFR 812.3(s)).

8.2 Classification of an Adverse Event

8.2.1 Severity of Event

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

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

8.2.2 Relationship to Study Quality Improvement Program

The PI or site PI will assess the AE's relationship to study quality improvement program, and will be part of the documentation process, but it is not a factor in determining what is or is not reported in the study. If there is any doubt as to whether a clinical observation is an AE, the event should be reported. All AEs must have their relationship to study agent assessed. In a clinical trial, the study product must always be suspect. To help assess, the following guidelines are used.

- **Related** – The AE is known to occur with the study agent, there is a reasonable possibility that the study agent caused the AE, or there is a temporal relationship between the study agent and event. Reasonable possibility means that there is evidence to suggest a causal relationship between the study agent and the AE.
- **Not Related** – There is not a reasonable possibility that the administration of the study agent caused the event, there is no temporal relationship between the study agent and event onset, or an alternate etiology has been established.

8.2.3 Expectedness

The site PI or PI will be responsible for determining whether an AE is expected or unexpected. An AE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the study agent.

8.3 Time Period and Frequency for Event Assessment and Follow-Up

The occurrence of an AE or SAE may come to the attention of study personnel during study visits and interviews of a study participant presenting for medical care, or upon review by a study monitor. All AEs including local and systemic reactions not meeting the criteria for SAEs will be captured on the appropriate RF. Information to be collected includes event description, time of onset, clinician's assessment of severity, relationship to study product (assessed only by those with the training and authority to make a diagnosis), and time of resolution/stabilization of the event. All AEs occurring while on study must be documented appropriately regardless of relationship. All AEs will be followed to adequate resolution.

Any medical condition that is present at the time that the participant is screened will be considered as baseline and not reported as an AE. However, if the study participant's condition deteriorates at any time during the study, it will be recorded as an AE. UPs will be recorded in the data collection system throughout the study.

Changes in the severity of an AE will be documented to allow an assessment of the duration of the event at each level of severity to be performed. AEs characterized as intermittent require documentation of onset and duration of each episode.

The PI will record all reportable events with start dates occurring any time after informed consent is obtained until 7 (for non-serious AEs) or 30 days (for SAEs) after the last day of study participation. At each study visit, the investigator will inquire about the occurrence of AE/SAEs since the last visit Events will be followed for outcome information until resolution or stabilization.

All unresolved adverse events should be followed by the investigator until the events are resolved, the subject is lost to follow-up, or the adverse event is otherwise explained. At the last scheduled visit, the investigator should instruct each subject to report any subsequent event(s) that the subject, or the subject's personal physician, believes might reasonably be related to participation in this study. The investigator should notify the study sponsor of any death or adverse event occurring at any time after a subject has discontinued or terminated study participation that may reasonably be related to this study. The sponsor should also be notified if the investigator should become aware of the development of cancer or of a congenital anomaly in a subsequently conceived offspring of a subject that has participated in this study.

8.4 Reporting Procedures – Notifying the IRB

All AEs and SAEs will be reported to the site-PI (if applicable) and study-PI immediately. The PI will assess the event for severity, consult with the co-investigators if necessary, and when an event has been determined to be severe, the site PI will follow SCP by notifying the subject's health care provider. The PI will report all study related SAEs to IRB and DSMB within 24 hours of their knowledge of the incident. The PI will be responsible for working with the DSMB, IRB, site-PIs and other individuals regarding related SAE to the trial. All AEs will be recorded and reviewed immediately and for patterns of AE on a quarterly basis and referred with a corresponding report to the IRB and DSMB.

8.4.1 **Unanticipated Problem Reporting**

Incidents or events that meet the OHRP criteria for UPs require the creation and completion of an UP report form. It is the site investigator's responsibility to report UPs to their IRB and to the DSMB/study sponsor. The UP report will include the following information:

- Protocol identifying information: protocol title and number, PI's name, and the IRB project number;
- A detailed description of the event, incident, experience, or outcome;
- An explanation of the basis for determining that the event, incident, experience, or outcome represents an UP;
- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the UP.

To satisfy the requirement for prompt reporting, UPs will be reported using the following timeline:

- UPs that are SAEs will be reported to the IRB and to the DSMB/study sponsor within 24 hours of the investigator becoming aware of the event.
- Any other UP will be reported to the IRB and to the DSMB/study sponsor within 3 days of the investigator becoming aware of the problem.
- All UPs should be reported to appropriate institutional officials (as required by an institution's written reporting procedures), the supporting agency head (or designee), and OHRP within<insert timeline in accordance with policy> of the IR's receipt of the report of the problem from the investigator.

