Care Ecosystem Trial Protocol

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Trial Protocol

Study Application (Version 1.3)

1.0 General Information

***Enter the full title of your study:**

Care Ecosystem: Navigating Patients and Families through Stages of Care

***Enter the study number or study alias**

Care Ecosystem
* This field allows you to enter an abbreviated version of the Study Title to quickly identify this study.

2.0 Add Department(s)

2.1 List the departments associated with this study. The Principal Investigator's department should be Primary.:

Primary Dept?	Department Name
○	**UCSF** - *140020* - M_Neurology
○	**UCSF** - *332008* - P_Clinical Pharmacy
○	**UCSF** - *707515* - SOM MEDICINE GERIATRICS MZ

3.0 List the key study personnel: (Note: external and affiliated collaborators who are not in the UCSF directory can be identified later in the Qualifications of Key Study Personnel section at the end of the form)

3.1 *Please add a Principal Investigator for the study:

Miller, Bruce L

Select if applicable
☐ Department Chair ☐ Resident
☐ Fellow
If the Principal Investigator is a Fellow, the name of the Faculty Advisor must be supplied below.

3.2 If applicable, please select the Research Staff personnel:

A) Additional Investigators

Boissier, Natasha
Study Clinician
Chiong, Winston W MDPhD
Other Investigator
Chodos, Anna H
Study Clinician

Finley, Ronald R Study Clinician Gearhart, Rosalie S Other Investigator Kao, Helen Other Investigator Koehn, Laura Other Investigator Lee, Kirby P Other Investigator Merrilees, Jennifer J Other Investigator Naasan, Georges Study Clinician Pierluissi, Edgar Study Clinician Possin, Katherine L Co-Principal Investigator Rosen, Howard J MD Other Investigator Schaffer, Michael W Other Investigator Wilson, Leslie PhD, PhD Other Investigator		
B) Research Support Staff		
Beagle, Alexander Clinical Research Associate Drew, Kathleen L Clinical Research Associate Johnson, Erica Clinical Research Associate Latham, Caroline Clinical Research Associate Linton, Deborah A Clinical Research Associate Tse, Marian M Clinical Research Associate		
3.3 *Please add a Study Contact:		
Chiong, Winston W MDPhD Fraser, James R Gearhart, Rosalie S Merrilees, Jennifer J Miller, Bruce L Possin, Katherine L The Study Contact(s) will receive all important system notifications along with the Principal Investigator. (e.g. The project contact(s) are typically either the Study Coordinator or the Principal Investigator themselves).		
3.4 If applicable, please add a Faculty Advisor/Mentor:		

3.5 If applicable, please select the Designated Department Approval(s):

Add the name of the individual authorized to approve and sign off on this protocol from your Department (e.g. the Department Chair or Dean).

4.0 Qualifications of Key Study Personnel

4.1 November, 2015 - NEW Definition of Key Study Personnel and CITI Training Requirements:

UCSF Key Study Personnel include the Principal Investigator, other investigators and research personnel who are directly involved in conducting research with study participants or who are directly involved in using study participants' identifiable private information during the course of the research. Key Personnel also include faculty mentors/advisors who provide direct oversight to Postdoctoral Fellows, Residents and Clinical Fellows serving as PI on the IRB application. **The IRB requires that all Key Study Personnel complete Human Subjects Protection Training through CITI prior to approval of a new study, or a modification in which KSP are being added. More information on the CITI training requirement can be found on our website.**

List the study responsibilities and qualifications of any individuals who qualify as Key Study Personnel (KSP) at UCSF and affiliated sites ONLY by clicking the "Add a new row" button. This information is required and your application will be considered incomplete without it.

KSP Name	Description of Study Responsibilities	Qualifications
Dr. Miller, Bruce MD	PI. He is responsible for organization and administration of the project, providing leadership and overseeing planning and execution of the research. He will ensure best use of resources and assure financial requirements set forth by CMS are adhered to according to terms and conditions of the award.	Professor of Neurology, directs UCSF's MAC and its AD Research Center.
Dr. Possin, Katherine PhD	Associate Director. With Dr. Miller, she will be accountable for efficient and effective project operations, strategy, quality and interactions establishing agreements with payer groups.	Career Development Award focused on cognition and dementia, and Investigator on a M.J. Fox Foundation award to elucidate the heterogeneity of Parkinson's disease. 2011 winner John S. Spice Award in Aging Research, and a 2013 UCSF Digital Health Catalyst Award for developing tablet-based cognitive diagnostic and monitoring tools for dementia. She diagnoses and cares for patients with dementia and supervises trainees.
Dr. Merrilees, Jennifer PhD, RN	Clinical & Education Core Director. Will direct Care Ecosystem UCSF clinical services, lead the Caregiver module, and oversee the UCSF	Clinical Nurse Specialist at the MAC and Associate Professor Nursing. She oversees clinical services of the MAC and leads a nurse-run Behavior

