HRP-592 - Protocol for Human Subject

Research with Use of Test Article(s)

Protocol Title:

Provide the full title of the study as listed in item 1 on the "Basic Information" page in CATS IRB (http://irb.psu.edu).

Reducing Disability via a Family-centered Intervention for Acutely Ill Persons with Alzheimer's disease and Related Dementias

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Version Date:

Provide the date of this submission. This date must be updated each time the submission is provided to the IRB office with

June 8, 2021

Clinicaltrials.gov Registration #:

Provide the registration number for this study, if applicable.

NCT03046121

Important Instructions for Using This Protocol Template:

1. Add this completed protocol template to your study in CATS IRB (http://irb.psu.edu) on the "Basic Information" page, item 7.
2. This template is provided to help investigators prepare a protocol that includes the necessary information needed by the IRB to determine whether a study meets all applicable criteria for approval.
3. **Type your protocol responses below the gray instructional boxes of guidance language. If the section or item is not applicable, indicate not applicable.**
4. **For research being conducted at Penn State Hershey or by Penn State Hershey researchers only, delete the instructional boxes from the final version of the protocol prior to upload to CATS IRB (http://irb.psu.edu). For all other research, do not delete the instructional boxes from the final version of the protocol.**
5. When making revisions to this protocol as requested by the IRB, please follow the instructions outlined in the Study Submission Guide available in the Help Center in CATS IRB (http://irb.psu.edu) for using track changes.

If you need help…	
University Park and other campuses: Office for Research Protections Human Research Protection Program The 330 Building, Suite 205 University Park, PA 16802-7014 Phone: 814-865-1775 Fax: 814-863-8699 Email: irb-orp@psu.edu	**College of Medicine and Hershey Medical Center:** Human Subjects Protection Office 90 Hope Drive, Mail Code A115, P.O. Box 855 Hershey, PA 17033 (Physical Office Location: Academic Support Building Room 1140) Phone: 717-531-5687 Fax number: 717-531-3937 Email: irb-hspo@psu.edu

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1.0 Objectives

1.1 Study Objectives

Describe the purpose, specific aims or objectives. State the hypotheses to be tested. Describe the treatment that is considered standard of care (i.e., indicate how patients would be treated in a non-investigational setting). Indicate if the study test article(s) is available to patients without taking part in the study.

The overall aim of this study is to conduct a formal, real world test of the efficacy of Family-centered function-focused care (Fam-FFC) on patient and caregiver-centered outcomes in community- dwelling, hospitalized older adults with very mild to moderate dementia.

Aim 1: Validate the efficacy of Fam-FFC on physical function (ADLs/ performance and physical activity), delirium occurrence and severity, behavior, and mood.

***H_1**: Patients exposed to Fam-FFC will demonstrate more return to baseline ADL function as compared to those in the control condition.*

***H_2:** Patients exposed to Fam-FFC will demonstrate increased physical activity, improved chair rise and less delirium occurrence and severity, less NPS, and less depression, as compared to those in the control condition.*

Aim 2: Evaluate the impact of Fam-FFC on CG –centered outcomes.

***H_3:** CGs exposed to Fam-FFC will demonstrate improved preparedness for caregiving, and less strain, burden, and desire to institutionalize as compared to those in the control condition.*

Aim 3: Evaluate the relative costs for Fam-FFC v. control condition, and calculate health care (post-acute health care utilization) costs and total cost savings for Fam-FFC.

***H_4**: Patients exposed to Fam-FFC will demonstrate higher intervention costs but lower post-discharge cost for health care services (emergency room admissions, hospital admissions, and long-term nursing home admissions) as compared to those in the control condition.*

***H_5**: Patients exposed to Fam-FFC will demonstrate total cost savings overtime as compared to those in the control condition.*

***Exploratory Aim**: Assess the cultural appropriateness of Fam-FCC for diverse families.*

1.2 Primary Study Endpoints

State the primary endpoints to be measured in the study. Clinical trials typically have a primary objective or endpoint. Additional objectives and endpoints are secondary. The endpoints (or outcomes), determined for each study subject, are the quantitative measurements required by the objectives. Measuring the selected endpoints is the goal of a trial (examples: response rate and survival).

P**atient outcomes**: physical function (return to baseline ADLs/ performance, physical activity), delirium occurrence and severity, neuro-psychiatric symptoms, and mood.
Family CG-centered outcomes: preparedness for caregiving, strain, burden, and desire to institutionalize.
Relative **costs** for Fam-FFC v. control condition,**health care cost** (post-acute health care utilization) and **total cost savings** for Fam-FFC.

1.3 Secondary Study Endpoints

State the secondary endpoints to be measured in the study.

Cultural appropriateness of Fam-FCC.

2.0 Background

2.1 Scientific Background and Gaps

Describe the scientific background and gaps in current knowledge.

Persons with Alzheimer's disease and related dementias (ADRD) account for 3.2 million hospital admissions per year and are about two times more likely to be hospitalized than their peers who are cognitively healthy.[1-4] Once hospitalized, individuals with ADRD are more likely to experience potentially preventable complications such as delirium, neuropsychiatric symptoms (NPS), pressure ulcers, falls, and nutritional deficiencies.[5-8] The unfortunate consequences of this combination of factors is that persons with ADRD often have clinically significant functional decline resulting in increased risk for hospital readmission, emergency department use, morbidity, earlier mortality,[9-14] and long-term care placement. [15,16]

Prior to hospitalization, approximately 75% of hospitalized patients with ADRD are living at home and receiving care from family members or friends,[2, 17,18] Upon hospitalization, the goal of most families is to have their relative return home.[19,20] However, family caregivers (CGs) are limited in the amount of physical care they can provide in terms of lifting, moving and providing incontinence care.[21] The additive stress of the hospitalization, and the patient's increased functional dependency, often co-existing with persistent delirium, compounds the strain of the family CG,[58] prompting the decision to seek long-term nursing home care.[22,23] It is particularly important, therefore, that patients with ADRD receive the type of care, beginning at admission and continuing through the post-acute transitional period, that optimizes function and physical activity and helps prevent or decrease functional decline.

In hospital settings, acute illness, superimposed upon baseline cognitive and functional vulnerabilities,[24-31] account for only some of the functional decline associated with hospitalization of the person with ADRD. Our team's extensive preliminary work identified factors associated with negative outcomes, including: 1) non-dementia friendly care processes (i.e., inadequate assessment of patient/CG needs and preferences),[32,33] 2) activity-restrictive policies and environments,[34-39] 3) staff under-prepared to care for persons with cognitive impairment,[40,41] and 4) patient, staff, and CG attitudes regarding physical activity in the acute setting. [42,43] Another salient finding was that patients were more likely to be involved in function–promoting activities (e.g., walking, using the toilet) when family CGs encouraged them and advocated for them to do so.[43-44]

Specialized hospital programs have effectively improved some patient outcomes, such as reduced delirium.[45-48] These programs do not, however, include the needed approaches to promote return of the person with ADRD to pre-hospital function, and the ability to return to home and remain at home. Researchers have identified that a social-ecological approach (function-focused care; FFC) improves functional outcomes in long-term care residents with ADRD.[49-53] FFC components include: 1) policy and environmental assessment; 2) staff education; and (3) mentoring and motivating nursing staff and patients. Our team has conducted a series of preliminary studies demonstrating the benefits of adapting this model for the hospital setting.[42-44, 54-58] In an intervention entitled, Family-centered function-focused care (Fam-FFC), we modified FFC components to the unique needs of hospitalized patients with ADRD and their family CGs.[59]

Fam-FFC provides expert dementia care by formal caregivers (nursing staff) through adaptations to the physical and care environment but, importantly, incorporates the additional component of the patient's family CG. In our *unique* family-centered care approach, nurses purposefully engage CGs in the assessment, decision-making, care delivery, and evaluation *beginning at admission, continuing through the hospital stay and the 60-day post-acute period*. Fam-FFC emphasizes the critical role of CGs as often the expert, voice, and advocate of the patient's needs and desires. In non-randomized, feasibility pilots, Fam-FFC demonstrated moderate effect sizes in improving ADL function and reducing delirium as well as increasing family CG preparedness for caregiving, without increasing CG strain.[59,60] ***These pilot findings warrant an efficacy trial.***

2.2 Previous Data

Describe any relevant preliminary data.

- **Understanding and documentation of functional decline in hospitalized older adults**. From our longitudinal, descriptive studies, [36, 55] we concluded: (a) most patients (70-80%) did not return to baseline function; (b) hospitalization is often preceded by a decline in functional status (worse in situations of high family caregiver strain[115]); and (c) factors associated with failure to return to baseline by discharge included lower baseline and admission ADL function, delirium, and cognitive impairment. We also found that controlling for baseline/admission ADL function and cognition, the degree to which nurses encouraged self-care and physical activity in routine interactions with patients (FFC) was associated less functional (ADL) loss from admission to discharge, and baseline

to discharge.[55]

- **Barriers and facilitators to the engagement of older adults in functional and physical activities**. Qualitative and mixed method approaches identified barriers: [42-44, 54, 56] (a) intrinsic patient factors including cognitive impairment, delirium, depression, fear of falling, and symptoms (emphasizing the need for individualized treatment plans); (b) inadequate staff knowledge regarding care of the patients with dementia including behavioral manifestations of distress, techniques to motivate, and communication and collaboration with families; (c) family beliefs and attitudes toward physical activity; (d) environmental impediments (e.g., inadequate bed/toilet height, seating, walking paths, lighting, access to assistive and sensory devices); (e) policy barriers such as inadequate assessment of physical and cognitive function; inadequate information of the patient's social profile and family roles; lack of a care planning process to address symptom management, delirium prevention, and function; and the need to incorporate plans for functional recovery into discharge planning and post-acute follow-up. The family CG can provide motivation, support, and encouragement to promote physical activity but was rarely engaged to do so. [42-44, 54, 56] This work informed the development of Family-centered Function-focused Care (Fam-FFC).

- **Development and Feasibility Testing of Fam-FFC**.

  The first pilot study (24% of eligible recruited; attrition less than 5%, 28% of sample with ADRD) demonstrated feasibility of the staff training, nurse champion role, environmental and policy assessments, systematic method of partnering with families in function-focused care, and post-acute follow-up.[60] Treatment fidelity observations of care delivery by nursing staff showed ≥ 90% agreement between the care plan and enactment of the plan. Qualitative data showed that families of persons with ADRD reported the need for education, support, and engagement unique to managing their relative with ADRD.[60] This pilot study identified the need for more robust recruitment/ enrollment strategies and customization of Fam-FFC for persons with ADRD (including adapted communication, motivation techniques, behavioral support). The subsequent pilot study addressed these issues.

  The second pilot study conducted with hospitalized medical patients with ADRD [60] incorporated recruitment approaches to include: a) twice a day phone contact with unit secretaries to capture potential participants,(b) incentives for unit managers to assist recruiting (free continuing education programs for staff unrelated to the study focus), and (c) the coordination of recruitment activity so as not to conflict with routine patient and staff activity (e.g., rounds, meals, peak personal care times). Enrollment of eligible patients increased from 24% in the first pilot [60] to 41% of potential and 97% of eligible participants enrolled in the second study.[59] Patients were able to participate in data collection and tasks. Attrition and missing data was less than 5% in both pilot studies.[59,60] Similar to the first pilot, patients exposed to Fam-FFC demonstrated closer return to baseline ADL performance (X^2 p = .003) at two months post-discharge, less 30-day hospital readmissions (X^2 = 5.8, p = .02), and less delirium (X^2 = 3.8, p = .05). CGs who participated in Fam-FFC reported better preparedness for caregiving (F (2.6) = 3.0, p =.04, partial η2= .06), from admission to two months post-discharge, with no significant increases in strain or decreased mutuality (relationship with the patient). [59, 60] These pilot studies however, were limited by a lack of randomization, single site selection, and lack of cost-effectiveness measurement.

2.3 Study Rationale

Provide the scientific rationale for the research.

In summary, we have demonstrated that Fam-FFC is feasible to implement for hospitalized persons with Alzheimer's disease and related dementias. We found that hospital nursing staff can integrate FFC into their practice and that CGs can adapt this approach in their various role functions.

The **next step** is to conduct a randomized, controlled trial to further our understanding of mechanisms of functional decline. This design will allow us to examine functional decline over a longer period of time, validate both the short and long term consequences of functional decline as well as cost, and determine how a multi-component intervention can alter this course. We are particularly interested in building caregiver science to understand whether and how caregivers become an essential part of the hospital care team, and whether this is associated with better overall CG outcomes as well.

3.0 Inclusion and Exclusion Criteria

Create a numbered list below in sections 3.1 and 3.2 of criteria subjects must meet to be eligible for study enrollment (e.g., age, gender, diagnosis, etc.). Indicate specifically whether you will include any of the following vulnerable populations: (You may not include members of these populations as subjects in your research unless you indicate this in your inclusion criteria.) Review the corresponding checklists to ensure that you have provided the necessary information.