8.5 Reporting Procedures – Notifying the Study Sponsor

The study clinician will complete a SAE Form within the following timelines:

- All deaths and immediately life-threatening events, whether related or unrelated, will be recorded on the SAE Form. SAE that have been determined to be related to the study will be submitted to the DSMB/study sponsor within 24 hours of site awareness. See Section 1, Key Roles for contact information.
- Other SAEs that are determined to be related to the study will be submitted to the DSMB/study sponsor within 72 hours of site awareness.

All SAEs will be followed until satisfactory resolution or until the site investigator deems the event to be chronic or the adherence to be stable. Other supporting documentation of the event may be requested by the DSMB/study sponsor and should be provided as soon as possible.

As a follow-up to the initial report, within the following 48 hours of awareness of the event, the investigator shall provide further information, as applicable, on the unanticipated event or the unanticipated problem in the form of a written narrative. This should include a copy of the completed Unanticipated Problem form,

and any other diagnostic information that will assist the understanding of the event. Significant new information on ongoing unanticipated adverse effects shall be provided promptly to the study sponsor.

8.6 Reporting Procedures – Participating Investigators

As noted in 8.4 all site PIs will take part in the classification of AEs, SAEs and UPs and will therefore be immediately contacted for discussion of the event.

8.7 Study Halting Rules

Temporary suspension of the trial will occur if there is a 20% or greater negative effect found in any of the primary outcomes. The study will also be halted if SAEs are found that are caused by the quality improvement program, or at the discretion of the IC or the DSMB in conjunction with the IC. Safety Oversight

It is the responsibility of the Principal Investigator to oversee the safety of the study at his/her site. This safety monitoring will include careful assessment and appropriate reporting of adverse events as noted above, as well as the construction and implementation of a site data and safety-monitoring plan. Medical monitoring will include a regular assessment of the number and type of serious adverse events.

8.8 Safety Oversight

8.8.1 Data Safety and Monitoring

The Principle Investigator will ensure overall safety of the subjects in the trial on a daily basis and will be responsible for all reporting. The site PIs will be responsible for managing safety at their sites in coordination with the PI. The study statistician will be responsible for running quarterly reports on data safety, consistency and outcomes and reviewing them with the study PI. A DSMB will act in an advisory capacity to the Primary IC Director in regards to the study.

8.8.2 Frequency and Reporting

As noted in section 8.4, all AE and SAE will be reported directly to the site PI and then study PI. All events will be reported within 24 hours to the DSMB and the IRB at both the study site and the primary IRB (NYU). The DSMB will then discuss whether and how to convene. Outside of SAE, the DSMB will meet at least prior to onset of the trial and every 6 months at a minimum. Safety reports will be sent twice yearly including analysis of study progress and data and safety issues. These reports will include descriptive analyses of participant demographic data, interim analyses of primary and secondary outcomes, as well as any adverse or serious adverse events, and quality improvement program fidelity. Individuals who withdraw from the trial will be examined in sensitivity analyses, however will be replaced with completed cases for the purposes of the trial. There are no cases where the quality improvement program will be discontinued but follow-up will still occur unless an individual withdraws from the study due to an AE or SAE, in which case we will ensure safety of the individual/dyad and referral to existing resources.

8.8.3 Data Safety and Monitoring Board

8.8.3.1.1 DSMB Composition

The investigators will develop with the IC a 3-member independent DSMB. The composition will include a chair who has experience performing Phase III behavioral clinical trials in dementia, a biostatistician, and an independent clinician-researcher with experience in home-based care of older adults. All members will

have no personal or professional conflict of interest in the study, a current affiliation with any of the study sites, has not served as an author or co-author on a grant or manuscript together with the PI or site PIs within the past 3 years.

8.8.3.1.2 DSMB Responsibilities and Powers

The principle responsibility of the DSMB is to protect the safety of study participant. The DSMB will initially meet to evaluate the protocol to ensure minimization of risk prior to initiation and recommend when subject recruitment can be initiated. The DSMB will then meet and monitor primary and secondary outcome data, SAEs and AEs, performance data by site, and recruitment data by site, as well as other safety issues or risks to the PWD, caregiver, or dyad through bi-annual meetings, or if needed more frequently via conference call or webex. The DSMB will have the power to recommend halting of the trial to the IC and PI should it find any of these factors cause safety issues, serious adverse events or outcomes, or significantly better outcomes. It also has the power to report directly to the IC and the PI on its findings or any issues with the conduct of the study or enrollment, sample size, or data collection issues. The quality improvement program will be discontinued or temporarily halted if the IC closes the trial or DSMB recommends discontinuing or halting the trial based on determining the study's subjects (care recipient and care giver) safety is compromised or at risk. (see section 8.7).

