

PROTOCOL TITLE:

Palliative care telehealth delivered Program of SUPPORT-D Intervention for persons with Alzheimer's Disease and caregivers.

Phase 2

PRINCIPAL INVESTIGATOR:

- *Diana Layne, PhD, RN*

1.0 Objectives / Specific Aims

Assess feasibility of implementing the adapted SUPPORT-(D) intervention in up to 30 individuals living with Alzheimer's disease (PWD)/caregiver (CG) dyads in terms of recruitment, use and acceptability of the intervention, data collection methods, and obtain estimates of variability for outcome measures (e.g., QoL, acceptability, feasibility, safety, symptom burden, knowledge) to be used in the design of a subsequent adequately powered randomized control trial (RCT).

2.0 Background

Severity of the problem. It is estimated that over 11 million Americans are providing unpaid care to persons with dementia (PWD).¹ In 2021, Alzheimer's and other related dementias are estimated to cost the nation \$355 billion dollars. This is projected to increase to \$1.1 trillion dollars by 2050.¹ Dementia is a progressive, irreversible condition defined as an acquired loss of cognition in multiple cognitive domains sufficiently severe to affect social or occupational function.² Primary treatment goals for this chronic condition are to decrease suffering caused by cognitive and behavioral changes and delay inevitable progressive decline.² Healthcare utilization and costs are significantly higher in persons living with dementia compared to a demographically matched cohort.³ This population experiences a higher burden of comorbid physical disease, polypharmacy⁴ and, in advanced stages, challenges with independent mobility, increasing falls risk.⁵

The unpredictable and often extended illness trajectory coupled with progressive decreases in cognitive functioning creates a complex environment for symptom self-management often requiring family caregiver assistance. Caregivers (CG) of PWD report needing support to manage stress related to caregiving responsibilities, identifying respite care, building a network of support, and managing behavioral symptoms.⁶ Many PWD/CG dyads experience unmet needs which vary based on severity of cognitive impairment of the PWD.^{6,7} PWD and their CGs could benefit from interventions for improving early access to palliative care.⁸

Palliative care uptake among PWD remains limited. Despite a recent increase in hospice enrollments for PWD (fewer than 1% in 1995, to 18% in 2017), challenges remain with palliative care, in particular, advance care planning (ACP).⁹ Caregiver education regarding prognosis of dementia and ACP is limited.^{10,11} Initiation of palliative care among PWD is inhibited by the inability to verbalize preferences due to illness progression coupled with an often lengthy end of life phase.¹² While debate regarding the timing of the initiation of palliative care continues, ACP exists as a key milestone in care. Several possible triggers for engaging in ACP conversations include time of diagnosis, changes in care setting, changes in health status of the CG, or completion of a Lasting Power of Attorney.¹³ Advance care planning as part of the palliative care model can reduce caregiver burden and stress.¹⁴ Early ACP prior to the onset of severe cognitive impairment promotes care delivery consistent with the desires of PWD/CG and minimizes caregiver burden and stress during the end of life phase of the illness.

PWD/CG dyads face serious stressors. Evidence suggests dyadic interventions versus those that focus on solely on the individual can improve mutual understanding, communication and relationship quality among PWD/CG dyads and may have broader implications for positive health outcomes in the pair, such as reducing stress.¹⁵ Commonly reported stressors for PWD include intense negative emotions and distress, challenges obtaining accurate and helpful information, difficulty understanding diagnosis and disease trajectory, and a sense of loss of anticipated future.¹⁶ Additional stressors reported by PWD included experiences of loss, changes in relationship dynamics, living with the symptoms of dementia, learning to do things differently and establishing coping mechanisms.¹⁷ In contrast, CG report stressors associated with personal care, housekeeping, medication administration, financial responsibilities, and difficulty maintaining professional and social connections.¹⁸ Concerns for safety of the PWD were also reported by CGs.⁶ While some interventions exist to address stressors for the PWD/CG dyad, comprehensive interventions addressing most or all stressors are limited. Palliative care interventions to improve PWD/CG quality of life and safety while reducing caregiver burden are necessary.