- **Adults unable to consent**
  - Review "CHECKLIST: Cognitively Impaired Adults (HRP-417)" to ensure that you have provided sufficient information. HRP-417 can be accessed by clicking the Library link in CATS IRB (http://irb.psu.edu).
- **Individuals who are not yet adults (infants, children, teenagers)**
  - If the research involves persons who have not attained the legal age for consent to treatments or procedures involved in the research ("children"), review the "CHECKLIST: Children (HRP-416)" to ensure that you have provided sufficient information. HRP-416 can be accessed by clicking the Library link in CATS IRB (http://irb.psu.edu).
- **Pregnant women**
  - Review "CHECKLIST: Pregnant Women (HRP-412)" to ensure that you have provided sufficient information. HRP-412 can be accessed by clicking the Library link in CATS IRB (http://irb.psu.edu).
- **Prisoners**
  - Review "CHECKLIST: Prisoners (HRP-415)" to ensure that you have provided sufficient information. HRP-415 can be accessed by clicking the Library link in CATS IRB (http://irb.psu.edu).
- **Neonates of uncertain viability or non-viable neonates**
  - Review "CHECKLIST: Neonates (HRP-413)" or "CHECKLIST: Neonates of Uncertain Viability (HRP-414)" to ensure that you have provide sufficient information. HRP-413 and HRP-414 can be accessed by clicking the Library link in CATS IRB (http://irb.psu.edu).

3.1 Inclusion Criteria

List the criteria that define who will be included in your study.

FOR THE PRIMARY STUDY AIMS

Patient

1. age ≥ 65
2. speak English or Spanish
3. live in the community prior to admission to the hospital
4. screen positive for dementia on well-validated scales (Montreal Cognitive Assessment {MoCA} ≤ 25[123-127] and AD8 ≥2 with symptoms evident for several years[128,129]
5. have a diagnosis of very mild to moderate stage dementia as confirmed by a score of 0.5 to 2.0 on the Clinical Dementia Rating Scale[130]
6. have a family caregiver as the designated study partner for the duration of the study.

Family caregiver

1. age 18 and above
2. are related to the patient by blood, marriage, adoption, or affinity as a significant other (defined by the legally authorized person as the primary person providing oversight and support on an ongoing basis)
3. speak English or Spanish
4. able to recall at least two words on the Three Word Recall
5. participate, at a minimum, in the initial assessment and development of FamPath

Nurses (at the conclusion of the intervention at each site)

1. identify the intervention unit as the primary unit worked
2. speak English or Spanish

FOR THE EXPLORATORY AIM of assessing the cultural appropriateness of the intervention, we will recruit ***family CGs*** who self-identify as black, Latino, Asian and white, randomly selected from the Fam-FFC sample. Approximately 10 percent of families from each ethnic group represented in the study will be approached for consent for participation in interviews. (If theoretical saturation is not reached, interviews will continue until saturation is reached). Additionally, the ***six nurse champions*** will be consented and interviewed after the study ends in his/her particular unit/setting to provide their perspective on the cultural appropriateness of Fam-FFC.

3.2 Exclusion Criteria

List the criteria that define who will be excluded in your study.

Patient

1. enrolled in hospice and/or have a life expectancy of six months or less
2. admitted from a nursing home
3. no family caregiver to participate
4. mild cognitive impairment (CDR 0.5 without functional or ADL impairments)
5. severe dementia (CDR 3)
6. any significant neurological condition associated with cognitive impairment other than dementia (e.g. brain tumor)
7. a major acute psychiatric disorder

Family caregiver

1. unable to recall at least two out of 3 words on the Three Word Recall

3.3 Early Withdrawal of Subjects

3.3.1 Criteria for removal from study

Insert subject withdrawal criteria (e.g., safety reasons, failure of subject to adhere to protocol requirements, subject consent withdrawal, disease progression, etc.).

For both patient and family caregiver:

1. Subject consent withdrawal
2. Death
3. Failure of subject to adhere to protocol

The Intent-To-Treat Principle will be followed to analyze data from the current proposed trial.

For the nurse/nurse champions:

1. Subject consent withdrawal

3.3.2 Follow-up for withdrawn subjects

Describe when and how to withdraw subjects from the investigational product or study; the type and timing of the data to be collected for withdrawal of subjects; whether and how subjects are to be replaced; the follow-up for subjects withdrawn from investigational treatment.

If the participant withdraws from this study, already collected data will not be removed from the study database. The participant will be asked whether the investigator can collect data from his /her clinical records in the facility. If the individual agrees, this data will be handled the same as all other research data. Subjects will not be replaced.

4.0 Recruitment Methods

4.1 Identification of subjects

Describe the methods that will be used to identify potential subjects or the source of the subjects. If not recruiting subjects directly (e.g., database query for eligible records or samples) state what will be queried, how and by whom.

The Project Manager, research evaluators and PI will work with identified setting staff to provide us with a list of potentially eligible patients and recruit 146 patient/family caregiver dyads per participating setting (total sample 438 dyads). We are requesting a partial waiver to allow identification and, as appropriate, contact of potential participants to determine their interest in study participation. A flyer posted in the nursing station will alert/remind nursing staff of the study and ask them to refer potential study participants. It is the study staff's responsibility to ask permission of the patient to explain the study to the patient.

4.2 Recruitment process

Describe how, where and when potential subjects will be recruited (e.g., approaching or providing information to potential subjects for participation in this research study).

The research evaluators will provide IRB-approved information about the study/invitation to participate will to all potentially eligible patients/legally authorized representative (LAR) admitted to the study units (six medical or medical/surgical units of three hospitals in Pennsylvania). The patient and LAR will be approached to visit and discuss the study, and if granted, will receive: 1) brief oral information about the study; and 2) a copy of the consent form. The requirement to have a family CG (defined as the primary person providing oversight and support on an ongoing basis) involved and consented is explained to the patient/LAR. The patient and LAR may decide that another person, a CG other than the LAR, is the best person to participate in the study. In that case, that CG is provided information and if agreeable, engaged in the consent process.

Additionally, for the exploratory aim of assessing the cultural appropriateness of the intervention, we will recruit ***family CGs*** who self-identify as black, Latino, Asian and white, randomly selected from the Fam-FFC sample. Approximately 10 percent of families from each ethnic group represented in the study will be provided verbal information and approached for consent for participation in these interviews. Additionally, ***the six nurse champions*** will be consented and interviewed after the study ends in his/her particular unit/setting to provide their perspective on the cultural appropriateness of Fam-FFC. At the conclusion of the intervention at each site, approximately 6-8 ***nurses*** representing both shifts will be recruited to participate voluntarily in focus groups evaluating nurse-reported perceptions of: influence of nurse managers, organizational culture, likelihood of continuing to implement the intervention, and satisfaction. The purpose, voluntary nature, confidentiality, setting, time, and duration of the focus group will be shared with staff nurses at a staff meeting. If more than 8 nurses volunteer, we will accommodate their involvement by holding a second focus group.

4.3 Recruitment materials

List the materials that will be used to recruit subjects. Add recruitment documents to your study in CATS IRB (http://irb.psu.edu) on the "Consent Forms and Recruitment Materials" page. For advertisements, upload the final copy of printed advertisements. When advertisements are taped for broadcast, attach the final audio/video tape. You may submit the wording of the advertisement prior to taping to preclude re-taping because of inappropriate wording, provided the IRB reviews the final audio/video tape.

The data evaluator, responsible for recruitment, will provide information to all potential participants, using a flyer and verbal script. This information will be provided in person, and in some cases over the phone to family members who are not present.

4.4 Eligibility/screening of subjects

If potential subjects will be asked eligibility questions before obtaining informed consent, describe the process. Add the script documents and a list of the eligibility questions that will be used to your study in CATS IRB (http://irb.psu.edu) on the "Consent Forms and Recruitment Materials" page.

Both patient and CG (who may or may not be the LAR) consent are required for the study process to proceed to screening. The research evaluator will check CG eligibility (able to recall at least two words on the Three Word Recall) in person or over the phone, and then screen the patient in person for dementia using the Montreal Cognitive Assessment (MoCA) [123] and AD8.[128] Patients who screen positive for dementia will then be assessed for severity of dementia using the Clinical Dementia Rating (CDR). A diagnosis of very mild to moderate stage dementia as confirmed by a score of 0.5 to 2.0 on the Clinical Dementia Rating Scale will be required. Functional ability will be assessed with the Pfeffer Functional Activities Questionnaire (FAQ) to discriminate MCI from dementia.

5.0 Consent Process and Documentation

Refer to "SOP: Informed Consent Process for Research (HRP-090)", for information about the process of obtaining informed consent from subjects. HRP-090 can be accessed by clicking the Library link in CATS IRB (http://irb.psu.edu).

5.1 Consent Process

5.1.1 Obtaining Informed Consent

5.1.1.1 Timing and Location of Consent

Describe where and when the consent process will take place.

The consent process of patient/family caregiver dyads will occur within 48 hours of admission to the unit. Patients will be consented in person. The family caregivers will also be consented in person unless they are unable to be present with the research staff within the 48- hour timeframe, in which case they will be consented over the telephone. Nurse champions will be consented at the beginning of the study, prior to patient/family caregiver enrollment. Hospital staff nurses will be consented for post-intervention focus groups at the conclusion of the intervention. All consenting will occur within a private setting.

5.1.1.2 Coercion or Undue Influence during Consent

Describe the steps that will be taken to minimize the possibility of coercion or undue influence in the consent process.

Patient/family caregivers will be informed about the study. Research staff are trained to give sufficient time for answers and questions and to offer to come back/give extra time for consideration. Because the focus of this study is partnership with the family caregiver to improve the care /outcomes of persons with dementia, we will inform patients/families that in order to be eligible to participate, both members of the dyad need to assent or consent. If one member of the chooses not to participate, we don't enroll the dyad, and assure them that there are no negative sequelae associated with this decision.

Both patient/family caregivers will need to pass the Evaluation to Sign Consent to fully consent. This will assure that they understand what they are volunteering to participate in the study. Both patient and family caregivers will be informed that the decision to participate or not will have no bearing on the care and services provided by the hospital to both patient and family caregivers.

We will provide a $20 gift certificate at three time points during the study, at discharge from the hospital, at the second post-discharge data collection, and upon conclusion of the study. The two

different time-periods and modest nature of this honorarium offset the potential for undue influence.

The inclusion of nurse champions and staff nurses in the study is purely voluntary. Those who volunteer will be consented. All staff will be informed that their decision to participate or not will not in any way influence their working conditions or standing.

5.1.2 Waiver or alteration of the informed consent requirement

If you are requesting a waiver or alteration of consent (consent will not be obtained, required information will not be disclosed, or the research involves deception), describe the rationale for the request in this section. If the alteration is because of deception or incomplete disclosure, explain whether and how subjects will be debriefed. Add any debriefing materials or document(s) to your study in CATS IRB (http://irb.psu.edu) on the "Supporting Documents" page. NOTE: Review the "CHECKLIST: Waiver or Alteration of Consent Process (HRP-410)" to ensure you have provided sufficient information for the IRB to make these determinations. HRP-410 can be accessed by clicking the Library link in CATS IRB (http://irb.psu.edu).

n/a

5.2 Consent Documentation

5.2.1 Written Documentation of Consent

Refer to "SOP: Written Documentation of Consent (HRP-091)" for information about the process to document the informed consent process in writing. HRP-091 can be accessed by clicking the Library link in CATS IRB (http://irb.psu.edu).

If you will document consent in writing, describe how consent of the subject will be documented in writing. Add the consent document(s) to your study in CATS IRB (http://irb.psu.edu) on the "Consent Forms and Recruitment Materials" page. Links to Penn State's consent templates are available in the same location where they are uploaded and their use is required.

The following participants will be consented: 1) patient and CG, 2) nurse champions, and 3) nurses.

Both patient and CG consent are required. After information is provided, and the patient and CG agree to participate, an evaluation of capacity to provide consent will be conducted, using the Evaluation to Sign Consent (ESC).[131] If capacity is determined the patient may provide his or her own consent. If decisional capacity is impaired, and the patient provides assent , the LAR will complete the consent process. The legally authorized representative will be encouraged to try and determine what the patient would do if competent and base his/her decision upon what he/she thinks is in the patient's best interest. The CG's ability to sign consent will also be evaluated using the ESC. Only CGs answering all ESC questions correctly will be enrolled. Both patient and CG (who may or may not be the LAR) consent are required for the study process to proceed to screening. The consenting party is requested to sign the consent form. If it is not possible to obtain written signature from the LAR, verbal consent may be documented. The research evaluator will check CG eligibility (including the ability to recall at least two words on the Three Word Recall) and then screen the patient for dementia using the Montreal Cognitive Assessment (MoCA) [123] and AD8.[128] Patients who screen positive for dementia will then be assessed for severity of dementia using the Clinical Dementia Rating (CDR). A diagnosis of very mild to moderate stage dementia as confirmed by a score of 0.5 to 2.0 on the Clinical Dementia Rating Scale will be required. Functional ability will be assessed with the Pfeffer Functional Activities Questionnaire (FAQ) to discriminate MCI from dementia.[132]

Prior to the study the PI will ask the unit manager of the three intervention units to identify two nurse champions (to cover both nursing shifts). The PI will emphasize that the nurse champions must be

volunteers, in order to support their right to refuse without losing any job standing, as well as to support the success of the study. The PI will meet with the prospective nurse champions in private, explain the purpose of the study, procedures, possible risks and benefits, time commitment, compensation, privacy/ confidentiality, payment, PI contact information, and voluntary nature of the research, including the interview that will be conducted at the end of the study. If the nurse declines to participate as champion, another potential participant will be recruited and asked to provide an informed consent. A total of six nurse champions will be recruited.