9 Clinical Monitoring

Clinical site monitoring is conducted to ensure that the rights and well-being of human subjects are protected, that the reported trial data are accurate, complete, and verifiable, and that the conduct of the trial is in compliance with the currently approved protocol/amendment(s), with GCP, and with applicable regulatory requirement(s). As this is a minimal risk study, limited clinical monitoring will be performed by the study biostatistician in ensuring data entry verification and completeness and, the lead site principal investigator in ensuring appropriate and complete targeting of prospective subjects. As noted in fidelity measurement, we will also hold monthly meetings to ensure quality improvement program fidelity. Additionally, each research site will perform internal quality management of study conduct, data collection, documentation and completion.

10 Statistical Considerations

10.1 Statistical and Analytical Plans (SAP)

A formal SAP will not be completed for this study.

10.2 Statistical Hypotheses

H1: PWD cared for by a HHC team utilizing the DSM-H will show reduced symptoms and improved ratings of pain, BPSD, and caregiver-rated QOL at the end of the first 60-day HHC certification period compared to the control (usual care) group.

H2: Informal caregivers of PWD cared for by a HHC team utilizing the DSM-H will show reduced ratings of burden, and depression, and improved functional health and well-being at the end of the first 60-day HHC certification period compared to the control (usual care) group.

H3: PWD cared for by a HHC team utilizing the DSM-H will show a reduction in emergency room visits and hospital admissions compared to the control (usual care) group, and a greater number of outpatient visits.

10.3 Analysis Datasets

PWD, caregivers, and clinicians will each have a separate data set. Additionally, a data set with combined will be created to examine the interaction between PWD-caregiver dyad interactions and interactions between outcomes and quality improvement program fidelity. Separate SAE and AE data sets will be maintained for caregivers and PWDs.

10.4 Description of Statistical Methods

10.4.1 General Approach

Data Analysis will be performed using SAS 9.4[120]. We will perform statistical tests to examine baseline differences between the quality improvement program and control groups. We will then perform unadjusted comparison of both primary outcomes (patient and caregiver quality of life, emergency room visits) and secondary outcomes (pain, BPSD, delirium, caregiver depression burden, and burnout, hospital and emergency room admissions) between groups. We will focus on the endpoint measure for quality of life, and 30 and 60-day outcomes for emergency room utilization. For primary and secondary outcomes, we will perform a time trend analysis using a mixed effects linear model (PROC MCM). Mixed effects regression is used to analyze longitudinal data with repeated measures accounting for intra-individual and group clustering. We intend to use multivariate mixed effects regression modeling as opposed to traditional linear modeling or ANOVA in order to control for unobservable confounding variables that are constant over time but differ across PWD and/or caregivers[121]. For both primary and secondary outcomes, we will then repeat the above analyses adjusting for baseline variables as covariates for a more efficient measurement of the effects of the quality improvement program. We will also perform correlation analyses to explore the relationship between pain and BPSD, and PWD and caregiver QOL through plotting scores over time and then if a significant correlation is present through adding to our mixed effect model. For utilization data, we will perform logistic regression to examine whether the patient is more or less likely to have a hospitalization or ER visit compared when receiving the quality improvement program at 30 and 60 days. We will then perform a Poisson Count Regression to compare the total number of hospitalizations and ER visits at each timepoint. In these models we will utilize a random effect to measure for clustering.

10.4.2 Safety Analyses

We will perform interim analyses using descriptive statistics and two-sided t-tests, monitoring for a significance of 0.05 starting at the end of year 1 of the grant for safety purposes. These results will be presented unblinded to the DSMB.

10.4.3 Adherence and Retention Analyses

We will perform sensitivity analyses to examine whether there are differences in those who are retained in the study vs those who withdraw/are terminated. As this is a cluster randomized trial, adherence is related to the quality improvement program implementation at the care team level and therefore falls under fidelity monitoring. We will examine differences in annual DSKA scores submitted by HHC clinicians across control and quality improvement program care teams through paired t-tests and repeated measures ANOVA.

10.4.4 Baseline Descriptive Statistics

We will compare quality improvement program cohorts based on baseline demographic variables including age, sex, education, race, ethnicity, healthcare literacy, functional status, and comorbidities using descriptive statistics and t-tests.