	CTNs. Will oversee the development and implementation of the Dementia Curriculum. Will coordinate with Brenda Keller, MD, who will direct the UNMC clinical services.	Management Clinic. Completed study "Life enhancing activities for family caregivers of people with frontotemporal dementia" that showed significant benefit for caregivers using a skill building intervention delivered with innovative technology. Funded for "Burden, depression, and health in dementia caregivers: The role of emotion."
Dr. Wilson, Leslie PhD, PhD	Administration & Health Economics Director. Will develop and test dementia care pay for performance model and health utilization survey instrument and review information from CMS claims records, and analyze the impact of the intervention on medical costs.	Professor Medicine, Co-Director of the Health Services and Policy Research Pathway, and Director of Program for Pharmaceutical Outcome and Policy Studies in UCSF Department of Pharmacy. Expertise health economics and outcomes studies, including comparative effectiveness, cost-effectiveness, and cost benefit analyses and teaches decision analysis, decision modeling and utility measurement, including standard gamble and choice based conjoint analyses. Experience examining differences in hospitalization rates and care utilization and costs for patients with and without dementia with Kaiser.
Schaffer, Michael	Technology & Strategy Director. Directs integration of technology solutions in Care Ecosystem, including the Dashboard.	Technology Consultant, contributes expertise in systems integrations, application design and technology management. He has over 30 years of software development, technology strategy and management experience, in a variety of both startups and enterprise software companies. As an independent consultant, Michael is currently advising a number of clients in system architecture and in organizational design; he also performs technical due diligence for private equity and similar investment funds.
Gearhart, Rosalie S	Administrative Nurse. Will work with team to ensure optimal operations. Liaison and communicate with all sites and partners. Oversee personnel, resource management and reporting duties.	MAC's administrative nurse and Associate Clinical Professor Department Physiology in School of Nursing. Administers UCSF AD Research Center.
Dr. Chiong, Winston MD, PhD	Strategic Leader of the	Assistant Professor of

	Decision-making Module. He will direct the Decision-Making Module, applying best practices and current research findings to improve decision-making by patients with dementia as well as by their caregivers.	Neurology at the MAC. Research elucidates the neural mechanisms underlying decision-making in dementia. Co-Directs Responsible Conduct of Research course UCSF CTSI, and member of Medical Center Ethics Committee and Training in Responsible Conduct of Research Subcommittee.
Dr. Lee, Kirby PharmD,MAS	Strategic Leader of the Medication Module. Will direct the Medication Module and work closely with all members of the Strategic and Clinical Teams to optimize medication use and clinical outcomes.	Associate Professor of Clinical Pharmacy and Director of the Patient Health Information Technology Lab. Research focuses on improving the quality and safety of medications and leads projects to understand barriers and solutions to optimal medication use by patient, provider and system level factors. Incorporating web and mobile technologies, develops novel programs that screen for medication related problems to assist providers and patients with medication management.
Finley, Ronald R	Clinical Pharmacist. Will provide medication consults to Care Ecosystem patients and the Clinical Team.	MAC clinical pharmacist for 18 years. Clinical Professor School of Pharmacy with specialized expertise in brain health and dementia.
Dr. Rosen, Howard MD	Co-Investigator. Will oversee the Chinatown cohort.	Professor Neurology, directs dementia care services for the Chinatown Clinics.
Tse, Marian M	Research Associate. She will support the Chinese cohort CTN with outreach, and will translate study materials.	Experienced translator, coordinates all current MAC outreach efforts to the Chinatown Clinics.
Dr. Naasan, Georges MD	Clinician. MAC Neurologist will provide clinical care direction.	Behavioral Neurologist and Medical Director of the Memory and Aging Center clinical services.
Dr. Chodos, Anna MD	Clinician. SFGH Geriatrician will provide clinical care direction.	San Francisco General Hospital geriatrician.
Pierluissi, Edgar	Clinician. SFGH Geriatrician will provide clinical care direction.	San Francisco General Hospital geriatrician.
Boissier, Natasha	Social Worker. Will work closely with Dr. Merrilees to connect Care Ecosystem patients with resources via the Dashboard, over the phone or via in-home visits, as needed.	Licensed Clinical Social Worker at the MAC. She serves on the diagnostic team and provides resource information, counseling and dementia care education to people with neurodegenerative illnesses and their family caregivers in

		clinic and research programs. She provides training and supervision for other professionals. Particular area of focus is working with the Huntington's Disease cohort.
Latham, Caroline	Content Manager. Oversee content for the dashboard, project materials, website, and brochures.	Creates, manages content for the MAC, including memory. ucsf.edu.
Drew, Kathleen L	Finance. Post-award and financial management duties.	Financial analyst at the Memory and Aging Center.
Linton, Deborah A	Information Architect and Content Curator (IACC). Will work closely with all members of the Care Ecosystem inter-professional team to design and organize the content and structure of the Dashboard.	Information architect and UX designer at the Memory and Aging Center.
Koehn, Laura	Will provide direction on clinical care issues and contribute palliative care expertise to study design.	UCSF Palliative Care specialist and neurologist.
6017195 Kao, Helen 6017195, MD	Will provide clinical care & recruitment direction.	UCSF Geriatrician.
Beagle, Alexander	Research Associate. Providing project support during study set-up.	Clinical Research Coordinator at Memory and Aging Center.
Johnson, Erica	Research Associate. Providing project support during study set-up.	Clinical Research Coordinator at Memory and Aging Center.

