Study Title: Randomized controlled trial to test the feasibility, acceptability, and preliminary effectiveness of a psychosocial intervention to support Alzheimer's family caregivers in Vietnam.

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Document Type: Study Protocol

1) Protocol Title

Title: Randomized controlled trial to test the feasibility, acceptability and preliminary effectiveness of a psychosocial intervention to support Alzheimer's family caregivers in Vietnam

Protocol Version Date: *4/2/2018*

2) Objectives

The objective of this study is to conduct a randomized controlled trial to test the preliminary effectiveness, feasibility and acceptability of a psychosocial intervention to support Alzheimer's family caregivers in Vietnam. In terms of preliminary effectiveness, our hypothesis is that caregivers in the intervention will show lower psychological distress and lower caregiver burden compared with those in the control group.

3) Background

Low and middle-income countries (LMIC) such as Vietnam are undergoing a dramatic demographic transition that will result in a substantial increase in the number of older adults, including those afflicted with Alzheimer's disease and related dementias, over the next several decades. Dementia is among the most disabling and costly neurodegenerative brain diseases. Strengthening LMIC capacity to support family caregivers of persons with dementia through low-cost and sustainable non-pharmacological approaches, such as education and skill-building to deal with difficult behaviors, is vital to avoid costly and ineffective alternatives such as psychotropic medications or institutionalization, and to reduce caregiver burdens and depression. While evidence-based non-pharmacological treatments exist in high income countries (HIC), these interventions have not been adapted for use in Vietnam and other LMIC.

This project addresses these gaps by testing a community-based and culturally adapted behavioral family caregiver intervention for use in Vietnam. The intervention has several components (psychoeducation, stress reduction, skill-building) and is designed to reduce caregiver stress and burden. This project also builds directly on two preliminary studies, including interviews with key stakeholder and a case series. These preliminary studies demonstrated the acceptability of the intervention model but also identified areas for modification to tailor the intervention to the social, economic, and cultural circumstances in Vietnam.

4) Inclusion and Exclusion Criteria

Alzheimer's family caregivers will be identified through a registry of persons with dementia at the Vietnam National Geriatric Hospital in Hanoi.

To be eligible, the person will be an adult who is the identified primary adult caregiver (i.e. the person spending the most time day-to-day providing care) to an older adult who is living in the community and has received a diagnosis of Alzheimer's disease or another degenerative dementia. All participants will be living in the Soc Son area outside Hanoi, Vietnam.

The final sample will be 50 family caregivers of persons diagnosed with dementia (25 in the active intervention and 25 in the control group). The study will exclude

- Adults unable to consent
- Individuals who are not yet adults (infants, children, teenagers)
- Prisoners
- Pregnant women.

5) Study Timelines

- Each family caregiver will participate in the study for 3 months.
- We will enroll subjects from April 1 through the end of September, 2018.
- We will complete preliminary analysis of the data by the end of January of 2019.

6) Study Endpoints

This is a time-limited intervention lasting up to 3 months.

7) Procedures Involved

This is cluster randomized controlled trial to pilot-test a culturally adapted behavioral intervention to support Alzheimer's family caregivers.

Participants in the intervention clusters will receive a manualized intervention that will consist of 3-6 one-hour sessions with a trained health professional (e.g. nurse, social worker, or physician) who has been certified to deliver the intervention. The sessions will be administered in the home (or other setting of the subject's choice such as a clinic) and include several components, including psychoeducation, stress reduction, skill-building. The intervention will be tailored to the needs and preferences of the caregiver.

Participants in the control clusters will receive education about Alzheimer's disease including written informational materials at the time of enrollment (i.e., 1 session). .

Participants in both clusters will also be assessed at baseline and at the end of the intervention. These assessments will occur at baselineand 3 months to and will assess primary and secondary outcomes using standardized instruments (i.e., items embedded in Risk Priority Intake Assessment).

A research protocol will be used that includes scripts, study scales detailed descriptions of the goals for each session, and standardized forms (see attached study manual).

8) Data and/or Specimen Management and Confidentiality

The primary study outcomesare burden of caregiving (Zarit Burden Inventory) and caregiver distress (PHQ-4), found on pages (RP)4 and (RP)5 of the REACH Interventionist Notebook respectively. Secondary outcomes include Alzheimer's disease knowledge (Alzheimer's knowledge scale)

Procedures for maintenance and confidentiality include 1) assigning each participant a unique identifier, 2) data collected will be labeled using the unique identifier and will be stored separately from the key linking personal information (e.g. name, date of birth, address, phone number) and identifiers, 3) all data will be kept under lock and key or on a secure server that is only accessible to research staff, 4) at the conclusion of the study, the key linking identifiers and personal information will be destroyed, 5) all research personnel in the US who have access to the patient data will receive training on conducting human research (e.g. NIH online course) – all investigators in Vietnam will participate in the local equivalent of this training.