10.4.5 Planned Interim Analysis

See. 10.4.2

10.4.5.1 Safety Review

See 8.7 and 10.4.2.

10.4.5.2 Efficacy Review

See 10.4.2. Efficacy will not be considered in halting the study.

10.4.6 Additional Sub-Group Analyses

We will perform sub-group analyses based on age, sex, and race/ethnicity. We will perform both descriptive and multivariate comparisons.

10.4.7 Multiple Comparison/Multiplicity

Not Applicable

10.4.8 Tabulation of Individual Response Data

Individual participant data will not be listed, with the exception of spaghetti plots of change over time.

10.4.9 Exploratory Analyses

We will examine the effect of ADL function on non-QOL outcomes. We will also examine the interaction of caregiver and PWD primary and secondary outcomes.

10.5 Sample Size

Power analyses were conducted using Optimal Design software[122]. Given that this study is randomized at the cluster level, we must control for intra-class correlation, and have therefore calculated all power with an intra-class coefficient of .05, which is more conservative than the most recent clustered palliative care study[123] and aligns well with prior community-based cluster trials[124]. The Quality of Life in Alzheimer's Disease as the primary outcome measure in aim 1 has an average score of 33.1, standard deviation of 5.9. A .5 standard deviation difference in this measure would be clinically meaningful. Therefore, in a 2-sample comparison with a power of .80, an alpha of .05 and covariates that account for a cumulative 15% of the variance in outcome would require 15 dyads per cluster, and 20 clusters (10 per arm) at 60 days to detect a medium effect (δ = .45). For mixed effects linear models, the projected sample size will also allow us to detect a medium linear treatment effect (δ = .45) between groups in unadjusted analyses (assuming 15 dyads per cluster, 20 clusters, 4 observations, and an ICC = .05). Although there are no closed-form equations for calculating the power of linear models that include covariates, any non-zero correlation between covariates and the outcome will reduce the unexplained (error) variance thus increasing the statistical power of our tests, and reducing the minimum detectable effect size. As such, the detectable effect size estimated for the unadjusted analyses can be considered an upper bound estimate for the jneffect size detectable in adjusted analyses. **We will recruit until we have reached 15 completed cases in each cluster (N=300).** Conservatively anticipating a 15% dropout[40,125] over the 60 days requires a **total recruitment goal of 345 dyads.** As almost 20,000 patients are seen each year in the three HHC agencies in this study, approximately 30% with ADRD, we do not expect any difficult recruiting this sample, even with an unanticipatedly high rate of dyads declining to participate.

In addition, for fidelity monitoring, as discussed in section 6.1.6.1, we will consent **300 clinicians** at the participating HHC agencies on usual care and quality improvement care teams to complete fidelity monitor by performing the DSKA survey. These clinicians are not study subjects but will be consented as they are

performing these surveys to assist the research team in monitoring fidelity of the quality improvement program.

10.6 Measures to Minimize Bias

10.6.1 Enrollment/Randomization/Masking Procedures

As randomization is done at the cluster (care team) level, this will only be performed at the beginning of the trial. The study statistician will perform the randomization utilizing SAS 9.4 stratified by agency. The PI will relay to the home care agencies which teams will serve as quality improvement program teams or control teams. The study RAs, study project director, and site-PIs will all be blinded to the assignment. Teams will be randomized in strata by agency and geographic location to ensure like care teams are assigned to each condition. Subjects will be assigned through usual practice to the care team that serves the geographic area they live in. We will sequentially recruit individuals as they are referred from agencies following the very clear, straightforward method described above in section 5.4.

Clinicians will be enrolled sequentially if they are eligible and all study personnel with the exception of the lead site PI and study statistician will be blinded as to the assignment of the clinicians within a performance improvement or usual care team.

10.6.2 Evaluation of Success of Blinding

Not applicable

10.6.3 Breaking the Study Blind/Participant Code

Intentional breaking of the blind will only be performed in case of SAE, and then only to the site PI, but not the site RA or project director.

11 Source Documents and Access to Source Data/Documents

Source data is all information, original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents. Examples of these original documents, and data records include: hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files, and records kept at the pharmacy, at the laboratories, and at medico-technical departments involved in the clinical trial. It is acceptable to use CRFs as source documents. If this is the case, it should be stated in this section what data will be collected on CRFs and what data will be collected from other sources.