5.0 Initial Screening Questions - Updated 9/13

(Note: You must answer every question on this page to proceed).
If you are converting to the new form, check questions 5.4, 5.6, 5.7, 5.8 and 5.10 before saving and continuing to the next section.

5.1 * Application type:

- (•) Full Committee
- ( ) Expedited
- ( ) Exempt

5.2 * Risk level (Help Text updated 9/13):

- (•) Minimal risk
- ( ) Greater than minimal risk

5.3 * Subject contact:

- (•) Yes (including phone, email or web contact)

		clinic and research programs. She provides training and supervision for other professionals. Particular area of focus is working with the Huntington's Disease cohort.
Latham, Caroline	Content Manager. Oversee content for the dashboard, project materials, website, and brochures.	Creates, manages content for the MAC, including memory. ucsf.edu.
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5.1 * Application type:

- (•) Full Committee
- ( ) Expedited
- ( ) Exempt

5.2 * Risk level (Help Text updated 9/13):

- (•) Minimal risk
- ( ) Greater than minimal risk

5.3 * Subject contact:

- (•) Yes (including phone, email or web contact)

○ No (limited to medical records review, biological specimen analysis, and/or data analysis)

5.4 * Funding (past or present):

◉ Funded or will be funded (external sponsor, gift, program or specific internal or departmental funds)
○ Unfunded (no specific funds earmarked for this project)
○ Unfunded student project

5.5 * The Principal Investigator and/or one or more of the key study personnel has financial interests related to this study:

○ Yes ◉ No

If **Yes**, the Conflict of Interest Advisory Committee (COIAC) office may contact you for additional information.

5.6 * This is an investigator-initiated study:

◉ Yes ○ No

5.7 * This study ONLY involves retrospective records review and/or identifiable biospecimen analysis:

○ Yes ◉ No

5.8 * This is a clinical trial:

◉ Yes ○ No

Clinical Trial Registration
"NCT" number for this trial:

NCT02213458

5.9 * This is a multicenter study:

◉ Yes ○ No

5.10 * This application involves the study of unapproved or approved drugs, devices, biologics or in vitro diagnostics:

○ Yes ◉ No

5.11 * This application involves a Humanitarian Use Device:

◉ No
○ Yes, and it includes a research component
○ Yes, and it involves clinical care ONLY

5.12 * This study involves human stem cells (including iPS cells and adult stem cells), gametes or embryos:

◉ No
○ Yes, and requires CHR and GESCR review

○ Yes, and requires GESCR review, but NOT CHR review

5.13 * This is a CIRB study (e.g. the NCI CIRB will be the IRB of record):

○ Yes ◉ No

5.14 * This application includes a request to rely on another IRB (other than NCI CIRB):

○ Yes ◉ No

Note: If this request is approved, the CHR will **NOT** review and approve this study. Another institution will be the IRB of record.

6.0 Funding

6.1 Identify all sponsors and provide the funding details. If funding comes from a Subcontract, please list only the Prime Sponsor: **Note: we require only a P Number *OR* an A Number for funding coming through UCSF. Please avoid these common errors in funding documentation:**

- **DO NOT add the A Number if a P Number was already provided OR update the A Number field when a new funding cycle begins. The IRB does NOT use this information or want these changes made.**
- **DO NOT add a grant continuation as a new funding source.**

External Sponsor:

View Details	Sponsor Name	Sponsor Type	Awardee Institution	Contract Type:	UCSF RAS "P number" or eProposal number	UCSF RAS System Award Number ("A" + 6 digits)
⊟	HHS Ctrs for Medicare and Medicaid Svcs	01	UCSF	Grant		124135A

Sponsor Name:	HHS Ctrs for Medicare and Medicaid Svcs
Sponsor Type:	01
Sponsor Role:	Funding
Grant/Contract Number:	1C1CMS331346-01-00
Awardee Institution:	UCSF
Is Institution the Primary Grant Holder:	Yes
Contract Type:	Grant
UCSF RAS "P number" or eProposal number:	
UCSF RAS System Award Number ("A" + 6 digits):	124135A
Grant Number for Studies Not Funded thru UCSF:	
Grant Title:	
PI Name:	

(If PI is not the same as identified on the study.)	
Significant Discrepancy:	

Gift, Program, or Internal Funding (check all that apply):

- ☐ Funded by gift (specify source below)
- ☐ Funded by UCSF or UC-wide program (specify source below)
- ☐ Specific departmental funding (specify source below, if applicable)

List the gift, program, or departmental funding source:

6.2 If you tried to add a sponsor in the question above and it was not in the list, follow these steps:

- **If funding has already been awarded or the contract is being processed by the Office of Sponsored Research (OSR) or Industry Contracts Division (ICD), your sponsor is already in the system and the project has an eProposal Proposal or Award number. Check with your department's OSR Staff or ICD Officer to ask how the sponsor is listed in the UC sponsor list and what the Proposal or Award number is. Click here to find your OSR staff and here to find your ICD staff.**
- **If your sponsor is not yet in the list, enter it in the box below.**

○ Sponsor not in list

Only if your sponsor is not yet in the list, type the sponsor's name:

If the funding is administered by the UCSF Office of Sponsored Research, your study will not receive CHR approval until the sponsor and funding details have been added to your application.