Safety is an overlooked component of dementia care. Caregivers of PWD seek to prevent harm in four primary areas including physical harm, economic harm, emotional harm and relational harm.¹⁹ Evidence suggests 90% of community dwelling PWD have unmet safety needs, specifically related to falls risk, wander risk management and home safety evaluation.⁷ A recent systematic review of interventions for family caregivers of PWD identified 16 psychotherapeutic or psychoeducational interventions of which only 2 incorporated content related to providing a safe environment for PWD.²⁰ Martindale-Adams²¹ (2013) included a telephone delivered program with information related to safety and Pahlavanzade²² (2010) incorporated a lecture and group discussion on safety measures at home. However, outcome measures for PWD safety were not measured for either study; additionally, only one of these studies was conducted within the United States. Thus, additional research is necessary to better understand the impact of including safety as part of a palliative care intervention for PWD/CG dyads.

3.0 Intervention to be studied (A Program of SUPPORT-D)

This protocol describes the second phase of the study in which the SUPPORT-D intervention will be delivered to up to 30 PWD/CG dyads over six weeks. The SUPPORT-D intervention consists educational materials will be presented in a format with enhanced content (face-to-face virtually delivered by nurse interventionist via telehealth (e.g., MS Teams), with printed booklet, and identical digital content (electronic pdf and recorded videos of printed content). The SUPPORT-D intervention will be addressed in four sequential sections including: 1) understanding the disease 2) caring for myself; 3) information for the caregiver; and 4) planning for the future. Within the four sections of the intervention seven topics are addressed included symptom management, understanding your disease, putting safety first, ongoing conversations, respite care, palliative care, and alternative treatments. Included content for each SUPPORT-D is described in **Table 1**. The intervention contents are assembled in a bound printed book and recorded for viewing on a mobile device (tablet or smartphone) along with a pdf version of the booklet for easy reference.

4.0 Study Endpoints

Study end points include successful study completions, consent withdrawals, PI terminations, Lost contact with the patient, and unexpected adverse events.

Table 1. Included content for A Program of SUPPORT™-D

Intervention Component	Current Topics	Included content
Part 1. Understanding the disease	Symptom Management	Define dementia, discuss causes of dementia, describe what happens in the brain with dementia, discuss diagnostic tests and monitoring
	Understanding your disease	Discuss disease trajectory mild, moderate, and severe, enhancing self-management based on dementia severity, commonly asked questions, common medications, support groups
Part 2. Caring for myself	Putting safety first	<i>Discuss how dementia affects safety, home safety tips including falls prevention, risks for wandering and mitigation strategies, what to do if wandering occurs</i>
Part 3. Caring for your caregiver	Ongoing conversations	Discuss strategies for self-care, asking for help, and avoiding burnout, finding local resources, online tools for communication, <i>safety strategies for caregivers</i> , commonly asked questions
	Respite care	<i>Define respite care and provide respite care resources</i>
Part 4. Plan for the future	Palliative care	Discuss informing family and friends of diagnosis, considerations for moving forward (new/evolving treatments, advanced treatments, research participation, future care considerations), overview of palliative care, differences between palliative care and hospice, preparing for the end of life and making future care decisions
Part 4. Plan for the future	Alternative Treatments	<i>Discuss herbal remedies, dietary supplements (e.g., Coenzyme Q10, Omega-3 fatty acids), concerns about alternative therapies</i>

5.0 Inclusion and Exclusion Criteria/ Study Population

The participants in this study include persons with Alzheimer's disease (PWD) and their caregivers (CG).

- *Inclusion Criteria:*

- *Persons with Alzheimer's Disease or Mild Cognitive Impairment (we anticipate cognitive impairment within this group)*
 - *18 years old or older*
 - *Diagnosis of Alzheimer's Disease, suspected Alzheimer's disease or Mild Cognitive Impairment with (FAST score ≤4)*
 - *Able to read and speak English (intervention in English)*
- *Caregivers (CG)*
 - *≥ 18 years old*
 - *Non-paid (eliminates professional caregivers)*
 - *Provides care to someone living with Alzheimer's, suspected Alzheimer's disease or Mild Cognitive Impairment. Able to read and speak English (written materials in English)*
 - *No diagnosis of cognitive impairment*

Exclusion Criteria

- Inability or unwillingness to provide informed consent

Inclusion of a diverse population

Families with loved-ones with Alzheimer's Disease from all racial and ethnic backgrounds will be approached and invited to participate as research participants.