At the end of the study at each of the three hospital cites, the PI will attend a staff meeting on the three intervention units. The PI will explain the plan for focus groups to obtain nurses' feedback on the effectiveness and sustainability of the intervention. Staff nurses will receive information on the focus groups and asked to participate. The nurses will receive information about the purpose, procedures, possible risks and benefits, time commitment, compensation, privacy/confidentiality, payment, PI contact information, and voluntary nature of the research

All participants will receive a copy of the consent to keep for future reference.

5.2.2 Waiver of Documentation of Consent (Implied consent, Verbal consent, etc.)

If you will obtain consent (verbal or implied), but not document consent in writing, describe how consent will be obtained. Add the consent script(s) and/or information sheet(s) to your study in CATS IRB (http://irb.psu.edu) on the "Consent Forms and Recruitment Materials" page. Links to Penn State's consent templates are available in the same location where they are uploaded and their use is required. Review "CHECKLIST: Waiver of Written Documentation of Consent (HRP-411)" to ensure that you have provided sufficient information. HRP-411 can be accessed by clicking the Library link in CATS IRB (http://irb.psu.edu).

If your research presents no more than minimal risk of harm to subjects and involves no procedures for which written documentation of consent is normally required outside of the research context, the IRB will generally waive the requirement to obtain written documentation of consent.

The research presents no more than minimal risk of harm to subjects and involves no procedures for which written documentation of consent is normally required in acute care settings. There are patients who are unable to write or unable to consent due to cognitive impairment (unable to pass the Evaluation to Sign Consent) but would like to participate in the study or are willing to have us speak with their LAR. There are also situations in which the LAR would really like to have the patient participate but can't meet face-to-face to sign the consent or HIPPA form; in this case the research staff will document verbal consent on the consent form.

5.3 Consent – Other Considerations

5.3.1 Non-English Speaking Subjects

Indicate what language(s) other than English are understood by prospective subjects or representatives.

If subjects who do not speak English will be enrolled, describe the process to ensure that the oral and written information provided to those subjects will be in that language. Indicate the language that will be used by those obtaining consent.

Indicate whether the consent process will be documented in writing with the long form of the consent documentation or with the short form of the consent documentation. Review the "SOP: Written Documentation of Consent (HRP-091)" and the "Investigator Manual (HRP-103)"

to ensure that you have provided sufficient information. HRP-091 and HRP-103 can be accessed by clicking the Library link in CATS IRB (http://irb.psu.edu).

Study participants will speak English or Spanish. The research evaluators will speak both English and Spanish. Study information, consents, and interventional material will be available in both English and Spanish. The long form of the consent documentation will be used.

5.3.2 Cognitively Impaired Adults

Refer to "CHECKLIST: Cognitively Impaired Adults (HRP-417)" for information about research involving cognitively impaired adults as subjects. HRP-417 can be accessed by clicking the Library link in CATS IRB (http://irb.psu.edu).

5.3.2.1 Capability of Providing Consent

Describe the process to determine whether an individual is capable of consent.

All potentially eligible patients and family caregivers (CGs), defined as or by the patient/legally authorized person (LAR) as the primary person providing oversight and support on an ongoing basis, will be approached to complete the Evaluation to Sign Consent (ESC). The Evaluation to Sign Consent is a four item measure with an opening question that is not scored. The opening question is used to indicate if the individual is alert and able to communicate. The five items reflect the participants' ability to name at least two potential risks incurred as a result of participating in the study; name two things that will be expected of him/her related to participation; explain what he/she would do if no longer interested in participating in the study; or if distress or discomfort was experienced associated with study participation. Evidence of ability to sign consent is based on correct responses to all five items on the ESC.

Both patient and CG (who may or may not be the LAR) consent are required for the study process to proceed to screening.

5.3.2.2 Adults Unable To Consent

Describe whether and how informed consent will be obtained from the legally authorized representative. Describe who will be allowed to provide informed consent. Describe the process used to determine these individual's authority to consent to research.

For research conducted in the state, review "SOP: Legally Authorized Representatives, Children and Guardians (HRP-013)" to be aware of which individuals in the state meet the definition of "legally authorized representative". HRP-013 can be accessed by clicking the Library link in CATS IRB (http://irb.psu.edu).

For research conducted outside of the state, provide information that describes which individuals are authorized under applicable law to consent on behalf of a prospective subject to their participation in the procedure(s) involved in this research. One method of obtaining this information is to have a legal counsel or authority review your protocol along with the definition of "children" in "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)." HRP-013 can be accessed by clicking the Library link in CATS IRB (http://irb.psu.edu).

If capacity is determined, based upon the ESC, the patient may provide his or her own consent. If decisional capacity is impaired, then assent, either verbal or written, will be obtained from the patient and the legally authorized representative

will be approached to complete the consent process. Therefore, we are requesting that Assent and Consent be either written or verbal. If the patient does not pass the Evaluation to Sign Consent and assents to participate the LAR will be approached. Many of the LARs live out of town and/or are unable to get to the facility to sign a face-to-face consent. We are therefore asking to be able to obtain verbal consent via phone communications if needed.

5.3.2.3 Assent of Adults Unable to Consent

Describe the process for assent of the subjects. Indicate whether assent will be required of all, some or none of the subjects. If some, indicate which subjects will be required to assent and which will not.

If assent will not be obtained from some or all subjects, provide an explanation of why not.

Describe whether assent of the subjects will be documented and the process to document assent. The IRB allows the person obtaining assent to document assent on the consent document and does not routinely require assent documents and does not routinely require subjects to sign assent documents.

After information is provided, and the patient and CG agree to participate, an evaluation of capacity to provide consent will be conducted, using the Evaluation to Sign Consent (ESC).[131] If capacity is determined the patient may provide his or her own consent. If decisional capacity is impaired, and the patient agrees to participate (provides assent), the legally authorized representative (LAR) will complete the consent process. The LAR will be encouraged to try and determine what the patient would do if competent and base his/her decision upon what he/she thinks is in the patient's best interest. The assent will be documented on the consent form by the research staff who are securing consent.

5.3.3 Subjects who are not yet adults (infants, children, teenagers)

5.3.3.1 Parental Permission

Describe whether and how parental permission will be obtained. If permission will be obtained from individuals other than parents, describe who will be allowed to provide permission. Describe the process used to determine these individual's authority to consent to each child's general medical care.

For research conducted in the state, review "SOP: Legally Authorized Representatives, Children and Guardians (HRP-013)" to be aware of which individuals in the state meet the definition of "children". HRP-013 can be accessed by clicking the Library link in CATS IRB (http://irb.psu.edu).

For research conducted outside of the state, provide information that describes which persons have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which research will be conducted. One method of obtaining this information is to have a legal counsel or authority review your protocol along with the definition of "children" in "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)." HRP-013 can be accessed by clicking the Library link in CATS IRB (http://irb.psu.edu).

n/a

5.3.3.2 Assent of subjects who are not yet adults

Indicate whether assent will be obtained from all, some, or none of the children. If assent will be obtained from some children, indicate which children will be required to assent. When assent of children is obtained describe whether and how it will be documented.

n/a

6.0 HIPAA Research Authorization and/or Waiver or Alteration of Authorization

This section is about the access, use or disclosure of Protected Health Information (PHI). PHI is individually identifiable health information (i.e., health information containing one or more 18 identifiers) that is transmitted or maintained in any form or medium by a Covered Entity or its Business Associate. A Covered Entity is a health plan, a health care clearinghouse or health care provider who transmits health information in electronic form. See the "Investigator Manual (HRP-103)" for a list of the 18 identifiers. HRP-103 can be accessed by clicking the Library link in CATS IRB (http://irb.psu.edu).

If requesting a waiver/alteration of HIPAA authorization, complete sections 6.2 and 6.3 in addition to section 6.1. The Privacy Rule permits waivers (or alterations) of authorization if the research meets certain conditions. Include only information that will be accessed with the waiver/alteration.

6.1 Authorization and/or Waiver or Alteration of Authorization for the Uses and Disclosures of PHI

Check all that apply:

☐ **Not applicable, no identifiable protected health information (PHI) is accessed, used or disclosed in this study.** *[Mark all parts of sections 6.2 and 6.3 as not applicable]*

X☐ **Authorization will be obtained and documented as part of the consent process.** *[If this is the only box checked, mark sections 6.2 and 6.3 as not applicable]*

X ☐ **Partial waiver is requested for recruitment purposes only (Check this box if patients' medical records will be accessed to determine eligibility before consent/authorization has been obtained).** *[Complete all parts of sections 6.2 and 6.3]*

☐ **Full waiver is requested for entire research study (e.g., medical record review studies).** *[Complete all parts of sections 6.2 and 6.3]*

☐ **Alteration is requested to waive requirement for written documentation of authorization (verbal authorization will be obtained).** *[Complete all parts of sections 6.2 and 6.3]*

6.2 Waiver or Alteration of Authorization for the Uses and Disclosures of PHI

6.2.1 Access, use or disclosure of PHI representing no more than a minimal risk to the privacy of the individual

6.2.1.1 Plan to protect PHI from improper use or disclosure

Include the following statement as written – DO NOT ALTER OR DELETE unless this section is not applicable because the research does not involve a waiver of authorization. If the section is not applicable, remove the statement and indicate as not applicable.

Information is included in the "Confidentiality, Privacy and Data Management" section of this protocol.

6.2.1.2 Plan to destroy identifiers or a justification for retaining identifiers

Describe the plan to destroy the identifiers at the earliest opportunity consistent with the conduct of the research. Include when and how identifiers will be destroyed. If identifiers will be retained, provide the legal, health or research justification for retaining the identifiers.

Because, we plan to follow up with post-acute visits after discharge, we will collect information on the discharge date, discharge location/address, and family caregiver telephone number, and email. We will maintain a separate file of this information, which will include names and ID number, maintained on RedCap and a separate hard copy file in a locked cabinet in the research office. This file will be deleted at the conclusion of the study.

6.2.2 Explanation for why the research could not practicably be conducted without access to and use of PHI

Provide an explanation for why the research could not practicably be conducted without access to and use of PHI.

In order to evaluate the effectiveness of the intervention, we need to collect data co-variate demographic, health and treatment data, as well as outcome measures such as physical function and delirium.

6.2.3 Explanation for why the research could not practicably be conducted without the waiver or alteration of authorization

Provide an explanation for why the research could not practicably be conducted without the waiver or alteration of authorization.

We are only seeking HIPAA documents for recruitment purposes. We are trying to avoid unnecessary use of patient/caregiver and research staff time and resources. This, we are asking hospital staff (unit secretary or nurse) to identify potentially eligible patient/caregiver dyads who meet inclusion/exclusion (e.g., age, not admitted from a nursing home, dementia diagnosis not hospice) criteria. If necessary we will access the hospital record to get inclusion/exclusion criteria and a family caregiver telephone number for recruiting purposes. We will not be accessing records for protected information such as treatments and medications until after consent is secured.

6.3 Waiver or alteration of authorization statements of agreement

By submitting this study for review with a waiver of authorization, you agree to the following statement – DO NOT ALTER OR DELETE unless this section is not applicable because the research does not involve a waiver or alteration of authorization. If the section is not applicable, remove the statement and indicate as not applicable.

Protected health information obtained as part of this research will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other permitted uses and disclosures according to federal regulations.

The research team will collect only information essential to the study and in accord with the 'Minimum Necessary' standard (information reasonably necessary to accomplish the objectives of the research) per federal regulations.

Access to the information will be limited, to the greatest extent possible, within the research team. All disclosures or releases of identifiable information granted under this waiver will be accounted for and documented.

7.0 Study Design and Procedures

7.1 Study Design

Describe the type/design of trial to be conducted (e.g., double-blind, placebo controlled, parallel design, etc.). Provide a schematic diagram of study design, procedures and stages, if appropriate.

The experimental design for this study is a repeated measures analysis with study units randomized by clustering to either treatment (Fam-FFC) or the control condition. This allows a within- and between-groups analysis to ascertain the effects of Fam-FFC.

7.2 Study Procedures

Provide a description of all research procedures being performed and when they are being performed (broken out by visit, if applicable), including procedures being performed to monitor subjects for safety or minimize risks. Include any long-term follow-up procedures and data collection, if applicable.

Describe where or how you will be obtaining information about subjects (e.g., medical records, school records, surveys, interview questions, focus group topics, audio or video recordings, data collection forms, and collection of specimens through invasive or non-invasive procedures to include the amount to be collected and how often). Add any data collection instruments that will be seen by subjects to your study in CATS IRB (http://irb.psu.edu) in the "Supporting Documents" page.

7.2.1 EXAMPLE: Visit 1 or Day 1 or Pre-test, etc. (format accordingly)

Provide a description as defined above and format accordingly.

7.2.2 EXAMPLE: Visit 2 or Day 2 or Post-test, etc. (format accordingly)

Provide a description as defined above and format accordingly.

Pre-intervention Procedures, <u>all three hospital sites</u>: The three hospital units will be randomized into treatment cohorts (time 1, time 2, time 3). The statistician will assist with randomization. There will be a meeting with all three hospitals to establish plans for implementation and randomization.

SITE Procedures (These procedures are repeated for Sites 1, 2 and 3.)
Pre-intervention: Baseline setting (census, ownership, etc.) as well as an environmental and policy information will be collected by the research evaluator on the two study units. T**he units will be randomized into treatment or control arm.** Nurse champions (two per the intervention unit) will be recruited and consented.

Month 1-2
INTERVENTION UNITS: 1) Component I: Nursing (nurses and nursing assistants) **staff education** and **2) Component II**: **environmental and policy assessment** conducted by the <u>research nurse</u> (TBN).