6.3 * This study is currently supported in whole or in part by Federal funding OR has received ANY Federal funding in the past (Help Text updated 9/13):

◉ Yes ○ No

If **yes**, indicate which portion of your grant you will be attaching:

- ☐ The Research Plan, including the Human Subjects Section of your NIH grant or subcontract
- ☐ For other federal proposals (contracts or grants), the section of the proposal describing human subjects work
- ☐ The section of your progress report if it provides the most current information about your human subjects work
- ☑ The grant is not attached. The study is funded by an award that does not describe specific plans for human subjects, such as career development awards (K awards), cooperative agreements, program projects, and training grants (T32 awards) OR UCSF (or the affiliate institution) is not the prime recipient of the award

7.0 Sites

7.1 Institutions (check all that apply):

- ☑ UCSF
- ☐ China Basin
- ☐ Helen Diller Family Comprehensive Cancer Center
- ☑ Mission Bay

- [ ] Mount Zion
- [x] San Francisco General Hospital (SFGH)
- [ ] SF VA Medical Center (SF VAMC)
- [ ] Blood Centers of the Pacific (BCP)
- [ ] Blood Systems Research Institute (BSRI)
- [ ] Fresno (Community Medical Center)
- [ ] Gallo
- [ ] Gladstone
- [ ] Institute on Aging (IOA)
- [ ] Jewish Home
- [ ] SF Dept of Public Health (DPH)

7.2 Check all the other types of sites not affiliated with UCSF with which you are cooperating or collaborating on this project (Help Text updated 9/13):

- [ ] Other UC Campus
- [x] Other institution
- [x] Other community-based site
- [ ] Foreign Country

List the foreign country/ies:

7.3 Check any research programs this study is associated with:

- [ ] Cancer Center
- [ ] Center for AIDS Prevention Sciences (CAPS)
- [ ] Global Health Sciences
- [ ] Immune Tolerance Network (ITN)
- [x] Neurosciences Clinical Research Unit (NCRU)
- [ ] Osher Center
- [ ] Positive Health Program

8.0 Studies Involving Other Sites

8.1 UCSF is the coordinating center:

(•) Yes ( ) No

If **Yes**, describe the plan for communicating safety updates, interim results, and other information that may impact risks to the subject or others among sites:

The University of Nebraska Medical Center (UNMC) is a major partner on this project, with plans to enroll 900 patient participants. They will be responsible for safety issues at their site and will sign a separate consent form from UNMC. With UNMC, our site will monitor safety, results, and other information that may impact risks to the subject. This will be handled immediately for urgent issues via phone meetings between the key personnel. There will be quarterly meetings of the executive team (Miller, Possin, Schafer, Merrilees, Wilson, Gearhart and key personnel from UNMC) to address non-urgent updates and results.

San Francisco General Hospital (SFGH) is a recruitment site. Anna Chodos, a geriatrician at SFGH and on this project, will be responsible for communicating safety concerns and concerns about subject risk. She will attend monthly meetings with our clinical team.

If **Yes**, describe the plan for sharing modification(s) to the protocol or consent document(s) among sites:

Modifications will be addressed at the quarterly meetings of the executive team as well as well as video conferencing to train UNMC staff on changes to the protocol and as needed.

8.2 Check any other UC campuses with which you are collaborating on this research study:

- ☐ UC Berkeley
- ☐ UC Davis
- ☐ Lawrence Berkeley National Laboratory (LBNL)
- ☐ UC Irvine
- ☐ UC Los Angeles
- ☐ UC Merced
- ☐ UC Riverside
- ☐ UC San Diego
- ☐ UC Santa Barbara
- ☐ UC Santa Cruz

8.3 Are the above UC campuses requesting to rely on UCSF's IRB (check all that apply):

- ☐ Yes (Submit a reliance request through the UC IRB Reliance Registry)
- ☐ No (Complete IRB Approval Certification section)

9.0 Outside Site Information

9.1 Outside Site Information

Click "Add a new row" to enter information for a site. Click it again to add a second site again to add a third site, a fourth site, etc.

Outside Site Information

Non-UCSF affiliated site information:

Site name:

University of Nebraska Medical Center (UNMC)

Contact name:

Steve Bonasera MD, PhD

Email:

Bonasera, Stephen J <sbonasera@unmc.edu>

Phone:

402-559-8409

For Federally-funded studies only, corresponding FWA#:

00002939

*** The research at this site will be reviewed by:**

- (●) The non-affiliated site's IRB or a private IRB
- ( ) The non-affiliated site is requesting UCSF to be the IRB of record for this study
- ( ) The non-affiliated site is not engaged in the human subjects research and has provided a letter of support

If the other site's IRB approval letter is available now, attach it to the application. If the IRB approval letter is not yet available, submit it once you receive it.