Statement on the non-inclusion of children

Alzheimer's disease is typically observed in older adults and not in children. Hence children are excluded from the study population.

6.0 Number of Subjects

Total of up to 60 participants (30 dyads) up to 30 persons with Alzheimer's or Mild Cognitive Impairment and 30 caregivers. Dyad members may participate individually if a caregiver is unavailable or PLWD chooses to not participate.

7.0 Setting

All aspects of this study will take place using virtual MUSC communication platforms means such as telephone, email or a meeting platform such as MS Teams. Initial study procedures (consent, basic demographic questionnaire and baseline measures) and subsequent visit measures will be completed remotely using REDCap survey. Post-intervention interviews will be conducted virtually. Participants will be able to participate in this study in the comfort and privacy of a setting of their own choosing.

8.0 Recruitment Methods

- **Person with Alzheimer's/Caregiver Recruitment**-Providers at MUSC Memory Disorder Clinic and/or MUSC Geriatric Clinic will identify potential participants dyads and ask permission from the patient/caregiver for the PI or program coordinator (PC) to contact the caregiver for screening. Once permission is granted, the PI, or PC will contact the caregiver and assess for eligibility and enrollment.
- Study participants from Dr. Kelechi's (Kelechi: R01 and Supplement) and Dr. Mintzer's (Multi-site R01) study population (those who agreed to be contacted for future studies) will be contacted.

- Study flyers will also be placed in clinic and public areas throughout the Medical University of South Carolina Enterprise. The flyers will include the PI/PC contact information; interested participants who call the PI/PC will be screened for eligibility.
- Electronic flyers, advertisements, and study information will be posted on social media channels (e.g., Facebook), on Research Match, and will be sent to professional and community-based organizations focused on care of people with Alzheimer's Disease to disseminate among their clients.
- Flyers will also be shared with local respite care centers offering early memory loss programs to share with potentially interested participants
- Families with loved ones that have been recently diagnosed with Alzheimer's Disease and are seen in the clinics of research team members who are MUSC clinicians will be approached and given a study flyer.
- The researchers will submit a BMIC honest broker Research Data Request to obtain a recruitment report of MUSC patients who potentially meet the study's eligibility criteria (ICD diagnosis of Alzheimer's Disease). The researchers will not cold-contact any patients who have chosen to opt-out of receiving contact about research and/or that have reached the maximum contact attempts at the time of recruitment. Researchers will use a Cold Calling telephone script to approach patients and follow MUSC policies and procedures for Cold Contact.

9.0 Consent Process

Electronic consenting-e-Consenting will be performed with eligible PWD/CG dyads that desire to participate in the study. Dyads identified through the recruitment process that are unavailable for face-to-face consenting will have spoken to the researchers by telephone to discuss the study and its demands as well as had any initial questions answered. Dyads will be asked to provide an email address to facilitate receipt of a REDCap survey link containing a scanned image of the most recently approved Informed Consent document (developed using the MUSC REDCap e-consent template). Dyads will be allowed as much time as necessary to read the consent document together in their own home or at a place/time of their choosing. They will be provided with contact information (telephone and email) for the researchers in the survey instruction header should they have additional questions prior to consenting to participation by adding their respective signatures to the form and submitting. Prior to providing physical e-consent researchers will coordinate with the dyads to ensure the availability of the researcher by telephone to answer any questions that may arise during the e-consent process. Once the e-consent is submitted a REDCap trigger will immediately notify the researchers, who will then countersign the document.