1) The **staff education** will be provided though instructor-led power-point presentations. Education in webinar format and one on one review will be provided for those unable to attend the training. Staff are requested to take a post-test after the training. *The educational material and post -test have been uploaded in the supporting document section.*
2) The **environmental and policy assessment** will be conducted by the research nurse who will include the nurse champions. The research nurse and champions will meet with the unit manager and discuss recommendations for change. Possible modifications include development of policies for: 1) labeling glasses/hearing aids, and 2) uninterrupted quiet times, and access to: 3) bedside white boards to promote family CG/patient communication

with the interdisciplinary team; and access to inexpensive hearing amplifiers, activity cart/supplies; mobility devices; and noise trackers. The site will be provided with up to $2000 to order supplies/equipment. *The environmental and policy assessment has been uploaded in the supporting document section.*

CONTROL UNITS: 1) **Staff education** (same content as in the intervention) conducted by a nurse member of the research team, who is not familiar with other components of the intervention.

Data Collected: Time spent in activity, recorded by the research nurse for cost study. Post-tests (Knowledge of Fam-FFC) collected by the research nurse and co-investigator.

Month: 3-14 Twelve months of recruitment/enrollment and intervention (Component III and IV).

I. Recruitment/enrollment

The research evaluators will work with unit staff to identify potentially eligible patients/family caregivers. A list of those who meet Information about the study/invitation to participate will be provided to all patients/legally authorized representative (LAR) admitted to the study units. The patient and LAR will be approached to visit and discuss the study, and if granted, will receive: 1) brief oral information about the study; and 2) a copy of the consent form. The requirement to have a family CG (defined as the primary person providing oversight and support on an ongoing basis) involved and consented is explained to the patient/LAR. The patient and LAR may decide that another person, a CG other than the LAR, is the best person to participate in the study. In that case, that CG is provided information and if agreeable, engaged in the consent process. Both patient and CG consent are required. After information is provided, and the patient and CG agree to participate, an evaluation of capacity to provide consent will be conducted, using the Evaluation to Sign Consent (ESC).[131] If capacity is determined the patient may provide his or her own consent. If decisional capacity is impaired, and the patient provides assent, the LAR will complete the consent process. The legally authorized representative will be encouraged to try and determine what the patient would do if competent and base his/her decision upon what he/she thinks is in the patient's best interest. The CG's ability to sign consent will also be evaluated using the ESC. Only CGs answering all ESC questions correctly will be enrolled. Both patient and CG (who may or may not be the LAR) consent are required for the study process to proceed to screening.

Upon consent, the research evaluator will check CG eligibility and then screen the patient for dementia using the Montreal Cognitive Assessment (MoCA) [123] and AD8.[128] Patients who screen positive for dementia will then be assessed for severity of dementia using the Clinical Dementia Rating (CDR). A diagnosis of very mild to moderate stage dementia as confirmed by a score of 0.5 to 2.0 on the Clinical Dementia Rating Scale will be required. Functional ability will be assessed with the Pfeffer Functional Activities Questionnaire (FAQ) to discriminate MCI from dementia.[132]

THE RECRUITMENT/ENROLLMENT PROCEDURES ARE THE SAME ON THE INTERVENTION AND CONTROL UNITS.

II. Intervention

FOR CONSENTED PATIENTS ON THE INTERVENTION UNITS:

The research nurse will provide **Component III*, the FamPath Care Pathway***: 1) Information to the patient and family caregiver on the admitting condition, diagnostics, and treatment; 2) Family/patient education: provided in lay terms (cueing and motivating techniques, support of physical activity, meals, cognitive stimulation, behavioral support, and safety, provided in written and CD format) linked to joint family CG/nurse assessment (baseline cognition, physical function and social profile); 3) Jointly developed bedside goals and treatment plans (updated daily); discharge checklist; and 4) Coaching of primary nurse to communicate and provide a copy of the FamPath plan to post-acute providers. ***The FamPath Care Pathway is initiated and continues throughout the hospitalization; it will vary based upon the patient's length of stay***. ***In addition, 5) post-acute follow-up will provide ongoing education and modification of the function-focused care plan*** (phone contact within 72 hours of discharge, weekly telephone calls for a total of 7 additional weeks, then monthly for 4 months), coaching of CGs to communicate FFC goals and expectations to the post-acute providers as indicated.

The *research nurse* will also provide **Component IV (mentoring**) Assistance to champions and nurses on above consented patients to: a) complete the Physical Capability Assessments*,[118] b) establish and update FFC goals with input from CGs/patients (Goal Attainment Scale*)[119] and c) develop a care plan with family CG/ patient addressing factors that impede FFC (e.g., acute illness, sedation, pain, fear/anxiety, pain, apathy, NPS, depression) 2) Support to the unit champions to mentor and motivate nursing staff (RN, LPN, nursing assistants) by: (a) role modeling; (b) highlighting staff role models and positive opinion leaders; (c) garnering support by sharing success stories with nursing council and

administration; (d) maintaining Fam-FFC bulletin board with updates /educational reinforcement; and (e) observing nursing staff during care interactions using the Function Focused Care Behavior Checklist*,[120] providing feedback to staff (See Tools).

FOR CONSENTED PATIENTS ON THE CONTROL UNITS: The CGs will receive information about hospital orientation and reinforcement of discharge teaching (medications/treatments, medical follow-up). ***This will be provided by a nurse member of the research team who is not familiar with Component II, III, and IV of the intervention.***

III. Data Collection

Patient data will be collected based on chart review, observations, actigraphy, and staff proxy informant interviews. ***Family CG data*** will be collected via electronic surveys on a tablet or by paper if a participant chooses. At all measurement time points, research evaluators will end data collection with the patient if he/she observes signs of dissent from the patient which includes: verbal refusal to answer a question, closing eyes and refusing to respond, asking the evaluator to leave, and moving away from the evaluator. The training of evaluators will include interrater reliability (minimum of 90%). Evaluators will not be informed of randomization results or provided with the details of the intervention. The research evaluators are fluent in Spanish and will use translated consents and study materials, in the event that Spanish is the primary language. The RedCap system will be used for screening of participants and data collection. **The same data is collected on the intervention and control units**. Descriptive (one-time) and outcome (multiple time-points) data are collected.

Upon enrollment, within 48 hours of admission to the unit, patient and family CG descriptive measures will be collected. Patient characteristics will include age, race/ethnicity, gender, marital status, education, medical diagnoses, medications, the use of sensory and mobility devices, and disease burden. Comorbid conditions will be classified with the *Charlson Comorbidity Index*.[133] Pre-admission function (ADL performance 2 weeks prior to admission) using the *Barthel Index* [134] (also an outcome measure) will be evaluated based on report from the family CG. Evaluation of hearing loss will be assessed using The Whisper Test. Pain will be measured using the Pain Assessment in Advanced Dementia and The Verbal Descriptor Scale. Upon discharge, length of stay, use of tethers (IV lines, pulse oximetry, urinary catheters, etc.), physical restraint use, and discharge disposition will be acquired. Cognitive *domains affected* by both dementia and delirium will be evaluated: executive function, orientation, memory, abstract thinking, and attention, evaluated by the subdomains of the *MoCA.* [123] The types of interventions provided on the FamPath assessment and care plan will be collected for descriptive purposes, extracted at the completion of the intervention.

We would like to test the efficiency of a new app to detect delirium and validate its use. The content includes 2 new questions (Ultra-brief CAM); the other questions are ones that we currently ask in the MoCA and CAM-Severity scale. We will test the app upon enrollment and each day until discharge. Thus, we will be extending our data collection time to less than one minute.

Here is the following description of the App: The READI delirium assessment app uses the REDCap application programming interface (API) for use on the iPad Air® tablet. The app executes the adaptive testing of the 2-step protocols using the Ultra-brief CAM and the 3D-CAM and together they take less than one minute to administer. The app allows the user to record accuracy of patient responses and automatically times each question. A pause button is available for interruptions. On subsequent days, the app retrieves information from the previous day's assessment to automatically assess for acute change. At the end of the assessment, the app reports the presence or absence of delirium, and uploads data into RedCAP, a HIPAA-compliant secure research database.

Family CG descriptive measures will include age, race, gender, marital status, education, relation to patient, employment status, other caregiving responsibilities, number of additional caregivers, and health literacy. General health and change in health compared to one year ago will be assessed using two widely used items from the SF-36.[135] **Health Literacy** (reading) will be measured with the *REALM-short form*). The *REALM-short form is highly correlated with* three other tests with a reported test-retest of 0.99.[136] Anxiety will be evaluated with the seven-item *Hospital Anxiety and Depression Scale (HADS*) subscale for Anxiety (HADS-A) and depression with the seven-item Hospital Anxiety and Depression Scale (HADS) subscale for Depression (HADS-D).[138] Suicidal ideation will be assessed using the Ask Suicide-Screening Questions (https://www.nimh.nih.gov/news/science-news/ask-suicide-screening-questions-asq.shtml) The type and level of caregivers' participation in hospital care will be measured by the researcher-developed tool that provides a self-report of the type of care and the number of hours per week spent providing care both in the hospital and post-discharge setting.[59,60]

The use of rehabilitation therapies and psychotropic medication prescribed during the hospitalization (drug, dose, frequency of antipsychotics, antidepressants, anxiolytics, sedatives/ hypnotics, mood stabilizers), length of stay, discharge disposition, setting and contact information, will be obtained through chart abstraction **at discharge**.

The following **outcome measure data collection/** will be initiated **within 48 hours of admission to the unit (T0), within 72 hours of discharge (T1), and 2 month (T2) and 6 month post-discharge (T3),** by research evaluators via observation, input from staff, chart abstracting or interview of the patient/family CG. Post-discharge data collection allows a one-week window post 72 hours of discharge. Also, a two-week window pre and post 2 month and 6 month time points to promote feasible and complete data collection.

The change in study procedure is due to COVID-19. The following **outcome measure data collection/** will be initiated **within 48 hours of admission to the unit (T0), within 72 hours of discharge (T1), and 2 month (T2) and 6 month post-discharge (T3),** by research evaluators via observation, input from staff, chart abstracting or interview of the patient/family CG. Outcome measures (and additional COVID-19 questions) collected at 72 hours of discharge, 2 month and 6 month post-discharge will be completed with family CG via telephone or zoom as able. Functional performance and physical activity (objective measure) will not be collected in post-acute setting. Post-discharge data collection allows a one-week window post 72 hours of discharge. Also, a two-week window pre and post 2 month and 6 month time points to promote feasible and complete data collection.

Patient outcome measures- collected for both control and intervention group.

Aim 1: Validate the efficacy of Fam-FFC on physical function (ADLs/ performance and physical activity), delirium occurrence and severity, behavior, mood, and adverse events.

Measure	Tool	Description
Physical Function		
ADLs (activities of daily living)	Barthel Index: verbal report of function will be obtained from the nurse who is assigned to the patient's care on the day of data collection..Return to baseline function (ADL function 2 weeks prior to admission) will be calculated	A 14-item measure of physical function that assesses ability for self-care.[134]There is sufficient evidence for the reliability and validity of the Barthel Index when used with older adults,[134, 140] individuals with progressive neurological conditions,[141] and when proxy respondents were utilized to report the functional abilities of dementia patients.[142]
Functional performance	Timed Chair Rise (observation)	An item on the Balance subscale of the Tinetti Gait and Balance Scale.[143] Previous work has identified this measure as a reliable and valid indication of function and strength.[140]
Physical activity	Objectively measured (actigraphy) for 24 hours using the Motionwatch.	The MotionWatch offers wrist-worn actigraphy that records activity in set epochs of time.[145] with established reliability and validity;[145-148] well-tolerated by cognitively impaired older adults.[148] The MotionWatch is applied within 24 hours of consent, and then upon subsequent data collection points.
Delirium		
Delirium occurrence	Structured interview consisting of questions from the MoCA observation [123] and the Confusion Assessment Method (CAM).[149]	The CAM has high sensitivity and specificity;[149, 150] validated in persons with dementia.[151] Delirium occurrence will be evaluated as the presence of full or subsyndromal delirium, a binary outcome (present or absent).[151,152]
Delirium severity	Confusion Assessment Method (CAM) [149]	An additive score for six items of the *CAM* (inattention, disorganized thinking, disorientation, memory impairment, perceptual disturbances, and psychomotor agitation/ retardation), scored as "absent" (0 points), present in mild form (1 point), or present in severe form (2 points). The seventh item, altered level of consciousness, will be scored as alert (0 points), vigilant or lethargic (1 point), and stupor or coma (2 points). Scores range 0 - 14, with a higher score indicating greater severity of delirium.[153]
Mood and Behavior		
Depression	Cornell Scale for Depression in Dementia (CSDD)[154,155]	A 19-item survey designed to assess depressive symptoms in individuals with dementia.[154, 155] There is sufficient evidence of reliability and validity.[155]
NPS	Brief Neuropsychiatric Inventory (NPI-Q)[156]	A 12-item, reliable, validated informant-based assessment of neuropsychiatric symptoms and associated caregiver distress. [156]

Adverse Events	Report of falls, hospitalizations, transfers to the emergency department	A monthly check of the patient hospital record to evaluate for hospitalizations/ED visits (in addition to the family caregiver report at month 2 and month 6).