Or, if the other site is **not engaged** in human subjects research, attach the letter of support to your application.

10.0 Study Design

10.1 * Study design (Help Text updated 9/13):

This is a 3 year pragmatic clinical trial evaluating the benefits of a program that supports care for patients with dementia and their family caregivers. Subjects will be recruited from several sites in San Francisco. Subjects determined to be eligible will be consented and randomized along with their caregiver into one of two groups. Two thirds of patients and their caregivers will be enrolled into the Navigated Care group that provides them with assistance in meeting important benchmarks in their care, for example completion of legal and financial planning and strategies for minimizing caregiver burden. One third of patients and their caregivers will be enrolled to the control group, entitled Survey of Care. Outcome measures include quality of life, caregiver burden, completion of advance planning, resource utilization, and medication side effects.

10.2 If this is a clinical trial, check the applicable phase(s) (Help Text updated 9/13):

- [ ] Phase I
- [ ] Phase II
- [ ] Phase III
- [ ] Phase IV

11.0 Scientific Considerations

11.1 Hypothesis (Help Text updated 9/13):

This study has a hypothesis:

( ) Yes ( ) No

If yes, state the hypothesis or hypotheses:

Our primary hypotheses are that we will improve the caregiver's satisfaction with the patient's care, improve the patient's quality of life, decrease caregiver burden, and decrease total cost of care in our treatment group as compared to our control group.

11.2 * List the specific aims:

We aim to refine and to implement a dementia care program that supplements and coordinates with the patient's care as usual.

11.3 Statistical analysis:

Our cohort of 1400 Navigated Cared/700 Survey of Care patients provides a sample size with sufficient power to detect a difference equivalent to 0.2*(standard deviation) in the five primary outcomes between the two treatment arms at the 0.05/5=0.01 significance level, based on a two-sided two-sample Mann-Whitney test. Because this minimum difference translates into an effect size smaller than observed in comparable studies[56], we will have adequate power to identify all expected treatment effects. *Analysis of Missing Data:* Participants who drop out will be replaced as appropriate to maintain sample size. Baseline characteristics of participants who drop out will be compared with the other participants to assess for non-random missing data bias. When the mechanism leading to missing data is informative (e.g. depends on severity of patients), we will describe this using logistic regression models and consider performing sensitivity analysis to weigh various approaches to imputing the missing data when appropriate. *Analysis of Confounds:* Baseline and follow-up characteristics of participants in each treatment arm (Intervention vs. Survey of Care) across the two sites (UNMC vs. UCSF) and within each site will be examined using tests of central tendency and proportions at baseline and each follow-up visit, and log-linear tests and analysis of variance (ANOVA) will be applied to investigate treatment by site interaction. If there is no between-site effect, primary outcomes between treatment arms will be grouped across the sites, otherwise will be stratified by site. *Differences in the primary and secondary outcomes* between treatment arms will be examined using appropriate tests of proportions (e.g. Chi-square, Fisher's exact, Binomial exact) for categorical outcomes and tests of mean (e.g. t-test, Wilcoxon test) for continuous outcomes. We will apply appropriate multiple testing corrections, such as Bonferroni and Benjamini-Hochberg. *Intervention by Diagnosis Interaction:* We will elucidate differences in the effect of the intervention across diagnostic groups and other clinical characteristics using log-linear tests and ANOVA. *Multivariate Regression Analysis:* Appropriate regression models will be used to examine differences in the outcomes while adjusting for potential confounders. *Analysis of Longitudinal Changes in Outcomes* Linear mixed effects models will be used to examine longitudinal changes in outcome measures. To examine potential nonlinearities in these changes, we will consider applying mixed effects models with a non-linear term or piece-wise linear mixed effects models. *Analysis of Survival Function* To examine effectiveness of intervention for time-to-event (e.g. time to nursing home placement), we will use Kaplan-Meier, Breslow, and logrank tests with the Cox Proportional Hazards model to adjust for other important variables. Proportional hazards assumption will be checked using log-minus-log curves and the Schoenfeld test, and with severe departures we will consider either a) parametric survival models, such as accelerated failure time models; or b) add time varying covariates into the Cox Proportional Hazards Model to delineate time intervals within which the assumption holds approximately true. *Model Selection, Assumptions and Validation:* To avoid overfitting, all analyses will involve model choice based on a combination of our *a priori* knowledge and statistical measures of assessment (e.g., Akaike Information Criteria and Bayesian Information Criteria) and potentially model averaging. Assumptions will be checked and non-parametric alternatives (e.g. validation of p-values based on permutation) or transformations (e.g., Box-Cox) considered. We will internally validate inferred models using bootstrapping or cross-validation.