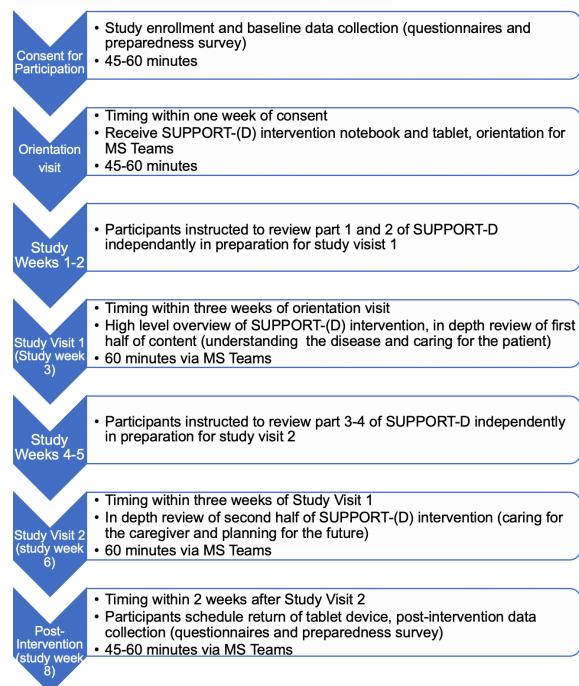
PWD with legal healthcare power of attorney: Caregivers that have a legal healthcare power of attorney for the PWD will provide consent for the PWD in addition to consenting for their participation as a caregiver.

PWD without legal healthcare power of attorney: PWD without legal healthcare power of attorney will be screened using the Evaluation to sign Consent (ESC) measures following review of the consent form. The ESC includes five items which determines the ability of a subject with cognitive impairment to sign consent using the following four questions; 1) name at least 2 potential risks incurred as a result of participating in the study 2) name at least 2 things that will be expected of him or her in terms of patient cooperation during the study, 3) explain what he or she would do if he or she no longer wished to participate in the study, 4) explain what he or she would do if he or she was experiencing distress or discomfort. Question 5 of the ESC was omitted as it relates to randomization which is not planned for this study. Subjects with dementia that correctly answer all four questions will complete an informed consent form. Ongoing consent will be assessed at the beginning of study visit 1 and 2 as well as during post intervention interviews. Caregivers will be instructed to notify the PI of any change in cognitive status of the PWD immediately. For any PWD with changes in cognitive status will be reevaluated with the ESC measures and reconsented.

10.0 Study Design / Methods

Intervention activities include delivering the intervention materials with up to 30 PWD/CG dyads with measurement of feasibility, process, and outcomes. Thirty enrolled PWD/CG dyads will be provided with the SUPPORT-D written materials, an electronic pdf of the SUPPORT-D booklet and links to electronic videos reviewing the content of the written booklet. Participants will be provided the option to utilize their personal mobile device to access digital content and MS Teams to determine which is method is preferred (print or digital) and to facilitate sharing of intervention materials with family members at a distance unable to review print materials. For those that do not have access to a personal mobile device a mobile device (tablet) with the digital content preloaded and MS Teams preloaded for use throughout the study period. Following consent and study enrollment, baseline measures will be completed electronically by participants via an email link or verbally by the PI or research assistant (RA). This is followed by an orientation visit with the PI or RA where participants will receive intervention materials, orientation for accessing digital material, instructions for sharing digital resources with friends and family and detailed instructions on how to access the video conferencing software MS Teams from the personal device/provided tablet for study visits and a support number to call for technical assistance if necessary. Participants will retain the device and printed materials for the length of the study. Participants will be asked to return provided tablet devices at the end of the 8-week study period. However, participants will retain printed materials and identical digital materials at the end of the study period. The first virtual study visit via telehealth (e.g., MS Teams) with the nurse interventionist will be scheduled within 1 week of receiving tablet device/orientation. During this first virtual study visit the SUPPORT-D intervention will be delivered via MS-Teams for approximately 60 minutes by the nurse interventionist using a manual for guidance and recorded for fidelity monitoring. To ensure standardized content is provided the nurse interventionist will respond to questions by referencing the provided materials. If questions go beyond content, the interventionist will advise patients to consult their provider and assist the PWD/CG dyad in crafting questions that address additional concerns. The focus of this visit will be to provide an overview of the intervention, review detailed content for the first two parts of the intervention (understanding the disease and caring for myself) and provide participants instruction in maintaining an electronic or paper self-report log of home use of SUPPORT-D materials including when, what and how (format), content was reviewed and if shared with others (who, when, feasibility). Dyads will be encouraged to review these materials at home and share information with other family members. The PI will conduct fidelity monitoring for 10% of all study visits. Two weeks after the first virtual study visit dyads will be scheduled for a second virtual study visit via with nurse interventionist for delivery of parts 3 and 4 (information for the caregiver and planning for the future) of the intervention via MS Teams and recorded for fidelity monitoring. This session should last approximately 60 minutes. The nurse interventionist will utilize a manual for guidance to tailor study visit discussions according to baseline data collection, emphasizing areas of evident knowledge deficit based on questionnaire responses. All participants will