The following **outcome measure** data collection will be initiated **within 72 hours of discharge (T1), and 2 month (T2) and 6 month post-discharge (T3),** by research evaluators via interview of the patient/family CG

Family Caregiver Outcome Measures- collected for both control and intervention group.		
Aim 2: Evaluate the impact of Fam-FFC on Family CG-centered outcomes.		
All measures are self-rated and will be initiated within: 72 hours of discharge (T1), 2 (T2) and 6 months post-discharge (T3). This data is collected via pen/paper tools completed by family CG.		
Measure	**Tool**	**Description**
Preparedness for caregiving	Preparedness for Caregiving Scale [157]	An 8-item instrument that asks caregivers how well prepared they believe they are for multiple domains of caregiving: physical care and emotional support, setting up support services, dealing with the stress of caregiving. Items are rated 0 (not at all prepared) to 4 (very well prepared); shows very good reliability and internal consistency,[157] including in family CGs of hospitalized persons with dementia.[59]
Caregiver Strain	Modified Caregiver Strain Index (CSI)[158]	A 13-question tool that measures strain (financial, physical, social, psychological, and personal) related to care provision, with excellent internal consistency and reliability.[158,159]
Caregiver Burden	Zarit Burden Interview (ZBI-12)[160] short version	12-item tool that measures caregiver perception of burden has shown high internal consistency and discriminative ability in caregivers of persons with dementia.[160,161]
Desire to Institutionalize	Desire to Institutionalize Scale[162]	6-item scale with moderate reliability; Cronbach alpha = 0.694.[162]

Nurse Champion Interviews: For the exploratory aim of assessing the cultural appropriateness of the intervention, the six nurse champions (intervention units) will be consented and interviewed, using a semi-structured interview guide, after the study ends in his/her particular unit/setting to provide their perspective. Qualitative content analysis of audiotaped, transcribed interviews will be conducted. The research evaluators will be trained to conduct these interviews.

Staff Nurse Interviews: Staff nurses will also be recruited at the end of the intervention at each study site, to participate in a focus group to determine their views on the effectiveness and sustainability of the intervention. We anticipate having 6-8 nurses per site (representing all three intervention units). This number is based upon our past experience recruiting for focus groups in this type setting, and the expected number to reach data saturation. However, if more than nurses volunteer/ want to participate, and/or the responses indicate the need to elicit more participation, we will add focus groups at the site. The PI and a member of the research team will conduct these interviews.

Family CG interviews: For the exploratory aim of assessing the cultural appropriateness of the intervention, we will recruit ***family CGs*** who self-identify as black, Latino, Asian and white, randomly selected from the Fam-FFC (intervention) sample. Approximately 10 percent of families from each ethnic group represented in the study will be approached for consent for participation in these interviews. Qualitative content analysis of audiotaped, transcribed interviews will be conducted at the six-month post-hospital discharge visit. A draft semi-structured interview guide will be refined with the input of a hospital patient /family council. Additional COVID-19 questions be asked during interview of the family CG. The research evaluators will be trained to conduct these interviews.

Cost Outcomes ***Aim3: Evaluate the relative costs for Fam-FFC v. control condition; calculate health care cost (post-acute health care utilization) and total cost savings for Fam-FFC***. We have developed cost-related data collection forms, specifically Activity Diaries, to help facilitate data collection for the champions, research nurse facilitators, and staff. These include staff and research nurse time and hours worked, training time (including replacement), supplies, and incentives. Post –acute utilization will be evaluated with a cumulative count of emergency room visits, number/days of hospitalizations, and long-term nursing home admissions six months after discharge, obtained from questioning of the family at each point of data collection. Health care unit charges and reimbursement rates will be obtained from yearly publications from the American Hospital Associations and other health data organizations.

Treatment Fidelity. Treatment fidelity will be evaluated with regard to delivery of the intervention, receipt, and

enactment[163,164] as shown in Table 5. *Assessment of Environment and Policy* will be conducted by the Fam-FFC Research Nurse with champions as part of the intervention (See Component 1).[59] *Knowledge of Fam-FFC* is a valid and reliable 15-item paper and pencil multiple choice exam that tests staff knowledge about Fam-FFC.[59] *The Goal Attainment Scale* [119] evaluates attainment of up to four patient goals and will be completed by the Fam-FFC Research Nurse with input from CGs, champions, nursing staff, and other health care professionals who work with the patient. This will be reviewed at discharge and post-discharge data collection points. The *FamPath Audit* tracks delivery of FamPath and *Family CG Activity Logs* monitor CG involvement and agreement with the care plan. The *Function Focused Care Behavior Checklist (FFC-BC)*[120] is a valid and reliable objective measure including a 19-item checklist reflecting nursing staff performance of Fam- FFC. Oversight of treatment fidelity will be provided by the co-investigator (BR) who will collaborate with the research team to ensure adherence to the study manual of operations and standardization across sites. See below for a comparison of treatment fidelity for treatment and control sites.

Treatment Fidelity (**Bolded** items: both treatment and control sites; items not bolded: treatment site only)		
Focus	Data (Appendix B)	Evidence of Treatment Fidelity
Delivery	Environment/Policy Assessments [59, 60] (Component I)	Completion of assessments by Fam-FFC Research Nurse
	Education: Percentage of nurses exposed (Component II)	**80% of all nursing staff working on participating nursing units (# exposed/total # nursing staff)**
	Goal Attainment Forms [119] (Comp. III)	Forms completed on all recruited patients in treatment units
	Fam-Path Audit (Component IV) [59, 60]	Completion of: bedside goals and treatment plans, discharge checklist, post-acute follow-up and plan update, communication with post-acute provider
Receipt	**Knowledge of Fam-FFC Test** [59, 60]	**Mean score of > 80% among nursing staff after Education**
	Environment/Policy Assessments [59, 60]	Evidence of change(s) made over the course of the study
	Goal Attainment Scale [119]	Positive goal attainment scores incorporated into care plans
Enactment	FFC Behavior Checklist [59, 60, 120]	Performance of Fam-FFC by nurses based on observations of care interactions in the hospital
	Family CG Activity Logs [59, 60]	Family CG involvement in care and follow-through on plan.

7.3 Duration of Participation

Describe the duration of an individual subject's participation in the study.

Six months (with a potential two week extra to complete data collection.)

7.4 Test Article(s) (Study Drug(s) and/or Study Device(s))

7.4.1 Description

Provide a brief description of all test articles (drugs (including any foods and dietary supplements), devices and/or biologics used in the research including the purpose of their use and their approval status with the Food and Drug Administration (FDA). Include information about the form of the drug product (e.g., tablets, capsules, liquid).

The **experimental condition**, Fam-FFC, will be coordinated and implemented by a Family-centered Function Focused Care Nurse (Fam-FFC Nurse), who will work in the treatment units 20 hours a week for 14 months to implement the four components of the intervention. In addition, the sites will identify two members of the nursing staff from each unit (one for day and one for evening shift) to be Family-centered Function Focused Function Focused Care Champions (Fam-FFC Champions). The four components of Fam-FFC include: **Component I-** Environmental and Policy Assessments; **Component II-** Education and Training of Nursing Staff; **Component III**- Ongoing Training and Motivation of Nursing Staff. The Fam-FFC Nurse will work with the champions to mentor and motivate nursing staff (RN, LPN, nursing assistants) to provide Fam-FFC by: (a) role modeling Fam-FFC, reinforcing performance of and benefits of Fam-FFC, and brainstorming about ways to overcome challenges; (b) highlighting staff role models and

positive opinion leaders; and (c) eliminating the influence of negative opinion leaders; **Component IV** Implementation of the FamPath Care Pathway which includes: (a) information on the admitting condition, diagnostics, and treatment, (b) family/patient education, (c) transitional hand-off to post-acute providers, and (d) post-acute follow-up to provide ongoing education and modification of the function-focused care plan**.**

The Attention Control condition (Fam- FFC Ed-only) consists of Component II, education of the nursing staff in participating hospital units (exactly as offered in treatment sites), and education of CGs about hospital orientation and reinforcement of discharge teaching (medications/treatments, medical follow-up). Research staff not familiar with Components I, III and IV will deliver the staff and CG education per manualized protocol.

7.4.2 Treatment Regimen

Describe dose, route of administration and treatment duration. Include information about dose adjustments.

The intervention begins during hospitalization. Post -acute follow-up will provide ongoing education and modification of the function-focused care plan (contact within 72 hours of discharge, weekly telephone calls for a total of 7 additional weeks, then monthly for 4 months).

7.4.3 Method for Assigning Subject to Treatment Groups

Describe the randomization process and how the associated treatment assignment will be made.

After the hospitals are randomized to the time cohort, within each six hospitals the two inpatient units will be randomly assigned so that one unit will receive Fam-FCC and the other unit will receive Staff-Ed (control) intervention. Random assignment will be completed by the statistician using SAS proc plan which specifically allows simultaneous randomization on multiple dimensions (time and units) as well as counterbalancing across units.

7.4.4 Subject Compliance Monitoring

Insert the procedures for monitoring subject compliance.

Treatment Fidelity. Treatment fidelity will be evaluated with regard to delivery of the intervention, receipt, and enactment. [163,164] *Assessment of Environment and Policy* will be conducted by the Fam-FFC Research Nurse with champions as part of the intervention (See Component 1).[59] *Knowledge of Fam-FFC* is a valid and reliable 15- item paper and pencil multiple choice exam that tests staff knowledge about Fam-FFC.[59] *The Goal Attainment Scale* [119] evaluates attainment of up to four patient goals and will be completed by the Fam-FFC Research Nurse with input from CGs, champions, nursing staff, and other health care professionals who work with the patient. This will be reviewed at discharge and post-discharge data collection points. The *FamPath Audit* tracks delivery of FamPath and *Family CG Activity Logs* monitor CG involvement and agreement with the care plan. The *Function Focused Care Behavior Checklist (FFC-BC)* [120] is a valid and reliable objective measure including a 19-item checklist reflecting nursing staff performance of Fam- FFC. Oversight of treatment fidelity will be provided by the co-investigator (BR) who will collaborate with the research team to ensure adherence to the study manual of operations and standardization across sites.

7.4.5 Blinding of the Test Article

Describe how the test article is blinded.

To ensure comparable samples in both the treatment and control condition participants will be blinded to treatment arm prior to consent, since the Fam-FFC treatment requires more effort that the control condition.

7.4.6 Receiving, Storage, Dispensing and Return

7.4.6.1 Receipt of Test Article

Describe how the test article will be obtained and from what source. Describe how the study test article will be packaged along with amounts (e.g., number of tablets/capsules or volume of liquid) and labeling. If drug kits are used, describe all the contents of the kit and associated labeling.

n/a

7.4.6.2 Storage

Describe the plans to store, handle the test article so they will be used only on subjects and only by authorized investigators. Describe storage temperature requirements and how temperature will be monitored and recorded.

n/a

7.4.6.3 Preparation and Dispensing

Describe how the test article will be assigned to each subject and dispensed. Describe the steps necessary to prepare the test article. Include where the test article preparation will be done and by whom. Fully describe how the study treatment is to be administered and by whom.

n/a

7.4.6.4 Return or Destruction of the Test Article

Describe the procedures for final reconciliation of the test article supply at the end of the study and whether the test article is to be shipped back to a source or destroyed on site.

n/a

7.4.6.5 Prior and Concomitant Therapy

Describe what prior and/or concomitant medical therapy will be collected. Describe which concomitant medicines/therapies are permitted during the study. Describe which concomitant medicines are not permitted during the study.

n/a

8.0 Subject Numbers and Statistical Plan

8.1 Number of Subjects

Indicate the total number of subjects to be accrued.

If applicable, distinguish between the number of subjects who are expected to be enrolled and screened, and the number of subjects needed to complete the research procedures (i.e., numbers of subjects excluding screen failures.)

We expect to screen 1000 dyads (patients/caregivers) and enroll 458-468.
We plan to enroll ten nurse champions (2 per intervention unit, a high estimate with a plan for replacement if needed).
We plan to enroll approximately 6-8 nurses for focus groups from each intervention unit at the conclusion of the intervention, with a high estimate of a total of 35 nurses. This number is based upon our past experience recruiting for focus groups in this type setting, and the expected number to reach data saturation. However, if more than nurses volunteer/ want to participate, and/or the responses indicate the need to elicit more participation, we will add focus groups at the site.

We will oversample by 20- 30 patients in order to continue promoting diversity.

8.2 Sample size determination

If applicable, provide a justification of the sample size outlined in section 8.1 – to include reflections on, or calculations of, the power of the study.

We target a total sample size of 438 with 73 per inpatient unit is sufficient to detect an intervention effect comparable to the observed effect size in our pilot study, with 80% statistical power assuming a 20% attrition rate.

Our last site afforded us the opportunity to increase diversity; we will oversample by 20-30 patients in order to continue promoting diversity.

8.3 Statistical methods

Describe the statistical methods (or non-statistical methods of analysis) that will be employed.