11.4 If this study has undergone scientific or scholarly review, please indicate which entity performed the review:

- ☐ Cancer Center Protocol Review Committee (PRC) (Full approval is required prior to final CHR approval for cancer-related protocols.)
- ☐ CTSI Clinical Research Center (CRC) advisory committee
- ☐ Departmental scientific review
- ☐ Other:

Specify **Other**:

Centers for Medicare & Medicaid Services

12.0 Background

12.1 Background:

Current health care systems are unprepared to meet the growing costs and burdens of Alzheimer's disease (AD) and related dementias. In 2011, U.S. dementia care costs were between $157 and $215 billion per year, including $11 billion paid by Medicare (Hurd et al., 2013). These exceeded even costs of cancer or heart disease. Without better therapies or major changes to how we care for dementia patients, AD-related costs will more than double by 2040. Often, families are ill prepared for the caregiving challenges they encounter, and dementia care becomes reactive, focusing on managing crises as they arise. Patients are frequently on inappropriate medication regimens, and few have advanced care plans in place. Family caregivers experience negative effects to their physical and emotional health as a result of the burdens in

providing care (Schulz et al., 1997). Without a care team that closely monitors the patient and is always available, families face care decisions alone and unprepared and patients suffer negative outcomes.

Personalized and continuous care focused on prevention and supported by innovative technologies could prevent many of the negative outcomes associated with dementia care. Such care could prevent medical emergencies, adverse drug reactions, help families plan for the challenges of advancing dementia, keep patients in the home longer, and offer cost-savings to health care systems. Our program, the Care Ecosystem, is a partnership between the UCSF Memory and Aging Center (MAC) and the University of Nebraska Medical Center (UNMC), organizations with long histories of providing exemplary dementia care. The Care Ecosystem emphasizes continuous and personalized care and is based on 3 modules: the Caregiver Module that includes educational forums and connects families with community resources, the Decision-Making Module that facilitates proactive medical, financial, and safety decisions, and the Medication Module that identifies inappropriate medication usage via pharmacist review. Resources and education target the stage of dementia, for example, issues around safe driving are typically managed during the early or mild stage of dementia while concerns about hospice care come up during the advanced stage of dementia. Innovative technology in the form of a "dashboard" functions as a patient care management system used by Care Team Navigators (CTNs). The CTNs have monthly contacts with patients and families, provide necessary education and links to services, and access a clinical team member (nurse, social worker, pharmacist, and physician) as needed. The Dementia Curriculum is a series of courses covering topics important in dementia care and will be available for patients and families.

We aim to improve costs of dementia care by delaying admission to long-term care, lower ER visits, preventing hospital costs, reducing ambulance costs, and cutting costs of prescription drugs. We aim to reduce family caregiver burden, improve satisfaction with care, increase proactive decision-making, protect patient and family finances and safety, improve medication management, and respond efficiently and effectively to issues facing patients and their caregivers. We plan to rigorously test our care model in a diverse sample of patients from urban (San Francisco and including an underserved Chinese-American cohort) and rural (Nebraska, Iowa) areas.

12.2 Preliminary studies:

In 2010, UCSF partnered with the Alzheimer's Association of Northern California and Kaiser San Francisco to form the San Francisco Dementia Support Network. This education and support program for family caregivers with particular attention to high risk individuals reduced ER visits by 48% and hospital days by 61%. It improved caregiver efficacy in managing dementia-related symptoms and in accessing needed services (Edgerly et al., 2013). In a survey of UCSF caregivers, we found that caregivers needed a roadmap of what to expect and how to prepare, and requested access to legal services and online resources. Families preferred specific education and support delivered at different stages in the illness trajectory (ArthurAssoc., 2013). The Indiana Healthy Aging Brain Center has improved outcomes for patients and caregivers by offering systematic assessment in the diagnosis, evaluation, and management of patients with dementia along with education and support for family caregivers (Boustani et al. 2011). These studies guided the development of the Care Ecosystem by incorporating the care management and continuous follow-up features in addition to other novel components such as 24/7 access to a dementia expert, careful attention to medications and decision-making, and targeted caregiver education and support.

12.3 References:

Arozullah, A.M., Yarnold, P.R., Bennett, C.L., Soltysik, R.C., Wolf, M.S., Ferreira, R.M., Lee, S.-Y.D., Costello, S., Shakir, A., Denwood, C., et al. (2007). Development and validation of a short-form, rapid estimate of adult literacy in medicine. Med Care 45, 1026–1033.

ArthurAssociates. UCSF Memory and Aging Center Qualitative market research regarding services provided for patients and caregivers. Arthur Associates 2013, June 12, 2013.

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If you have a separate bibliography, attach it to the submission with your other study documents.

13.0 Sample Size and Eligibility

13.1 Number of subjects that will be enrolled at UCSF and affiliated institutions:

1200

13.2 Total number of subjects that will be enrolled at all sites (Help Text updated 9/13):

2100

13.3 Estimated number of people that you will need to consent and screen here (but not necessarily enroll) to get the needed subjects:

1600

13.4 Explain how and why the number of subjects was chosen (Help Text updated 9/13):

Power analysis (see statistical analysis section) and also to target diverse patient groups (urban, rural, range of socioeconomic, and an underserved Chinese-American cohort). The above numbers represent patient and caregiver dyads that will enroll into our study.