All assessment data, which has no PHI, will be collected using Qualtrics, which is hosted by NYU Data Services. Any data with PHI will be collected and entered directly into REDCap, which is hosted by NYU Langone Medical Center. In order to access REDCap or Qualtrics, you must use your NYULMC or NYU login credential respectively to access through a secure portal. Data will be transferred from Qualtrics to REDCap by the study project director. All Qualtrics assessments will require a forced entry to ensure missing data is minimized

PHI will only be collected in Redcap. A study ID will be created in NYU REDCap and used for all Qualtrics data that is collecting surveys. Once data is collected, it will be downloaded from Qualtrics to a NYU MCIT-managed network drive on a weekly basis that will only be accessible to the appropriate study personnel

and added to RedCAP. The MCIT drive It is HIPAA compliant and approved by NYU MCIT for maintaining sensitive information.

Data will be collected electronically through the use of computers or utilizing iPADs that are owned, centrally managed, passcode required, and distributed to the study RAs across sites by NYU MCIT. The iPads will be encrypted and locked so that only secure and approved apps, such as for collecting data offline (Qualtrics App) will be made available. Once data is collected through the use of Qualtrics surveys, it can only be transferred to the secure Qualtrics server and not extracted by other means. Thus, when the iPad is connected to secure wifi, the data will be automatically uploaded to the Qualtrics server and removed from the iPad. Electronic informed consent documents with subject information will be collected, stored and maintained on the REDCap system.

Access to study records will be limited to IRB-approved members of the study team. The investigator will permit study-related monitoring, audits, and inspections by the IRB/EC, the sponsor, government regulatory bodies, and University compliance and quality assurance groups of all study related documents (e.g. source documents, regulatory documents, data collection instruments, study data etc.). The investigator will ensure the capability for inspections of applicable study-related facilities (e.g. pharmacy, diagnostic laboratory, etc.).

Participation as an investigator in this study implies acceptance of potential inspection by government regulatory authorities and applicable University compliance and quality assurance offices.

12 Quality Assurance and Quality Control

QC procedures will be implemented beginning with the data entry system and data QC checks that will be run on the database will be generated. Any missing data or data anomalies will be communicated to the site(s) for clarification/resolution.

The lead PI will verify that the clinical trial is conducted and data are generated, documented (recorded), and reported in compliance with the protocol, and GCP in coordination with the study statistician.

The investigational site will provide direct access to all trial related sites, source data/documents, and reports for the purpose of monitoring and auditing by the sponsor, and inspection by local and regulatory authorities.

13 Ethics/Protection of Human Subjects

13.1 Ethical Standard

The investigator will ensure that this study is conducted in full conformity with Regulations for the Protection of Human Subjects of Research codified in 45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, and/or the ICH E6.

13.2 Institutional Review Board

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the IRB for review and approval. Approval of both the protocol and the consent form must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. All changes to the consent form will be IRB approved; a determination will be made regarding whether previously consented participants need to be re-consented.

13.3 Informed Consent Process

13.3.1 **Consent/Assent and Other Informational Documents Provided to Participants**

Consent forms describing in detail the quality improvement program, study procedures, and risks are provided to each participant electronically through the REDCap database. The completion of all consent documents will include electronic signatures that will be obtained and maintained through the REDCap system prior to starting study-related activities. The following consent materials are submitted with this protocol.

Consent-PWD
Assent Form-PWD
Consent-Caregiver
Telephone Consent Script-PWD Surrogate
Application for Waiver of documentation of consent-PWD and Caregiver
Application for Waiver of Documentation of Informed Consent-Clinician
Study Information Survey Header-Clinician