Aim 1: Validate the efficacy of Fam-FFC on physical function (ADLs/ performance and physical activity), delirium occurrence and severity, behavior, and mood. For each outcome, an appropriate mixed effects model (either a LME or a GLMM) will be identified for model fitting. For delirium occurrence (a binary variable) we will use generalized linear mixed models with a logistic link function. The primary independent variables will be GROUP (Fam FCC v. control), TIME (day of admission, day of discharge, 2-month post discharge and 6-month post discharge*)* and SITE (for the three hospitals*).* The TIME x GROUP interaction will be tested for differential rate of change in the outcome. The GROUP x SITE interaction will be tested for heterogeneous center effects. Three-level models using an unstructured correlation will be fitted for the repeated measures within individuals who are nested within the same inpatient unit.[181-184] Time will be modeled continuously using day since admission so that trajectories can vary across individuals depending on time spent in the inpatient unit. This also allows us to examine non-linear time functions (e.g., quadratic) that allow the rate of change to vary over the different intervals. Covariates identified from the baseline analyses will be included in the mixed model to adjust for their influences. We will also consider interactive effects among demographic variables of interest (e.g., age, gender of patient and caregiver, ethnicity) and treatment condition to identify moderators of the treatment effects. Bootstrap methods will be applied to the mixed effects models in addition to the Wald test and the likelihood ratio test within the mixed effects models.[185-187] Subject level propensity score matching will be applied to improve the statistical power of the planned hypothesis tests.[175] To address the multiple endpoints issue in this trial, $P<0.05$ for the primary hypothesis and then multiple testing procedures such as closed testing implemented in PROC MULTTEST will be applied to adjust p values.[188-190]

Aim 2: Evaluate the impact of Fam-FFC on family CG-centered outcomes (family CG preparedness for caregiving, strain, burden, and desire to institutionalize). LME similar to Aim 1, will be used.

Aim 3: Evaluate the relative costs for Fam-FFC v. control condition, and calculate health care and total cost savings for Fam-FFC. Standard micro-costing methods will be used to estimate costs. Using the guidelines offered by Chatterji and colleagues,[191] total intervention costs will be based on expenditures/outlays for each of the following: (1) intervention; (2) consultant fees; (3) personnel costs, (4) incentives, meals, travel for study participants; (5) utilities, maintenance, security and other operating costs; and (6) administrative costs. We will identify all of the "inputs" that go into the implementation and then assign unit costs to these inputs (wages/salaries acquired from the unit managers, cost of materials, etc.). Then, we will multiply the units of inputs by their unit costs and sum this across all of inputs to determine the total cost of implementation per setting. An average across all settings will then be calculated. To estimate the cost of healthcare for each group, we will collect unit costs from existing literature including data published yearly by the American Medical Association, the American Hospital Association, the National Hospital Discharge Survey, and the American Managed Behavioral Healthcare Association. Similarly, these unit cost estimates for each type of health care utilization (emergency room, hospital and long-term nursing home admissions) will then be multiplied by the number of units used by each individual in the sample. A variable will be created for total health care cost by summing across conditions while exercising care to avoid any double counting of services. Health care and total cost savings will be calculated for each treatment condition. Mean costs and savings will be computed and subsequently tested for statistical significances across conditions using a t-test. In calculating cost we will also take into account fixed versus variable costs adjusting for variation over time in wages, benefits, and supplies using a standard micro-costing approach. We will then use multivariable regressions to determine whether Fam-FCC is significantly related to lower costs of healthcare and total cost savings controlling for covariates. Moreover, we will compare health care costs in terms of changes over time with paired t-test (within group differences) and with parametric Analysis of Variance (between group differences).

Assessment of the cultural appropriateness of Fam-FCC for diverse families in our sample: We employ the Ecological Model (EM) originally developed by Bernal and colleagues as a framework to assess the cultural appropriateness of the Fam-CC intervention[192,193] and to refine Fam-FCC for future studies. See below for analysis plan.

EM Model Component	Sample/Data Source	Analysis
I. Family-CG experiences of EM model constructs (categories 1,3,4,5,6,8)	Caregivers who self-identify as black, Latino, Asian and white will be randomly selected (Approximately 10% of families from each ethnic group; if theoretical saturation is not reached, interviews will continue until saturation is reached.) A draft semi-structured interview guide will be refined with the input of a hospital patient /family council.	Qualitative content analysis of audiotaped, transcribed interviews conducted at the six-month post-hospital discharge contact. Trustworthiness[194] is enhanced by the team's methodological expertise, random sampling, rigorous analytic approaches, member checking, and a detailed audit trail.
II. Nurse champion experiences of EM model constructs (categories 1,3,4,5,6,8)	The six champions (2 per setting) will be interviewed using a semi-structured interview guide.	Qualitative content analysis of audiotaped, transcribed interviews at conclusion of intervention at each site.
III. Evaluation of measures for reliability and validity for the ethnic groups represented in the study (category 7)	1)The internal consistency of the caregiver outcome measures as well as relationships with known correlates (e.g., educational level) will be evaluated in the first 20 Spanish-speaking respondents and 2) Both content and face validity of each measure will be discussed in participant interviews outlined in Component I above.	Cronbach's alphas for caregiver outcomes will be assessed. The participants will be asked to assess their perceptions of measures and identify potential cultural gaps in measurement content in Component I above.
IV. Assessment of whether ethnic concordance moderates the relationship between treatment group and patient/ family outcomes (category 2).	The ethnicities of nurse champions and each family will be documented as concordant or not.	Concordance will potentially be used as a covariate in analyses for specific aims 1, 2.

9.0 Confidentiality, Privacy and Data Management

For research being conducted at Penn State Hershey or by Penn State Hershey researchers only, the research data security and integrity plan is submitted using "HRP-598 – Research Data Plan Review Form Application Supplement", which is available in the Library in CATS IRB (http://irb.psu.edu). Refer to Penn State College of Medicine IRB's "Standard Operating Procedure Addendum: Security and Integrity of Human Research Data", which is available on the IRB's website. **In order to avoid redundancy, for this section state "See the Research**

Data Plan Review Form" in section 9.0 if you are conducting Penn State Hershey research and move on to section 10.

For all other research, in the sections below, describe the steps that will be taken to secure the data during storage, use and transmission.

9.1 Confidentiality

//

9.1.1 Identifiers associated with data and/or specimens

List the identifiers that will be included or associated with the data and/or specimens in any way (e.g., names, addresses, telephone/fax numbers, email addresses, dates (date of birth, admission/discharge dates, etc.), medical record numbers, social security numbers, health plan beneficiary numbers, etc.).

If no identifiers will be included or associated with the data in any way, whether directly or indirectly, please indicate this instead.

All data will be coded with an arbitrary subject number to allow for linking of data over time. The linkage to individual names will be kept in a locked file in the project office. Additionally, we plan to follow up with post-acute visits after discharge. Thus we will collect information on the discharge date, discharge location/address, and family caregiver telephone number, and email. We will maintain a separate file of this information, which will include names and ID number, maintained in a separate file on RedCap or HIPAA-secure BOX so research evaluators can access, and a separate hard copy file in a locked cabinet in the research office.

9.1.1.1 Use of Codes, Master List

If identifiers will be associated with the data and/or specimens (as indicated in section 9.1.1 above), describe whether a master record or list containing a code (i.e., code number, pseudonyms) will be used to separate the data collected from identifiable information, where that master code list will be stored, who will have access to the master code list, and when it will be destroyed.

If identifiers are included or associated with the data as described in section 9.1.1 above, but no master record or list containing a code will be used, it will be assumed by the IRB that the investigator plans to directly link the identifiers with the data.

Identifying information (name, address, telephone number, email, discharge date) along with the study ID number will be maintained in a separate master file (on secure server and locked file), not linked to the data. Only the project manager and research evaluators will have access to this information. Master files/codes will be deleted/ destroyed three years after the conclusion of the study.

9.1.2 Storage of Data and/or Specimens

Describe where, how and for how long the data (hardcopy (paper) and/or electronic data) and/or specimens will be stored. NOTE: Data can include paper files, data on the internet or websites, computer files, audio/video files, photographs, etc. and should be considered in the responses. Refer to the "Investigator Manual (HRP-103)" for information about how long research records must be stored following the completion of the research prior to completing this section. HRP-103 can be accessed by clicking the Library link in CATS IRB (http://irb.psu.edu).

Please review Penn State's Data Categorization Project for detailed information regarding the appropriate and allowable storage of research data collected according to Penn State Policy AD71. Although the IRB can impose greater confidentiality/security requirements (particularly for sensitive data), the IRB cannot approve storage of research data in any way or using any service that is not permissible by Penn State Policy AD71.

The RedCap system, an electronic system used by universities worldwide, will be used for both data entry and data storage. The RedCap system will be accessed via the Penn State Clinical and Translational Science Institute (CTSI). RedCap is HIPAA compliant, with all data stored on a secure server, and encrypted. Data entry modules and stored data access is password protected and based on the individual's role on project. RedCap provides logging and audit trails on all data interactions. Consents and enrollment tracking, and contact information will be stored on a secure server (HIPAA compliant Box or RedCap) Hard copies of data will be stored in a locked cabinet in a locked office. We will store data for six years.

Consistent with NIH's Certificate of Confidentiality, the researchers will not disclose or use information, documents, or biospecimens that may identify subjects in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless study subjects have consented for this as participants about the protections afforded by the Certificate and any exceptions to that protection. Information, documents, or biospecimens will not be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse and neglect, elder mistreatment, harm to self or others, or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings), if subjects have consented to the disclosure, including for medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The researchers will comply with requests for information from personnel of the National Institute of Health which is funding this project.

The audio recording is uploaded into PSU BOX (approved for PHI) immediately and then transferred to the transcription service. Within 72 hours, the transcription is reviewed for accuracy and the recording is deleted from the device. The transcriptions will be destroyed 6 years after the completion of this evaluation.

9.1.3 Access to Data and/or Specimens

Identify who will have access to the data and/or specimens. This information should not conflict with information provided in section 9.1.1.1 regarding who has access to identifiable information, if applicable.

Only the Project Manager and data collectors/evaluators will have access to participant names/identifying information. The investigators and other members of the research team will have access only to de-identified data.

9.1.4 Transferring Data and/or Specimens

If the data and/or specimens will be transferred to and/or from outside collaborators, identify the collaborator to whom the data and/or specimens will be transferred and how the data and/or specimens will be transferred. This information should not conflict with information provided in section 9.1.1.1 regarding who has access to identifiable information, if applicable.

Data will not be transferred. Only the investigators and members of the research team will access data via a secure server.

9.2 Subject Privacy

This section must address subject privacy and NOT data confidentiality.

Indicate how the research team is permitted to access any sources of information about the subjects.

Describe the steps that will be taken to protect subjects' privacy interests. "Privacy interest" refers to a person's desire to place limits on whom they interact with or to whom they provide personal information.

Describe what steps you will take to make the subjects feel at ease with the research situation in terms of the questions being asked and the procedures being performed. "At ease" does not refer to physical discomfort, but the sense of intrusiveness a subject might experience in response to questions, examinations, and procedures.

Data will be obtained in a private area within the setting and all data will entered into RedCap data collection system. The only way to access the RedCap database is to have permission from Penn State Hershey. Only the study team will have access to this data on the RedCap server.

Participants in the focus groups and interviews will not provide any identifiable data. Members of the research team will have access to the data.

10.0 Data and Safety Monitoring Plan

This section is required when research involves more than Minimal Risk to subjects. As defined in "SOP: Definitions (HRP-001)", available in the Library in CATS IRB (http://irb.psu.edu), Minimal Risk is defined as the probability and magnitude of harm or discomfort anticipated in the research that are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. For research involving prisoners, Minimal Risk is the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons. **Please complete the sections below if the research involves more than minimal risk to subjects OR indicate as not applicable.**

We will have a DSMB and this information is located in the supporting documents.

10.1 Periodic evaluation of data

Describe the plan to periodically evaluate the data collected regarding both harms and benefits to determine whether subjects remain safe.

n/a

10.2 Data that are reviewed

Describe the data that are reviewed, including safety data, untoward events, and efficacy data.

n/a

10.3 Method of collection of safety information

Describe the method by which the safety information will be collected (e.g., with case report forms, at study visits, by telephone calls and with subjects).

n/a

10.4 Frequency of data collection

Describe the frequency of data collection, including when safety data collection starts.

n/a

10.5 Individuals reviewing the data

Identify the individuals who will review the data. The plan might include establishing a data and safety monitoring committee and a plan for reporting data monitoring committee findings to the IRB and the sponsor.

n/a

10.6 Frequency of review of cumulative data

Describe the frequency or periodicity of review of cumulative data.

n/a

10.7 Statistical tests

Describe the statistical tests for analyzing the safety data to determine whether harms are occurring.

n/a]

10.8 Suspension of research

Describe any conditions that trigger an immediate suspension of research.

n/a]

11.0 Risks

List the reasonably foreseeable risks, discomforts, hazards, or inconveniences to the subjects related the subjects' participation in the research. For each potential risk, describe the probability, magnitude, duration, and reversibility. Consider all types of risk including physical, psychological, social, legal, and economic risks. If applicable, indicate which procedures may have risks to the subjects that are currently unforeseeable. If applicable, indicate which procedures may have risks to an embryo or fetus should the subject be or become pregnant. If applicable, describe risks to others who are not subjects.

Please keep in mind that loss of confidentiality is a potential risk when conducting human subject research and should be addressed as such.

Risks associated with survey and observational data collection for patients in this study includes some concerns about privacy and embarrassment. The collection of actigraphy data from the MotionWatch may be mildly uncomfortable for participants, similar to the sensation of wearing a watch. Lastly, the **patient** may experience some stress completing study-related activities while trying to participate optimally in treatments and assessments that occur as part of hospital care. Research evaluators will be members of the research team, with health-related and/or research-related experience. We will train the research evaluators on safety precautions, including fall prevention and signs of patient stress. We also will train them on communicating with persons with dementia and their family caregivers.