13.5 * Eligible age range(s):

- [ ] 0-6 years
- [ ] 7-12 years
- [ ] 13-17 years
- [x] 18+ years

13.6 Inclusion criteria:

For Patient Participants:

Patient has a diagnosis of dementia,
Patient has a primary caregiver (identified as having primary responsibility for patient) that is eligible for and agrees to join the study
Patient is covered by Medicare or Medi-caid or is Medi-pending,
Patient death is not imminent (assessed by asking the referring provider "Would you be surprised if this patient died in the
next 6 months or is hospice eligible?"),
Patient speaks either English, Cantonese, Mandarin, or Spanish,
Patient lives in California or Nebraska or Iowa,
Patient is age 18 or older

For Caregiver Participants:

18 or older
Speaks either English, Cantonese, Mandarin, or Spanish,
Has primary responsibility for dementia patient that is eligible for and agrees to join the study

13.7 Exclusion criteria:

Patient has unstable mental illness that precedes the dementia
Patient resides in a nursing home or skilled nursing facility at time of enrollment
Caregiver has unstable mental illness or condition that negatively affects ability to be a caregiver

13.8 There are inclusion or exclusion criteria based on gender, race or ethnicity:

○ Yes ◉ No

If **yes**, please explain the nature and rationale for the restrictions:

14.0 Other Approvals and Registrations

14.1 * Do any study activities take place on patient care units:

○ Yes ◉ No

If **Yes**, attach a letter of support for the study from the involved patient care manager(s).

14.2 * Does your protocol involve any radiation exposure to patients/subjects? The UCSF Radiation Safety Committee requires review of your protocol if it includes administration of radiation as part of standard of care OR research exposures:

○ Yes ◉ No

14.3 * This study may generate genetic data that may be broadly shared (e.g. submitted to NIH for Genome-Wide Association Studies (GWAS) in dbGaP, TCGA, etc):

○ Yes ◉ No

14.4 * This study involves administration of vaccines produced using recombinant DNA technologies to human subjects:

○ Yes ◉ No

14.5 * This study involves human gene transfer (NOTE: Requires NIH Recombinant DNA Advisory Committee (RAC) review prior to CHR approval):

○ Yes ◉ No

14.6 This study involves other regulated materials and requires approval and/or authorization from the following regulatory committees:

☐ Institutional Biological Safety Committee (IBC)

Specify BUA #:

☐ Institutional Animal Care and Use Committee (IACUC)

Specify IACUC #:

☐ Radiation Safety Committee

Specify RUA #:

☐ Radioactive Drug Research Committee (RDRC)

Specify RDRC #:

☐ Controlled Substances

15.0 Procedures

15.1 * Procedures/Methods (Help Text updated 9/13) For clinical research list all study procedures, test and treatments required for this study, including when and how often they will be performed. If there are no clinical procedures, describe the Methods:

Pre-screening procedures:
Prior to the in-person screening evaluation of patient participants, potential patient participants will be identified by providers at the various recruitment sites. The Research Coordinator (RC) will conduct a preliminary chart review to confirm patient subject's eligibility and to determine if the patient meets the inclusion criteria (a request for a "waiver for consent for screening" is attached).

Screening visit:

The RC contacts the potential subject and their caregiver to discuss the study and to assess their interest in participating. The RC meets with the potential subject and caregiver in-person. The primary purpose of this visit is to determine eligibility and to sign the consent forms, one for the patient and one for the caregiver.

Consent:
Consent will be completed once the patient and caregiver have demonstrated understanding of the study, have had their questions answered, and agree to participate. Additionally, the Capacity Assessment Record will be used for each patient participant during the consent process and the caregiver (surrogate consent) will be involved as needed.

Baseline Outcome Assessment:
A Baseline Outcome Assessment will be performed following the consent. This includes all baseline measures, the Montreal Cognitive Assessment (MOCA) for the patient, the Functional Assessment Staging of AD (FAST) for the patient, a test of literacy (NIH Toolbox Reading level assessment) for the patient and caregiver, and demographic data and baseline characteristics for the patient and the caregiver. If the patient has a personal medication list, the RC will obtain a copy. Tasks and tests that require in-person completion (for example, the MOCA) will be done following the consent. If participants prefer, the portions of the Baseline Outcome Assessment that do not need to be completed in person, will be completed over the phone at a later date.

Randomization:
Patient subjects will be randomized with their caregiver (2:1) to Navigated Care or to Survey of Care. The Project Manager will be responsible for randomization. We will randomize participants to one of the two arms of the trial in a 2:1 ratio in Navigated Care vs. Survey of Care treatment arms. Allocation concealment will be ensured, as the randomization code will not be released until the participants are recruited into the trial and all baseline measures, including diagnostic evaluation, are taken. Following randomization, the subject and their caregiver will be informed of the next steps (when they will be contacted by study staff).