Figure 2. Intervention Delivery Timeline



attend a virtual post-intervention meeting (study week 8) with the PI via MS-Teams during which post-intervention data will be collected and a time scheduled for returning the tablet device. The PI will meet with the nurse interventionist weekly during the intervention. Each dyad will receive the SUPPORT-D intervention for a span of six-weeks with a two-week post intervention follow up (8-week total study period). The timeline for intervention delivery is also described in Table 2.

Post-intervention interviews. At the conclusion of the study period all dyads (30 dyads) will be asked their willingness to participate in post-intervention key informant interviews. Of those that express a desire to participate 10 dyads will be randomly selected via computer to participate in a post intervention interview with the PI to obtain more in-depth feasibility data related to accessibility, usability, and adherence to the intervention. A qualitative descriptive approach will be used to conduct the semi-structured interviews, which will last 45-60 minutes. An interview guide with open-ended questions and probes will be used to guide the semi-structured interview. Interviews will be recorded for the purposes of transcription for data analysis.

Table 2: Variables for Aims 1 and 2

McMillan Good Death Model Domain and major tasks	Measure/Instrument/ Psychometrics/Instrument scoring	Data sources and time points
Fixed characteristics of the patient		
Demographics/clinical characteristics	Age, gender, race, education, health history, date of diagnosis, diagnosis, # comorbidities	PWD/ CG, baseline
Modifiable dimensions of patient experience		
Knowledge	Alzheimer's Disease Knowledge Scale (ADKS), 30-items (TF), Cronbach's alpha .80 ²³ , summed total of correct items	PWD/CG, baseline and post-intervention
Acceptability of Intervention	Acceptability of Intervention Measure (AIM), 4 items; Cronbach's alpha 0.75-0.90 ²⁴ , calculated mean	PWD/CG, post-intervention
Feasibility	# days intervention use recorded, # times intervention materials shared, rates of recruitment, % eligible, consented, # times unable to access digital materials or meeting software; Intervention Appropriateness Measure (IAM) 8 items; Cronbach's alpha (0.77-0.87) ²⁴ , calculated mean Feasibility of Intervention Measure (FIM) (0.79-0.94) ²⁴ , calculated mean, content analysis from key informant and post-intervention interviews	PWD/CG, baseline, study visits 1 and 2, post intervention
Caregiver Burden	Zarit Caregiver Burden, 12 items; Cronbach's alpha 0.88 ²⁵ , summed score across items	Caregiver, baseline, post intervention
Perceived Stress Scale	Perceived Stress Scale (PSS); 10 items Cronbach's alpha > .70 ²⁶ , summed score across all items	PWD/CG, baseline, and post-intervention
Symptom Burden	Promis-29 v. 2.1, 29 items; Cronbach's alpha 0.89-0.95 ²⁷ , summed score converted to T-score ²⁸ Physical function, anxiety, depression, fatigue, sleep, quality, satisfaction with social role, and pain	CG/PWD (if able), baseline and post-intervention
Quality of Life	Quality of life-Alzheimer's Disease (QOL-AD); 13 items; Cronbach's alpha 0.74 for patients 0.66 for proxies ²⁹ , summed score	PWD (if able)/CG proxy, baseline, and post-intervention
Disease Preparedness	Self-Efficacy for Caregiving; 8 items; Cronbach's alpha 0.88, test-retest reliability .79, mean score across items Carer Support Needs Assessment Tool, 14 items summed score ³⁰	CG, baseline, and post-intervention
Safety	Safety Assessment Scale, 32 items, ICC 0.91, test-retest reliability 0.88 ³¹ , summed score across items	CG, baseline, post-intervention
Technology literacy	Digital Health Literacy Instrument; 21 items, Cronbach's alpha 0.87 ³² , total mean score	PWD/CG baseline and post-intervention
Care-system interventions		
Advance Care Planning (ACP)	ACP Survey, 2 items (Y/N) Pt completed >50% ACP-Y/N	PWD/CG, post-intervention

Additionally, those that complete the study will be invited to participate in a semi-structured interview to provide additional feedback on the digital version of the SUPPORT-D intervention. The same process described for the post-intervention interviews will be used to gather this feedback.