Family CGs may also experience embarrassment, emotional discomfort, and increased stress. We will train research evaluators on observing for signs of distress and preventive strategies (e.g., pacing, active listening, and flexibility in scheduling study activity). The evaluators will be trained for to observe for, detect, and report signs of depression and suicidal ideation in both patients and family CGs.

There is also a potential risk of a loss in confidentiality since **patients/family CGs** are sharing personal information with the study staff. Several measures will be taken to safeguard personal information: 1) All study documents will be coded with a special identifier number; 2) study data will be stored on a secured electronic system (RedCap) which can be accessed only by the study team; and 3) study related interviews will take place in a private setting, away from others; and 4) information provided by participating in this study will not be shared with the facility staff or administration.

During interviews and focus groups, **nurse champions and staff nurses** respectively, may experience stress, embarrassment, or the feeling that they need to offer only positive comments about the intervention. We will train evaluators on techniques to support the participants' comfort and emphasize the need to identify any needed improvements in the intervention. We will schedule interviews and focus groups at a time convenient. Releases for using audio recordings will be secured since such recordings cannot be entirely de-identified. Participants will be informed that the purpose of the interviews and focus groups will be to evaluate the intervention, not the hospital or unit, and results will not be shared with the facility. Nurses who participate in focus groups and interviews that confidentiality cannot be assured.

We will protect the rights of the patients, family CGs and champions to refuse to participate in, or withdraw from, the research without penalty and to have an opportunity to communicate directly with the researchers about their participation should they have any concerns. The informed consent preamble will provide participants with a way to reach the researchers directly. Participant data will not be shared with administrators except in the aggregate.

12.0 Potential Benefits to Subjects and Others

12.1 Potential Benefits to Subjects

Describe the potential benefits that individual subjects may experience from taking part in the research. If there is no direct benefit to subjects, indicate as such. Compensation is not considered a benefit. Compensation should be addressed in section 14.0.

Potential benefits to patients include improved functional performance, less delirium, less inappropriate psychotropic medication use, improved behavioral symptoms, and less hospital readmissions and admissions to a nursing home for long-term stay. Family CGs may experience decreased burden/strain and improved skills in sharing information, making decisions, advocating, coordinating, and providing direct care related to function-promoting care, during and after hospitalization. Nursing staff will learn skills in communicating and motivating patients with dementia and gain knowledge around alternatives to restrictive interventions when managing fall prevention and behavioral manifestations of distress. They will also learn how to promote function and physical activity and how to support family CG effectiveness through sound communication, information-sharing, and partnership, including shared decision-making. In addition, the nurses will learn that providing Fam-FFC does not place patients at risk for adverse events (e.g., falls) and may save nurses time by decreasing time spent doing tasks that patients can perform themselves or with less assistance. Our intervention also views the acute illness of the person with dementia across settings, offering approaches that may have long-term positive effects on the person with dementia.

12.2 Potential Benefits to Others

Include benefits to society or others.

Fam-FFC has the potential to reduce poor health outcomes that are major sources of today's spiraling health care costs. This study will have direct implications for clinical practice and informing policy related to effective care delivery for persons with dementia in acute care, a neglected area of research and program development. The societal implications of helping older individuals with dementia avoid functional decline, adverse events, long-term nursing home admissions, and hospitalizations are

enormous in terms of aging in place, quality of life, cost, and caregiver burden. Further this study will provide information about the theoretical utility of using Social Ecological Models, Social Cognitive Theory to facilitate behavior change related to optimizing function and physical activity in real world clinical settings. These findings will be relevant for other areas of behavior change research in acute care.

13.0 Sharing Results with Subjects

Describe whether results (study results or individual subject results, such as results of investigational diagnostic tests, genetic tests, or incidental findings) will be shared with subjects or others (e.g., the subject's primary care physicians) and if so, describe how it will be shared.

Results will not be shared with individuals. We will share full study results with facility leadership and they can determine if they would like to disseminate findings to staff.

14.0 Subject Stipend (Compensation) and/or Travel Reimbursements

Describe the amount and timing of any subject stipend/payment or travel reimbursement here. If there is no subject stipend/payment or travel reimbursement, indicate as not applicable.

If course credit or extra credit is offered to subjects, describe the amount of credit and the available alternatives. Alternatives should be equal in time and effort to the amount of course or extra credit offered.

If an existing, approved student subject pool will be used to enroll subjects, please indicate as such and indicate that course credit will be given and alternatives will be offered as per the approved subject pool procedures.

We will offer a modest honorarium ($20 gift card) to family caregivers at discharge from the hospital, month 2 and month 6.

15.0 Economic Burden to Subjects

15.1 Costs

Describe any costs that subjects may be responsible for because of participation in the research.

Participants will not incur any additional costs for the intervention above what their hospital costs are.

15.2 Compensation for research-related injury

If the research involves more than Minimal Risk to subjects, describe the available compensation in the event of research related injury.

If there is no sponsor agreement that addresses compensation for medical care for research subjects with a research-related injury, include the following text as written - DO NOT ALTER OR DELETE:
It is the policy of the institution to provide neither financial compensation nor free medical treatment for research-related injury. In the event of injury resulting from this research, medical treatment is available but will be provided at the usual charge. Costs for the treatment of research-related injuries will be charged to subjects or their insurance carriers.

For sponsored research studies with a research agreement with the sponsor that addresses compensation for medical care for research-related injuries, include the following text as written - DO NOT ALTER OR DELETE:
It is the policy of the institution to provide neither financial compensation nor free medical treatment for research-related injury. In the event of injury resulting from this research, medical treatment is available but will be provided at the usual charge. Such charges may be paid by the study sponsor as outlined in the research agreement and explained in the consent form.

n/a. The research involves minimal risk

16.0 Resources Available

16.1 Facilities and locations

Identify and describe the facilities, sites and locations where recruitment and study procedures will be performed.

If research will be conducted outside the United States, describe site-specific regulations or customs affecting the research, and describe the process for obtaining local ethical review. Also, describe the principal investigator's experience conducting research at these locations and familiarity with local culture.

We will recruit from six medical or medical/surgical units of three hospitals in Philadelphia, Pennsylvania.

16.2 Feasibility of recruiting the required number of subjects

Indicate the number of potential subjects to which the study team has access. Indicate the percentage of those potential subjects needed for recruitment.

We estimate that approximately 7.5 patients per week on average will be eligible for the study in the study units. Based on our past recruitment/ enrollment activity [59,60] (24%-97% from the eligible pool), we will be able to enroll more than the 1.5/week necessary to meet the required sample

16.3 PI Time devoted to conducting the research

Describe how the PI will ensure that a sufficient amount of time will be devoted to conducting and completing the research. Please consider outside responsibilities as well as other on-going research for which the PI is responsible.

The PI has allocated 30% of her time to this study.

16.4 Availability of medical or psychological resources

Describe the availability of medical or psychological resources that subject might need as a result of their participation in the study, if applicable.

Those family caregivers who screen positive for suicide or demonstrate a high level of depression (score 15–21) on the Hospital Anxiety and Depression Scale (HADS) subscale will be referred to psychiatry services at the participating hospital. This is in the consent form.

16.5 Process for informing Study Team

Describe the training plans to ensure members of the research team are informed about the protocol and their duties, if applicable.

With regard to testing of patients in the proposed study, we will use a training manual that details how to safely complete each measure with cognitively impaired patients. The evaluators are trained to be particularly sensitive to any changes in mood/behavior, evidence of fatigue, shortness of breath, acute pain or evidence of a desire to stop the assessment in which case the evaluators will stop testing. In the event that the research evaluator feels a participant has had an acute change in condition or behavior, all testing will be stopped and the evaluator will inform the patient's nurse.

Training of evaluators for this study will be conducted by Dr. Boltz and the project manager. Throughout the study, Dr. Boltz will be available to provide additional support with training and "on call" availability to answer questions for evaluators should they arise. All of the measures utilized have been developed for and/or used with cognitively impaired and physically frail older adults and allow for a broad range of function and activity. There are response options that include inability to perform an activity or performance of an activity with assistance. Thus, patients will not be required to perform an activity beyond his or her capability to safely do so. Cardiovascular events associated with performance of activities of daily living and physical activity, including moderate intensity physical activity are extremely rare. To prevent and decrease any risk of injury or harm during physical activity the Fam-FFC research nurse will work closely with other members of the health care team (e. g., physicians, physical therapists) and investigative team members (Drs. Boltz and Resnick) to assure that patient goals involve only those activities that can be safely performed. Dr. Boltz will train the Fam-FFC research nurse in her ability to continually reinforce safety measures throughout the study period. We have integrated safety materials into Component II (staff training). Additionally, we have incorporated safety training into the family CG education, including fall prevention and general safety considerations.

The PI and an expert in family health disparities will train the study nurse evaluator to conduct the qualitative interviews that assess cultural appropriateness and perceptions/satisfaction. The interview guide will be reviewed by a representative group of a patient/family council for content as well as clarity.

17.0 Other Approvals

17.1 Other Approvals from External Entities

Describe any approvals that will be obtained prior to commencing the research (e.g., from cooperating institutions, community leaders, schools, external sites, funding agencies).

After PSU approval, we will seek approval from the University of Pennsylvania Health System for the three participating hospitals

17.2 Internal PSU Committee Approvals

Check all that apply:

☐ Anatomic Pathology – Hershey only – Research involves the collection of tissues or use of pathologic specimens. Upload a copy of HRP-902 - Human Tissue For Research Form on the "Supporting Documents" page in CATS IRB. This form is available in the CATS IRB Library.

☐ Animal Care and Use – All campuses – Human research involves animals and humans or the use of human tissues in animals

☐ Biosafety – All campuses – Research involves biohazardous materials (human biological specimens in a PSU research lab, biological toxins, carcinogens, infectious agents, recombinant viruses or DNA or gene therapy).

☐ Clinical Laboratories – Hershey only – Collection, processing and/or storage of extra tubes of body fluid specimens for research purposes by the Clinical Laboratories; and/or use of body fluids that had been collected for clinical purposes, but are no longer needed for clinical use. Upload a copy of HRP-901 - Human Body Fluids for Research Form on the "Supporting Documents" page in CATS IRB. This form is available in the CATS IRB Library.

☐ Clinical Research Center (CRC) Advisory Committee– All campuses – Research involves the use of CRC services in any way.

☐ Conflict of Interest Review – All campuses – Research has one or more of study team members indicated as having a financial interest.

☐ Radiation Safety – Hershey only – Research involves research-related radiation procedures. All research involving radiation procedures (standard of care and/or research-related) must upload a copy of HRP-903 - Radiation Review Form on the "Supporting Documents" page in CATS IRB. This form is available in the CATS IRB Library.

☐ IND/IDE Audit – All campuses – Research in which the PSU researcher holds the IND or IDE or intends to hold the IND or IDE.

☐ Scientific Review – Hershey only – All investigator-written research studies requiring review by the convened IRB must provide documentation of scientific review with the IRB submission. The scientific review requirement may be fulfilled by one of the following: (1) external peer-review process; (2) department/institute scientific review committee; or (3) scientific review by the Clinical Research Center Advisory committee. NOTE: Review by the Penn State Hershey Cancer Institute Scientific Review Committee is required if the study involves cancer prevention studies or cancer patients, records and/or tissues. For more information about this requirement see the IRB website at: http://www.pennstatehershey.org/web/irb/home/resources/investigator

18.0 Multi-Site Research

If this is a multi-site study (i.e., the study will be conducted at other institutions each with its own principal investigator) and you are the lead investigator, describe the processes to ensure communication among sites in the sections below.

n/a

18.1 Communication Plans

Describe the plan for regular communication between the overall study director and the other sites to ensure that all sites have the most current version of the protocol, consent document, etc. Describe the process to ensure all modifications have been communicated to sites. Describe the process to ensure that all required approvals have been obtained at each site (including approval by the site's IRB of record). Describe the process for communication of problems with the research, interim results and closure of the study.

n/a

18.2 Data Submission and Security Plan

Describe the process and schedule for data submission and provide the data security plan for data collected from other sites. Describe the process to ensure all engaged participating sites will safeguard data as required by local information security policies.

n/a

18.3 Subject Enrollment

Describe the procedures for coordination of subject enrollment and randomization for the overall project.

n/a

18.4 Reporting of Adverse Events and New Information

Describe how adverse events and other information will be reported from the clinical sites to the overall study director. Provide the timeframe for this reporting.

n/a

18.5 Audit and Monitoring Plans

Describe the process to ensure all local site investigators conduct the study appropriately. Describe any on-site auditing and monitoring plans for the study.

n/a

19.0 Adverse Event Reporting

19.1 Adverse Event Definitions

For drug studies, incorporate the following definitions into the below responses, as written:	
Adverse event	Any untoward medical occurrence associated with the use of the drug in humans, whether or not considered drug related
Adverse reaction	Any adverse event caused by a drug
Suspected adverse reaction	Any adverse event for which there is a reasonable possibility that the drug caused the adverse event. Suspected adverse reaction implies a lesser degree of certainty about causality than "adverse reaction". • *Reasonable possibility.* For the purpose of IND safety reporting, "reasonable possibility" means there is evidence to suggest a causal relationship between the drug and the adverse event.
Serious adverse event or Serious suspected adverse reaction	Serious adverse event or Serious suspected adverse reaction: An adverse event or suspected adverse reaction that in the view of either the investigator or sponsor, it results in any of the following outcomes: Death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.
Life-threatening adverse event or life-threatening suspected adverse reaction	An adverse event or suspected adverse reaction is considered "life-threatening" if, in the view of either the Investigator (i.e., the study site principal investigator) or Sponsor, its occurrence places the patient or research subject at immediate risk of death. It does not include an adverse event or suspected adverse reaction that had it occurred in a more severe form, might have caused death.
Unexpected adverse event or Unexpected suspected adverse reaction.	An adverse event or suspected adverse reaction is considered "unexpected" if it is not listed in the investigator brochure, general investigational plan, clinical protocol, or elsewhere in the current IND application; or is not listed at the specificity or severity that has been previously observed and/or specified.