13.3.2 **Consent Procedures and Documentation**

Informed consent is a process that is initiated prior to the individual's agreeing to participate in the study and continues throughout the individual's study participation. Extensive discussion of risks and possible benefits of participation will be provided to the participants and their families. Consent forms will be IRB-approved and the participant will be asked to read and review the document. The investigator will explain the research study to the participant and answer any questions that may arise. All participants will receive a verbal explanation in terms suited to their comprehension of the purposes, procedures, and potential risks of the study and of their rights as research participants. Following the COVID-19 pandemic the method of completing informed consent with participants has transitioned from an in-person written consent to remote with electronic signature. Where verbal consent is needed, the researcher will incorporate HIPAA authorization language to describe the study purpose, the type of questions asked and their ability to refrain from answering, the length of time expected of their participation, the method for keeping information confidential and who they may contact (PI; IRB) with questions, and that their participation is voluntary and can be stopped at any time without consequence to the PLWD's treatment. The participants are given an opportunity to discuss the study with their surrogates or think about it prior to agreeing to participate. Participants will have the opportunity to carefully review the electronic consent form and ask questions prior to signing and/or providing verbal consent. The participant will electronically sign the informed consent document prior to any procedures being done specifically for the study. Only in cases where the subject due to lack of internet or poor computer literacy cannot electronically sign the consent form, we will accept their verbal consent to participate after all information on the consent document has been presented to them ensuring that regulatory HIPAA language has been heard and all questions have been answered. In these situations where verbal consent is received, the research will date and sign the informed consent document and advise the participant of their enrollment status, confirm with the subject that they want to participate, and then ask the subject if the researcher may begin the visit one assessments. In the cases where verbal consent, as a secondary option has been provided by the participant, a copy of the consent form completed with the researcher's signature will be sent to them and we will reconfirm their participation at visit 2. Where one part of the caregiver-PWD dyad can sign electronically and the other cannot, we will capture the signature of the individual who can sign, and verbal consent of the individual who cannot following said process, as they may be in different locations with differential access to internet. The participants may withdraw consent at any time throughout the course of the trial. A copy of the electronically signed informed consent document will be downloaded by participants for their records. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.

A copy of the executed informed consent document will be stored in the subject's research record on REDCap. The consent process, including the name of the individual obtaining consent, will be thoroughly documented in the subject's research record. Any alteration to the standard consent process (e.g. use of a translator, consent from a legally authorized representative, consent document presented orally, etc.) and the justification for such alteration will likewise be documented.

Consent will be performed remotely by study RAs or the study lead site project director. Determination of capacity for consent is discussed in section 5.4. Once the determination is made, the written informed consent will be completed by the RA or project director. Signatures for each subject's informed consent will be collected electronically and stored in the subject record on REDCap. If the PWD does not have capacity, and verbal or electronic consent is provided by the surrogate decision maker for the patient to participate, the PWD will be asked for their assent.

In addition to consent, in PWD who are determined to lack capacity, we will ask for their assent if they are verbally able to do so. If they chose not to assent, we will not enroll them in the study.

13.4 Participant and Data Confidentiality

Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Those regulations require a signed subject authorization informing the subject of the following:

- What protected health information (PHI) will be collected from subjects in this study
- Who will have access to that information and why
- Who will use or disclose that information
- The rights of a research subject to revoke their authorization for use of their PHI.

In the event that a subject revokes authorization to collect or use PHI, the investigator, by regulation, retains the ability to use all information collected prior to the revocation of subject authorization. For subjects that have revoked authorization to collect or use PHI, attempts should be made to obtain permission to collect at least vital status (i.e. that the subject is alive) at the end of their scheduled study period.

Participant confidentiality is strictly held in trust by the participating investigators, their staff, and the sponsor(s) and their agents. This confidentiality is extended to cover testing of biological samples and genetic tests in addition to the clinical information relating to participants. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party without prior written approval of the sponsor.

Authorized representatives of the sponsor and representatives of the IRB may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) and pharmacy records for the participants in this study. The clinical study site will permit access to such records.

The study participant's contact information will be securely stored at each clinical site for internal use during the study. At the end of the study, all records will continue to be kept in REDCAP or an MCIT managed networked drive for as long a period as dictated by local IRB and Institutional regulations.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored at NYU Langone Medical Center and the NYU School of Nursing. Transmission from external sites will be performed securely through the MCIT managed iPADs, or through secure

encrypted email. This will not include the participant's contact or identifying information. Rather, individual participants and their research data will be identified by a unique study identification number. The study data entry and study management systems used by clinical sites and by NYU School of Nursing research staff will be secured and password protected. At the end of the study, all study databases will be de-identified and archived at the NYU Langone Medical Center and NYU School of Nursing.

13.4.1 **Research Use of Stored Human Samples, Specimens, or Data**

Not Applicable

13.5 Future Use of Stored Specimens

Not Applicable

14 Data Handling and Record Keeping

14.1 Data Collection and Management Responsibilities

All data including the consent forms will be collected and maintained electronically in NYULMC RedCap or on an MCIT-managed network drive. Referral submissions sent via encrypted transfer or secure email will be uploaded directly into redcap, the study log, by the research coordinator or project director.