Measures. Self-report and proxy assessments will be completed by PWD, and CG utilizing participant personal mobile device or provided tablet to electronically answer the study measures directly into REDCap or asked verbally by the PI or PC. Measures of knowledge, acceptability, feasibility, stress, symptom burden, quality of life, disease preparedness, safety, technology literacy and advanced care planning will be collected from PWD/CG dyads. Specific instruments, scoring and psychometric properties are described within Table 2. The PI or PC will be present during baseline and post-intervention data collection to answer questions but will be unobtrusive during data collection. The data will be stored in REDCap.

Statistical Analysis Plan: We will obtain multiple measures to assess feasibility and inform future efficacy and effectiveness trials. Variables pertaining to the study procedures and participant demographic variables will also be collected. Data to be collected is described within Table 2. Specifically, 95% confidence intervals for proportions will be used to estimate dichotomous outcomes including proportion of participants who agree to participate out of those approached, and the proportion adherent to the intervention protocol (i.e., attendance at all study visits). Frequency distributions, median and mean responses (with 95% confidence intervals) will be obtained for continuous feasibility measures (e.g., time spent using SUPPORT materials between study visits, number of times SUPPORT content shared with others) as well as measure of practicability (e.g., number of calls for assistance, inability to access telehealth meeting software, number of chat messages received for intervention content related questions). Qualitative data gathered from post-intervention key informant interviews will be analyzed using directed content analysis.³⁴

Outcome measures and estimates of preliminary impacts: Measures of central tendency (mean, median), variability and frequency distributions as appropriate will be used to analyze demographic and clinical characteristics. Variability estimates of changes from baseline to post intervention for knowledge, quality of life, symptom burden, stress, and safety with 95% confidence intervals (without p-values) will be provided.

Sample size considerations: The purpose of this study is to establish feasibility, acceptability, and practicability of implementing the SUPPORT-D intervention, therefore a sample size calculation was not performed. Sample size for Phase II was determined for pragmatic reasons including time to deliver intervention, and availability of mobile devices for intervention delivery, The PI and PC plan to recruit participants over a three-month period using methods described within section 8 of this protocol. To ensure a consistent workload of the PI and interventionist we anticipate recruiting 1-2 dyads weekly during the recruitment period for up to 30 PWD/CG dyads.

Compensation: Reimbursement for dyads will be \$100 provided in \$25 increments over four time periods (enrollment/baseline data collection, study visit 1, study visit 2, and post intervention visit) with dyads in key informant interviews receiving an additional \$25.

12.0 Data Management

Data Capture and Management. This study will use Research Electronic Data Capture (REDCap) for data capture and management. REDCap is a software toolset and workflow methodology for the electronic collection and management of research and clinical trials data. REDCap provides secure, web-based, flexible applications, including real-time validation rules with automated data type and range checks at the time of data entry. Exports are made available for several statistical packages including SPSS, SAS, SATA, R and Microsoft Excel. The study-specific REDCap database will be designed and developed by MUSC research team. The provision of REDCap is made available through the South Carolina Clinical & Translational Research (SCTR) Institute at MUSC with NIH Grant awards UL1RR029882 and UL1TR000062.

Participant screening and enrollment-Data from participants screened for study enrollment will be entered into an electronic study database. Designated research staff will collect, gather, and enter required data (written informed consent, medical history, and demographics) onto study data forms. Screened patients who do not meet study eligibility will have specific screening data entered in the study database. The collected data will be helpful in examining the patient population and feasibility of enrollment criteria and will include gender, age, race, and reason for exclusion. All dates will be shifted, and other Personal Health Information (PHI) will be removed from the study database upon study completion. All data obtained from this study will be used for research purposes only and will comply with Federal HIPAA regulations. Master Screening and Enrollment Logs will be maintained electronically and will be used to prepare reports on accrual and attrition for the PI and SMC.

Case report forms-This study will utilize electronic case report forms (e-CRFs). All study specific e-CRFs will be designed by the PI or PC and transferred for use in the study's centralized REDCap database. These study specific eCRFs (study logs for correspondence, compensation, and other forms such as pre-eligibility screens) will be coded by the participant's unique study ID# for all data collected and will be maintained within the participant research record.