For device studies, incorporate the following definitions into the below responses, as written:	
Unanticipated adverse device effect	Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or IDE 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.

19.2 Recording of Adverse Events

Address the frequency and process for eliciting adverse event information from research subject, e.g., "Research subjects will be routinely questioned about adverse events at study visits."

In the response, incorporate the following as written:
All adverse events (serious or non-serious) and abnormal test findings observed or reported to study team believed to be associated with the study drug(s) or device(s) will be followed until the event (or its sequelae) or the abnormal test finding resolves or stabilizes at a level acceptable to the investigator.

An abnormal test finding will be classified as an adverse event if one or more of the following criteria are met:

- The test finding is accompanied by clinical symptoms
- The test finding necessitates additional diagnostic evaluation(s) or medical/surgical intervention; including significant additional concomitant drug treatment or other therapy **NOTE:** Simply repeating a test finding, in the absence of any of the other listed criteria, does not constitute an adverse event.
- The test finding leads to a change in study drug dosing or discontinuation of subject participation in the clinical research study
- The test finding is considered an adverse event by the investigator.

Based upon our past pilot research as well as other related studies, we don't expect serious adverse events, such as fall-related injury.

Risks associated with survey and observational data collection for patients in this study includes some concerns about privacy and embarrassment. The collection of actigraphy data from the MotionWatch may be mildly uncomfortable for participants, similar to the sensation of wearing a watch. Lastly, the patient may experience some stress completing study-related activities while trying to participate optimally in treatments and assessments that occur as part of hospital care. We will train evaluators on safety precautions, including fall prevention and signs of patient stress.

Family CGs may also experience embarrassment, emotional discomfort, and increased stress. We will train research evaluators on observing for signs of distress and preventive strategies (e.g., pacing, active listening, and flexibility in scheduling study activity). The evaluators will be trained for to observe for, detect, and report signs of depression and suicidal ideation in both patients and family CGs.

During interviews, champions and nurses may experience stress, embarrassment, or the feeling that they need to offer only positive comments about the intervention. We will train evaluators on techniques to support the participants' comfort, and emphasize the need to identify any needed improvements in the intervention. We will schedule interviews at a time convenient for the participants. HIPAA releases for using audio recordings will be secured since such recordings cannot be entirely de-identified. Participants will be informed that the purpose of the recordings will be to evaluate cultural competency and effectiveness of the intervention, not the hospital or unit.

19.3 Causality and Severity Assessments

By submitting this study for review, you agree to the following statement – DO NOT ALTER OR DELETE:

The investigator will promptly review documented adverse events and abnormal test findings to determine 1) if the abnormal test finding should be classified as an adverse event; 2) if there is a reasonable possibility that the adverse event was caused by the study drug(s) or device(s); and 3) if the adverse event meets the criteria for a serious adverse event.

If the investigator's final determination of causality is "unknown and of questionable relationship to the study drug(s) or device(s)", the adverse event will be classified as associated with the use of the study drug(s) or device(s) for reporting purposes. If the investigator's final determination of causality is

"unknown but not related to the study drug(s) or device(s)", this determination and the rationale for the determination will be documented in the respective subject's case history.

19.4 Reporting of Adverse Reactions and Unanticipated Problems to the FDA

19.4.1 Written IND/IDE Safety Reports

For a drug study under an IND, incorporate the following from 21 CFR 312.32 as written – DO NOT ALTER OR DELETE:
The Sponsor-Investigator will submit a written IND Safety Report (i.e., completed FDA Form 3500A) to the responsible new drug review division of the FDA for any observed or volunteered adverse event that is determined to be a serious and unexpected, suspected adverse reaction. Each IND Safety Report will be prominently labeled, "IND Safety Report", and a copy will be provided to all participating investigators (if applicable) and sub-investigators.

Written IND Safety Reports will be submitted to the FDA as soon as possible and, in no event, later than 15 calendar days following the Sponsor-Investigator's receipt of the respective adverse event information and determination that it meets the respective criteria for reporting.

For each written IND Safety Report, the Sponsor-Investigator will identify all previously submitted IND Safety Reports that addressed a similar suspected adverse reaction experience and will provide an analysis of the significance of newly reported, suspected adverse reaction in light of the previous, similar report(s) or any other relevant information.

Relevant follow-up information to an IND Safety Report will be submitted to the applicable review division of the FDA as soon as the information is available and will be identified as such (i.e., "Follow-up IND Safety Report").

If the results of the Sponsor-Investigator's follow-up investigation show that an adverse event that was initially determined to not require a written IND Safety Report does, in fact, meet the requirements for reporting; the Sponsor-Investigator will submit a written IND Safety Report as soon as possible, but in no event later than 15 calendar days, after the determination was made.

For a device study under an IDE, incorporate the following from 21 CFR 812.150 as written – DO NOT ALTER OR DELETE:
The Sponsor-Investigator will submit a completed FDA Form 3500Ato the FDA's Center for Devices and Radiological Health for any observed or volunteered adverse effect that is determined to be an unanticipated adverse device effect. A copy of this completed form will be provided to all participating sub-investigators.

The completed FDA Form 3500Awill be submitted to the FDA as soon as possible and, in no event, later than 10 working days after the Sponsor-Investigator first receives notice of the adverse effect.

If the results of the Sponsor-Investigator's follow-up evaluation show that an adverse effect that was initially determined to not constitute an unanticipated adverse device effect does, in fact, meet the requirements for reporting; the Sponsor-Investigator will submit a completed FDA Form 3500Aas soon as possible, but in no event later than 10 working days, after the determination was made.

For each submitted FDA Form 3500A, the Sponsor-Investigator will identify all previously submitted reports that that addressed a similar adverse effect experience and will provide an analysis of the significance of newly reported adverse effect in light of the previous, similar report(s).

Subsequent to the initial submission of a completed FDA Form 3500A, the Sponsor-Investigator will submit additional information concerning the reported adverse effect as requested by the FDA.

n/a. There are no drugs or devices evaluated.

19.4.2 Telephoned IND Safety Reports – Fatal or Life-threatening Suspected Adverse Reactions

For a drug study under an IND, incorporate the following from 21 CFR 312.32 into the response, as written:
In addition to the subsequent submission of a written IND Safety Report (i.e., completed FDA Form 3500A), the Sponsor-Investigator will notify the responsible review division of the FDA by telephone or facsimile transmission of any unexpected, fatal or life-threatening suspected adverse reaction.

The telephone or facsimile transmission of applicable IND Safety Reports will be made as soon as possible but in no event later than 7 calendar days after the Sponsor-Investigator's receipt of the respective adverse event information and determination that it meets the respective criteria for reporting.

n/a

19.5 Reporting Adverse Reactions and Unanticipated Problems to the Responsible IRB

By submitting this study for review, you agree to the following statement – DO NOT ALTER OR DELETE:

In accordance with applicable policies of The Pennsylvania State University Institutional Review Board (IRB), the investigator will report, to the IRB, any observed or reported harm (adverse event) experienced by a subject or other individual, which in the opinion of the investigator is determined to be (1) unexpected; and (2) probably related to the research procedures. Harms (adverse events) will be submitted to the IRB in accordance with the IRB policies and procedures.

19.6 Unblinding Procedures

Describe the procedures for unblinding study therapy on a subject, including documentation of this in the subject's source document. Include example(s) here why someone might unblind a study. In most cases, the unblinding will be part of managing a serious adverse reaction and will be reported with the serious adverse event. However, in cases where unblinding was not associated with a serious adverse event, such actions should be reported in a timely manner.

n/a

19.7 Stopping Rules

In studies with a primary safety endpoint or studies with high risk to study subjects, provide the rules that define the circumstances and procedures for interrupting or stopping the study. If an independent Data and Safety Monitoring (DSMB) or Committee (DSMC) is set up for the study, the same stopping rules should be incorporated into the safety analysis plan as well.

n/a

20.0 Study Monitoring, Auditing and Inspecting

20.1 Study Monitoring Plan

20.1.1 Quality Assurance and Quality Control

Include this section if FDA regulations apply to this study (see "WORKSHEET: Drugs (HRP-306)" and "WORKSHEET: Devices (HRP-307)". HRP-306 and HRP-307 can be accessed by clicking the Library link in CATS IRB (http://irb.psu.edu).

Describe how you will ensure that this study is conducted and that the data are generated, documented (recorded) and reported in compliance with this protocol, with institutional and IRB policies, with Good Clinical Practice guidelines and any other applicable regulatory requirements.

Indicate who is responsible for monitoring the conduct of the study and specify how often the study will be monitored.

For single-site studies with low risk, it may be appropriate for the principal investigator to monitor the study.

For multi-center studies or single site studies involving significant risk, an independent monitor may be required (e.g., monitoring by the staff of the PSU quality assurance program office(s) or by a clinical research organization).

We plan the use a **Data Safety Monitoring Board (DSMB)** for this study. Upon review and approval by the National Institute on Aging Program Official (PO), we plan the DSMB to be chaired by a researcher who has extensive expertise in data safety and monitoring, clinical trials, and dementia caregiving research including bioethical considerations. The additional members of the DMSB will include two biostatisticians who have experience on a DSMB and a nurse with extensive experience in behavior change research and care of older adults with dementia. Potential members who fulfill these qualifications include a dementia caregiving researcher (Meredeth Rowe, PhD), a statistician (Shijun Zhu, PhD), and a dementia expert clinician and nurse researcher (Elizabeth Galik, PhD, CRNP).

The group will meet at least annually via web conferencing. Telephone conferencing and email may be used for additional interactions as needed. The first meeting of the DSMB will be prior to recruitment of participants and will focus on review of the study protocol and recruitment plan, consideration of participant burden, a review of our plan for participant safety and comfort, and approval of monitoring and reporting forms and a plan for PI blinding to closed forms. The subsequent meetings will focus on the progress of the study with regard to data quality and timeliness, participant consent, accrual and retention of participants, participant risk versus benefit, performance of intervention units, and any adverse events that occur during the course of the study to date. One or more major adverse events will also trigger a DSMB meeting. At the end of each meeting the committee will make recommendations to NIH, institutional review board(s) and the PI and investigative team concerning continuation or conclusion of the trial.

20.1.2 Safety Monitoring

Include this section if FDA regulations apply to this study (see "WORKSHEET: Drugs (HRP-306)" and "WORKSHEET: Devices (HRP-307)". HRP-306 and HRP-307 can be accessed by clicking the Library link in CATS IRB (http://irb.psu.edu).

Indicate the process for identifying, recording and reporting adverse events.

Specify roles for adverse event recording and monitoring. Indicate each staff member's role in the adverse event reporting process. Include the following if applicable:

The **Principal Investigator** will confirm that all adverse events (AE) are correctly entered into the AE case report forms by the coordinator; be available to answer any questions that the coordinators may have concerning AEs; and will notify the IRB, FDA, sponsor and/or DSMB of all applicable AEs as appropriate. All assessments of AEs will be made by a licensed medical professional who is an investigator on the research.

The **Research Coordinator** will complete the appropriate report form and logs; assist the PI to prepare reports and notify the IRB, FDA and/or DSMB of all Unanticipated Problems/SAE's.

The **Monitor** will confirm that the AEs are correctly entered into the case report forms. The Monitor will also confirm that the adverse events are consistent with the source documents and are reported to the appropriate regulatory bodies as required.

21.0 Future Undetermined Research: Data and Specimen Banking

If this study is collecting identifiable data and/or specimens that will be banked for future undetermined research, please describe this process in the sections below. This information should not conflict with information provided in section 9.1.1 regarding whether or not data and/or specimens will be associated with identifiers (directly or indirectly).

21.1 Data and/or specimens being stored

Identify what data and/or specimens will be stored and the data associated with each specimen.

The data collected may be used for future secondary analyses.

21.2 Location of storage

Identify the location where the data and/or specimens will be stored.

The data will be stored on RedCap.

21.3 Duration of storage

Identify how long the data and/or specimens will be stored.

The data will stored for at least six years after the data collection is completed.

21.4 Access to data and/or specimens

Identify who will have access to the data and/or specimens.

Only members of the research team will have access to the data.

21.5 Procedures to release data or specimens

Describe the procedures to release the data and/or specimens, including: the process to request a release, approvals required for release, who can obtain data and/or specimens, and the data to be provided with the specimens.

Data will be released only upon request to the Office of Human Research Protections in the U.S. Dept. of Health and Human Services; The Pennsylvania State University Institutional Review Board; The Pennsylvania State University Office for Research Protections, and the University of Pennsylvania Health System Institutional Review Board.

21.6 Process for returning results

Describe the process for returning results about the use of the data and/or specimens.

n/a

22.0 References

List relevant references in the literature which highlight methods, controversies, and study outcomes.

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