Enrolled subjects who request to receive an email or text message to reminder them of upcoming study visits, will receive a notification through REDCap. Email notifications will be performed using REDCap survey function. SMS (text) messages will be completed through a linked REDCap and Twilio account. When a subject requests to receive a text message to their cell phone, REDCap requests that action through Twilio. When the subject responds to the message, Twilio relays the information back to REDCap. The data from this exchange is stored in the REDCap database. Twilio does not store any data nor does it keep a log of its actions. Further, REDCap goes to great length to ensure that SMS transcriptions do not stay in Twilio's logs but are removed shortly after being completed. This is done for security and privacy concerns (e.g., HIPPA), in which the subject's phone number and response to confirm the visit are not permanently logged on Twilio's servers but instead remain securely in REDCap.

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

All source documents should be completed in a neat, legible manner to ensure accurate interpretation of data. Black ink is required to ensure clarity of reproduced copies. When making changes or corrections, cross out the original entry with a single line, and initial and date the change. DO NOT ERASE, OVERWRITE, OR USE CORRECTION FLUID OR TAPE ON THE ORIGINAL.

Copies of the electronic CRF (eCRF) will be provided for use as source documents and maintained for recording data for each participant enrolled in the study. Data reported in the eCRF derived from source documents should be consistent with the source documents or the discrepancies should be explained and captured in a progress note and maintained in the participant's official electronic study record.

Clinical data (including AEs, concomitant medications, and expected adverse reactions data) and clinical laboratory data will be entered into RedCap, a 21 CFR Part 11-compliant data capture system provided by the NYU Langone School of Medicine and NYU College of Nursing. The data system includes password

protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate. Clinical data will be entered directly from the source documents.

14.2 Study Records Retention

Study documents will be retained for the longer of 3 years after close-out, 5 years after final reporting/publication.

14.3 Protocol Deviations

A protocol deviation is any noncompliance with the clinical trial protocol, GCP, or Manual of Procedures (MOP) requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. As a result of deviations, corrective actions are to be developed by the site and implemented promptly.

These practices are consistent with ICH E6:

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

It is the responsibility of the site PI/study staff to use continuous vigilance to identify and report deviations within 5 working days of identification of the protocol deviation, or within 5 working days of the scheduled protocol-required activity.

All protocol deviations must be addressed in study source documents, reported to the NIA Program Official.

Protocol deviations must be reported to the local IRB per their guidelines. The site PI/study staff is responsible for knowing and adhering to their IRB requirements. Further details about the handling of protocol deviations will be included in the MOP.

14.4 Publication and Data Sharing Policy

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

The International Committee of Medical Journal Editors (ICMJE) member journals have adopted a clinical trials registration policy as a condition for publication. The ICMJE defines a clinical trial as any research project that prospectively assigns human subjects to intervention or concurrent comparison or control groups to study the cause-and-effect relationship between a medical intervention and a health outcome. Medical interventions include drugs, surgical procedures, devices, behavioral treatments, process-of-care changes, and the like. Health outcomes include any biomedical or health-related measures obtained in patients or participants, including pharmacokinetic measures and adverse events. The ICMJE policy, and the Section 801 of the Food and Drug Administration Amendments Act of 2007, requires that all clinical trials be registered in a public trials registry such as ClinicalTrials.gov, which is sponsored by the National Library of Medicine. Other biomedical journals are considering adopting similar policies. For interventional clinical trials performed under NIH IC grants and cooperative agreements, it is the grantee's responsibility to register the trial in an acceptable registry, so the research results may be considered for publication in ICMJE member journals. The ICMJE does not review specific studies to determine whether registration is necessary; instead, the committee recommends that researchers who have questions about the need to

register err on the side of registration or consult the editorial office of the journal in which they wish to publish.

The trial will be registered through clinicaltrials.gov prior to starting.

The investigators will follow the NIH policy on making available an anonymized, publicly available data set following conclusion of the study.

15 Study Finances

15.1 Funding Source

This study is financed through a grant from the US National Institutes of Health.

15.2 Costs to the Participant

There will be no costs to participate outside of usual care that is performed.

15.3 Participant Reimbursements or Payments

PWD and caregivers will each receive $25 gift cards at visits 1 and 4 and $10 gift cards at visits 2 and 3. The gift cards will be sent to the subjects based on their preference for either post-mail or electronically via REDCap. Should the PWD or caregiver miss a visit, they will not receive compensation for the visit missed.

15.4 Study Leadership

The steering committee includes the Principle Investigator, two local site PIs, one representative designated by each HHC agency, and the biostatistician co-investigator. The Steering Committee will govern the conduct of the study in coordination with the program officer of the NIA.