Binders-The PC will maintain a unique electronic study record for participants containing all eCRFs records. A regulatory e-file will also be maintained to include the IRB-approved Protocol, original Informed Consent documents, and other study-related regulatory documents. Access to the research record, (study database and PHI's) will be restricted to study personnel as approved by the PI and MUSC IRB. As with all studies conducted at MUSC, this study is also eligible for a random audit by MUSC Office of Compliance.

Data security-Ensuring data security, compliance with 45 CFR 46 and maintaining the integrity of PHI is a top priority. MUSC has Standard Operating Procedures (SOP) to ensure a high level of data security while coordinating electronic and paper data management activities for clinical research trials. The REDCap study database will be hosted in the Biomedical Informatics secure data center at MUSC, a secure environment for data systems and servers on campus, and includes firewall, redundancy, failover capability, backups, and extensive security checks. The secure data center has strict access control; only authorized core personnel may access the facility un-escorted. Only authorized users are allowed to connect to the network, and the security of the network is actively monitored. Power and environmental controls have several layers of backups, from interruptible power supplies to alternate and redundant feeds to the local utility company. The REDCap system administrator contributes to the maintenance of institutional disaster recovery and business continuity plans. Load balancers and a highly fault tolerant SAN infrastructure contribute to high availability.

Data entry-Only MUSC IRB approved study personnel that are authorized to have access to the REDCap study database will be granted password access. Study personnel using computers that are connected to the Internet will directly enter data into the remotely housed database. As such, no electronic study data will be stored on hard drives and/or any portable electronic devices. Additionally, all personnel with access to the database will have current University of Miami CITI training in the Conduct of Human Subject Protections, and Good Clinical Practice (GCP) training in the Conduct of Human Subject Protections, and HIPAA and Information Security trainings that are completed annually. Each participant will be assigned a unique study identifier, all PHIs will be masked, and data exports will be limited to the PI, the PC, and the BS for generating reports and the conduct of statistical data analysis.

Data monitoring-The PI or PC will conduct routine monitoring of the study database and generate a report for the PI to review at study team meetings. Standing agenda items for these meetings will include participant recruitment and retention, AE's, protocol deviations, data integrity and overall study conduct. The PI will work with the PC to resolve and validate discrepant data. Discrepancies that warrant clarification will be sent to appropriate parties for review and resolution. All data entry and changes made in the study database by authorized study personnel will be automatically logged by REDCap and provide a transparent visible audit trail for reviewers. Protocol deviations will be reported by the PI in accordance with Institutional policy.

Audio Recordings and Transcriptions: Participant interviews will be recorded using audio voice recorders. Audio recordings will be uploaded for transcription within 48 hours to an outside agency with which MUSC has established a Business Associates Agreement (BAA). Once uploaded, all audio recordings will be deleted from the portable storage device. The recorded interview will then be immediately erased from the portable voice recorder. Transcription will only include the study ID number without PHI. Interview transcriptions will be stored in a standard file format in REDCap. Research staff will conduct daily checks of data transfer. A linkage file for the study ID number and PHI will be maintained in a password-protected server behind the MUSC firewall in order to link the questionnaire and interview data.

13.0 Provisions to Monitor the Data to Ensure the Safety of Subjects

The PI, Dr. Layne will be responsible for the overall monitoring of the safety of the study and the Program Coordinator (PC) Mrs. Pittman will be responsible for the daily monitoring and safeguarding of study data to ensure the safety and protection of all human study participants. Mrs. Pittman will report observed and solicited adverse events, and protocol deviations to Dr. Layne. Dr. Layne will be responsible for the classification of all reported adverse events (AE) and for ensuring that all serious adverse events (SAE), protocol deviations, and 'other' reportable events are forwarded to MUSC IRB in compliance with institutional policies and procedures. Mrs. Pittman will also be responsible for maintaining the electronic

regulatory binder, ensuring data management validation and verification of the electronic study research database.