9) Data and/or Specimen Banking

All data will be stored on a secure server at in Vietnam. De-identified data will be transferred to UC Davis and the University of South Carolina electronically through an encrypted zip file. After the study, the key linking personal identifiers to the survey data will be destroyed.

10) Provisions to Monitor the Data to Ensure the Safety of Subjects

The goal of this randomized controlled trial care is to assess feasibility, acceptability, and preliminary effectiveness of the behavioral intervention to support Alzheimer's family caregivers. Case review will occur on a weekly basis with a team that includes the care manager and the local PI and one investigators from the UC Davis and the U of SC. The caregiver's level of distress and any indicators of elder abuse/neglect will be reviewed at each session.

This study will have a Safety Officer (SO) but will not have a DSMB. The rationale for not having a DSMB is that this is a single-site, minimal risk clinical trial with a relatively small number of subjects at a single site. The lead investigators (i.e. Co-PIs Hinton and Nguyen as well as the lead investigator at the National Geriatric Hospital, Dr. Thang) will meet quarterly with Safety Officer during the clinical trial. During these meetings, the SO responsibility will be to review the progress of the study, adverse events, procedures for maintaining the confidentiality of data, and the quality of data collection, management, and analyses. The SO will also review any issues that arise in terms of conflict of interest. The SO will be a senior neurology faculty from the National Geriatric Hospital who is not directly involved in the study.

For this study, Dr. Hinton will have primary responsibility for coordinating the collection, review and reporting of adverse events. Adverse events (AE) including serious adverse events (SAE) will be collected and reported to the IRBs at all three collaborating institutions on a regular basis. At the monthly meetings of the research team, all incident adverse events will be graded in terms of their seriousness and their likely relationship to the psychosocial intervention. All serious adverse events determined to have a likely relationship to the psychosocial intervention will be reported to the SO for this study, to the IRBs for each institution, and to NIA by the next business day (e.g. usually within 24 hours). Consistent with NIA guidelines, we will define serious adverse events as those that results in death, are life threatening, or places the participant at immediate risk of death from the event as it occurred, requires or prolongs hospitalization, causes persistent or significant disability or incapacity, is another condition which investigators judge to represent significant hazards.

Cases of potential elder abuse/neglect and caregiver suicidal ideation will be handled according to study protocols that are consistent with local practice in Vietnam. Field staff will report all suspected cases of elder abuse/neglect within 24 hours to study investigators Dr. Hung (neurologist) and Dr. Thang (a geriatrician) at the National Geriatric Hospital. After consultation with the research team including Drs. Hinton (a geriatric psychiatrist) and Nguyen (a social worker), Dr. Hung may take additional steps, including contacting and directly assessing the situation, educating family members about abuse, and referring families to local services (e.g. temples, elder clubs, social work services) for counseling and support. Similarly, field staff will report to Dr. Hung any caregivers who express suicidal ideation. Dr. Hung will then directly contact and assess the caregiver and determine if additional steps are necessary, including referring the caregiver for counseling, support and/or hospital-based mental health and social services. Field staff, usually nurses or social workers, will be trained in these written protocols by the study staff (i.e. Dr. Hung and Dr. Nguyen). All cases of elder abuse and caregiver suicidal ideation will be treated as adverse events and discussed at monthly research meetings and reported to each institution's IRB. Dr. Hinton will report serious adverse events to the SO and NIA.

11) Withdrawal of Subjects

Subjects (patients and family members) may withdraw at any time. If they withdraw from the study, they will be given the option of having their records destroyed.

12) Risks to Subjects

There are two main risks associated with this study: 1) discomfort or mild distress because of the intervention and 2) inconvenience because of the need to fill out the study questionnaires. These risks are similar to the risk of undergoing routine assessments in healthcare clinics in Vietnam. Specific steps are being taken to address each category of risk.

Discomfort due to the intervention: Even though this study builds on evidence-based strategies for support of family caregivers, subjects may experience discomfort or mild distress when discussing their caregiving experience or because of concerns about confidentiality. These risks are being minimized in several ways. First, caregiver will be given the option of discussing issues privately with the care manager during the intervention. Second, the care manager will be trained to monitor the nature of interactions between patients and family members and any serious issues that emerge will be discussed with the supervising team so that strategies can be developed to address any issues that arise. Finally, subjects will have the opportunity to drop out of the family-centered arm of the study and complete treatment by themselves or drop out of the study altogether.