16 Conflict of Interest Policy

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

Any investigator who has a conflict of interest with this study (patent ownership, royalties, or financial gain greater than the minimum allowable by their institution, etc.) must have the conflict reviewed by the NYU Langone Conflict of Interest Management Unit (CIMU) with a Committee-sanctioned conflict management plan that has been reviewed and approved by the study sponsor prior to participation in this study. All NYULMC investigators will follow the applicable conflict of interest policies.

17 References

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18 Attachments

These documents are relevant to the protocol, but they are not considered part of the protocol. They are stored and modified separately. As such, modifications to these documents do not require protocol amendments.

- Consent Form-PWD
- Consent Form-Caregiver
- Assent Form-PWD
- Application for Temporary Waiver of documentation of consent-PWD
- Application for Waiver of Documentation of Consent-Clinicians
- Vulnerable Populations: Cognitive Impaired Subject Appendix
- Study Manual
- Assessment Instruments-PWD/Caregiver Dyads
- Dementia Symptom Knowledge Assessment-Clinicians
- Originally Submitted Grant
- Follow-up requested modifications by NIA as submitted by NYU Campus OSP
- COVID Questionnaire
- Email and text templates

19 Schedule of Events

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Table 2. Variables and Timing of Data Collection from PWD-Caregiver Dyads

Variable	Instruments or Measures	Items	Min.	Timing of Data Collection (Days)							
				Patient				Caregiver			
				0	15	30	60	0	15	30	60
Consent				✓				✓			
Patient-Centered Outcomes											
Stage of Dementia	Quick Dementia Rating Scale[119]	10	5					✓			
BPSD	Neuropsychiatric Inventory Questionnaire	13	5					✓	✓	✓	✓
Quality of life	Quality of Life in Alzheimer's Disease[99]	13	5					✓			✓
Pain	Brief Pain Inventory Short Form	9	5	✓	✓	✓	✓				
Pain	PAINAD	5	3	✓	✓	✓	✓				
Patient Satisfaction	HHCAHPS	32	7								✓
Pain	Analgesic use (collected by RA on each dyad visit)	1	1					✓	✓	✓	✓
BPSD	Antipsychotic use (collected by RA on each dyad visit)	1	1					✓	✓	✓	✓
Delirium	FAM-CAM[126]	11	3					✓	✓	✓	✓
Caregiver Centered Outcomes											
Quality of Life	Caregiver Targeted Quality of Life[100]	80	20					✓			✓
Depression	Public Health Questionnaire 9[104]	9	3					✓			✓
Burden	Zarit Burden Inventory[105]	22	10					✓			✓
Health	SF-12[127]	12	3					✓			✓
Utilization Outcomes											
Healthcare Utilization	Resource Utilization Inventory[101]	13	5					✓		✓	✓
Sociodemographics											
Sociodemographics	Date of birth, sex, education, race, ethnicity	6	4	✓				✓			
Language, Religion and Culture	Primary language, religion, literacy (SAHL-SE)[128]	3	3	✓				✓			
Supports											
Social Support	Marital status, household members	2	<1	✓				✓			
Other unpaid caregivers	# individuals, # visits, #hrs/week	3	1	✓	✓	✓	✓				
Paid Caregiver	# visits, hrs/week	2	1	✓	✓	✓	✓	✓			
Home nurse visits	# visits (chart)	1				✓	✓				
Physical/occupational therapy	# visits (chart)	2				✓	✓				
COVID-19 Effects on Caregiving	University of Pittsburgh COVID Caregiving Questionnaire and Investigator Derived from the Resource Utilization Inventory	18	6					✓			
Health and Functional Status											
Functional Status	Katz Activities of Daily Living[129], Lawton Instrumental Activities of Daily Living[130]	12	2	✓	✓	✓	✓				
Comorbidities	Charlson comorbidity Questionnaire[131] (chart for patient, interview for caregiver)	17	3	✓				✓			

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Table 3. GANTT Chart

TASK DESCRIPTION	Pre-Funding	YR1				YR2				YR3				YR4				YR5			
	-1	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
IRB approval and finalize procedures																					
Hire and Train Project Director																					
Develop and test Redcap database																					
Hire and Train RAs																					
Implement HHC EHR changes																					
Finalize sites, cluster randomization																					
Identify and train champions																					
Train non-champions					Ongoing as turnover occurs---------->																
Dyad enrollment																					
Quality Improvement fidelity monitoring																					
Clinician Knowledge and Attitudes Assessment																					
Data collection																					
DSMB meetings																					
Data analysis																					
Manuscripts and Dissemination																					