Monitoring Study Safety. From initial screening of study participants utilizing inclusion and exclusion criteria; to the informed consent process; to intervention delivery; to training in Good Clinical practices (GCP) and regulations pertaining to the Conduct of Human Participant Research for study personnel; to routinely scheduled study contact with enrolled participants; to protocol fidelity monitoring; to the real time review of AEs; and oversight of MUSC's IRB-procedures for examining study safety are consistently afforded throughout the study. Specific procedures include:

- Participant screening using established inclusion/exclusion criteria per the protocol.
- Full disclosure of all known risks and the possibility of risk from study participation to participants during the informed consent process. Note these risks are minimal.
- Participants will be informed to notify the researchers of any/all suspected or experienced adverse events whether the event is believed to be related or not to the intervention.
- PI or PC will track all reported AE through to resolution.
- All members of the research team will maintain CITI and GCP training.
- PI or PC will maintain weekly contact with all participants to enquire about AE's, monitor study progress, compliance, and safety.
- Participant study logs will be reviewed by the PI or PC to monitor for fidelity compliance with the intervention.
- Quarterly internal quality control audits by the PI or PC of all participant records are planned to ensure compliance with MUSC IRB regulations. The PI and PC will collaborate to resolve any identified errors.
- MUSC IRB and ORI will monitor Investigator compliance and performance.

Minimizing Research-Associated Risk. Study safety monitoring will be conducted by the PI and members of the research team throughout the conduct of this study in compliance with MUSC IRB's continuing review process:

- Tracking and follow-up of participant accrual including withdrawn consents will minimize risk by identifying, disclosing, and mitigating any potentially unknown risk(s) of harm to study participants.
- Timely and appropriate reporting of informed consent process deficiencies, protocol deviations, privacy breaches, conflicts of interest, and/or changes in personnel.
- Ongoing soliciting, monitoring, and appropriate reporting of adverse event activities.
- Timely and appropriate IRB submission of safety-related documents such as audit reports, sponsor progress reports, ISM reports, and other materials or communications that might impact the safe conduct of this study.
- Active cooperation with the IRB, ACO, sponsor, and other applicable entities in the event of a random or for-cause internal or external audit.

14.0 Withdrawal of Subjects

Participants (PWD and CG) may withdraw their consent at any time for any or no given reason while enrolled in the study. The PI may withdrawal a participant at any time if it is in the best interest of the participant, if they do not follow the investigator's instructions, or if they fail to keep study visits. Withdrawal may also occur in the event of a protocol violation or early closure of the study.

15.0 Risks to Subjects

We do not anticipate any significant risks related to participation in survey completion, or post intervention interviews. However, as with all studies, there are inherent risks involved with the conduct of human subject research that gathers Protected Health Information (PHI). Participants will be made aware of these risks during the Informed Consent process. Identified study risks include: Loss of privacy, emotional distress, and physical discomfort

Loss of privacy: PHI from participants will be gathered and stored electronically on secure and encrypted servers and there are risks associated for the loss of privacy and confidentiality. We will further minimize the potential for loss of confidentiality through the physical separation of participant names from their research record according to the process described above. Audio recordings of participants interviews will be uploaded for transcription within 48 hours to an outside agency with which MUSC has established a Business Associates Agreement (BAA). Once uploaded, all audio recordings will be deleted from the portable storage device.

Emotional distress: Some of the questions asked may be upsetting to participants or make them feel uncomfortable answering them. Participants will be instructed that if they do not wish to answer a question, they can skip it and go to the next question. In the rare and unexpected event of serious or life-threatening levels of distress, participants will be instructed to call 911 and/or visit the closest Emergency Department. In the event the caregiver expresses concern for the person living with Alzheimer's disease they will be referred to their primary care physician.

Physical fatigue: Completion of the sessions, questionnaire, measures and interviews may be tiring to some participants. Participants will be given ample time to complete the questionnaire and may take breaks as necessary throughout all study procedures.

In the rare and unexpected event of serious or life-threatening levels of distress, participants will be instructed to call 911 and/or visit the closest Emergency Department. In the event the caregiver expresses concern for the person living with Alzheimer's disease they will be referred to their primary care physician.

16.0 Potential Benefits to Subjects or Others

Participating in this study provides no direct medical benefit. We hope information learned from this study will aid patients with Alzheimer's Disease, their caregivers, and clinicians in the future.

17.0 Sharing of Results with Subjects

The results of this study will not be shared with research participants.

References

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