Inconvenience due to questionnaires: To address the inconvenience associate with completing study questionnaires, we will give subjects the option of completing these in the home or by phone. In addition, during the consent process, participants will be advised that they can choose not to answer any questions that make them feel uncomfortable. Risks to subjects are minimal for several reasons.

This is a behavioral intervention and does not involve drug treatment. In prior studies conducted in the US with multi-cultural populations in the United States there have not been any serious adverse side events attributable to the intervention (personal communication with one of the PIs of a large-scale national study). It is also possible that elder/abuse or neglect may be detected during the study and require intervention. A protocol for handling cases of abuse/neglect according to local norms/resources has been developed in collaboration with our colleagues in Vietnam.

13) Potential Benefits to Subjects

There are several potential direct benefits to subjects. Subject may experience an increase in their knowledge and skills because of the intervention. In addition, caregivers will learn stress reduction techniques that may help reduce caregiving-related distress.

Participants will receive $10 at the end of each study visit (including both intervention sessions and visits for administration of questionnaires).

14) Multi-Site Research

This is a single-site, multiple PI, international study and Dr. Hinton is the lead investigator. Dr. Hinton will be responsible for ensuring that all sites have the most current version of the protocol and consent document. He will also be responsible for ensuring that 1) All required approvals have been obtained at each site (including approval by the site's IRB of record), 2) All modifications have been communicated to sites, and approved (including approval by the site's IRB of record) before the modification is implemented, 3) All engaged participating sites will safeguard data as required by local information security policies, 4) All local site investigators conduct the study appropriately, and 5) All non-compliance with the study protocol or applicable requirements will reported in accordance with local policy.

15) Community-Based Participatory Research

NA

16) Provisions to Protect the Privacy Interests of 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 or 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.

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

17) Compensation for Research-Related Injury

NA – minimal risk study

18) Economic Burden to Subjects

There are no costs that subjects may be responsible for because of participation in the research.

19) Drugs or Devices

NA

20) ClinicalTrials.gov Registration

Section 1: NIH Funded Studies

If yes to BOTH, the study must be registered on Clinicaltrials.gov.

Yes	
☒	This study is funded by the NIH. (If this study is not funded by NIH, go to Section 2.)
☐	One or more human subjects will be prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.

Section 2: Studies subject to FDA jurisdiction

If yes to ANY the study must be registered on Clinicaltrials.gov.

Yes	
☐	This is a prospective clinical study of health outcomes in human subjects that compares an intervention with an FDA-regulated device against a control. This is not a small clinical trial to determine the feasibility of a device, or a clinical trial to test prototype devices where the primary outcome measure relates to feasibility and not to health outcomes.
☐	This is a pediatric postmarket surveillance of a device as required under section 522 of the Federal Food, Drug, and Cosmetic Act.
☐	This is a controlled clinical investigation, other than a phase I clinical investigation, of a drug subject to section 505 of the Federal Food, Drug, and Cosmetic Act or to section 351 of the Public Health Service Act.

To view a flowchart describing applicable clinical trials subject to FDA jurisdiction click here.

Section 3: Publishing the results

If yes to BOTH the study must be registered on Clinicaltrials.gov.

Yes	
☐	This study prospectively assigns people or a group of people to an intervention, with or without concurrent comparison or control groups, to study the cause-and-effect relationship between a health-related intervention *and* a health outcome.
☒	The PI has access to and control over all the data from the clinical trial and has the right to publish the results of the trial and plans to publish the results in a journal that follows the ICMJE recommendations.

This requirement includes studies of behavioral interventions.

Section 4: Registration on Clinicaltrials.gov is not required

Yes	
☐	I have read sections 1-3 above and registration on clinicaltrials.gov is not required for this research.

21) Criteria for 10 Year Approval

If yes to all items below this research may qualify for a 10-year approval period.

Yes	
☒	This research involves no more than minimal risk.
☐	This research does not receive any federal or state government funding or funding from a private funder who requires annual review per contract.
☐	This research is not subject to FDA jurisdiction.
☐	This research does not include prisoners as participants.
☐	This research is not subject to SCRO oversight.
☐	This research is not subject to oversight by the Research Advisory Panel of California (RAP of C).
☐	This research does not involve identifiable information held by the State of California Department or Agency
☐	No personnel involved in the design, conduct, or reporting of this research have a new unreported related financial interest (RFI) in this study.