Outcome Measures:
Outcome measures will be completed at different stages during the study. These stages are selected to both provide important information regarding the Care Ecosystem and patient/caregiver concerns while minimizing subject burden. There are 4 categories of outcome measures: Baseline, Agile (Navigated Care only, every 3 months), Short (every 6 months), and Full (annually). All subjects (patients and caregivers), regardless of randomization assignment receive Baseline, Short and Full measures. Outcome survey questions will be answered by patients on themselves (if they have capacity to respond), by caregivers on behalf of the patient, and caregivers on themselves. specifically, we will be asking caregivers about their experience with the patient's care, their needs regarding care, how prepared they are for changes in the patient's health, their mood (depression, anxiety), and how they are feeling overall about their health. Subjects in Navigated Care complete the Agile measures that rate their satisfaction with the program so that improvements can be made in a responsive and efficient manner. Outcome measures will be administered by a research coordinator who is not involved with the provision of care. Names will not be linked to the questionnaires when results are presented to the care team unless requested by the caregiver.

Contact initiated by study staff:
Care Team Navigators (CTNs) will contact subjects (patients and caregivers) who are enrolled in Navigated Care on a monthly basis to help guide and support the caregiver and patient with their dementia care. CTNs will not require a formal medical background but likely have a relevant BA or successful experience working with this population. CTNs will inquire about new problems, medication changes, experience with care, needs regarding care, how prepared the caregiver and the patient are for future changes in their health, how the patient and caregiver are feeling, and caregiver well-being. See the sample script in the appendix. CTNs will also provide help with dementia care education, planning for the future, managing stress, and dealing with medications. Patients and caregivers can contact their CTN at any time for questions, problems, and concerns, and clinic staff will be providing after-hours coverage for calls from patients and caregivers. The CTN will refer to a member of the clinical team as appropriate. If pertinent, the CTN will generate a message (fax, email, phone call) to the patient's provider describing the outcome of the contact. We estimate the caseload for each CTN to be approximately 80-90 patients with monthly touchpoints lasting 15 minutes on average. Detailed models of CTN activity were developed on our experience as health care professionals interacting with patients and their families throughout the course of disease.

RCs will contact Navigated Care (intervention group) and Survey of Care (control group) participants at scheduled intervals (Baseline, 6 months, and annually) in order to complete outcome measures. If the RC identifies a risk or concern, they will contact the patient or caregiver's provider so that the provider can follow-up.

Participant withdrawal:

While enrollment is targeted to our dementia patient participants, we are also consenting and enrolling their caregiver into the study. Delivery of our intervention and measurement of it's effectiveness is reliant upon enrolling and following dementia patients and their caregivers as a dyad. Because we are measuring effectiveness partly using surveys for each participant (patient and caregiver) over time, both participants are required. If we were delivering care without measurement, it would be permissible for caregivers to change for a given patient in our Care Ecosystem. It is for this reason
that we have decided and communicated in each consent (caregiver and patient) that if either participant decides to leave the study, patient or caregiver, that we will stop the other from continuing to participate in the study.

If you have a procedure table, attach it to the submission with your other study documents.

15.2 Interviews, questionnaires, and/or surveys will be administered or focus groups will be conducted:

◉ Yes ○ No

List any standard instruments used for this study:

Please see our Measurement Schedule for a schedule of when these are each administered.

Caregiver completes:
Zarit Burden Interview (Zarit et al., 1980)
QoL-AD (if patient unable to complete – Logsdon et al. 1999; Logsdon et al. 2002)
Rapid Assessment of Adult Literacy (Arozullah et al., 2007)
Functional Assessment Staging (FAST – Reisberg et al., 1988)
Neuropsychiatric Inventory (NPI-Q – Kaufer et al., 2000)
Geriatric Depression Scale, short form (GDS – Yeasavage & Sheikh, 1986)
Caregiver Strain Index (CSI – Robinson et al., 1983)
Generalized Anxiety (GAD7 – Spitzer et al., 2006)
Pittsburgh Sleep Quality Index (PSQI – Buysse et al., 1989)
Emotional Support (PROMIS - http://www.nihpromis.org)
Informational Support (PROMIS - http://www.nihpromis.org)
Instrumental Support (PROMIS - http://www.nihpromis.org)
Revised Scale for Caregiving Self-Efficacy (Steffen et al., 2002)
Edmonton Symptom Assessment Scale (if patient unable to participate – Bruera et al., 1991)
Pain Assessment in Advance Dementia Tool (PAIN-AD – Warden et al., 2003)

Patient completes:
The Montreal Cognitive Assessment (MOCA - http://www.mocatest.org)
Rapid Assessment of Adult Literacy (Arozullah et al., 2007)
Edmonton Symptom Assessment Scale (Bruera et al., 1991)
QoL-AD (Logsdon et al. 1999; Logsdon et al. 2002)
Standard demographic information (date of birth, gender, race/ethnicity, years of education)

Non-Standard Assessments (Attached):
Rates of Medication-Related Problems
Modified Health and Retirement Survey
Follow-up Annual Survey
Willingness to Pay
DCE-DM Baseline characteristics questions
DCE-DM Advance planning knowledge and attitudes
DCE-DM Errors and Events
Modified Satisfaction with Care at End-of-Life in Dementia (SWC-EOLD)
Agile Development Questionnaire
DCE-DM Post-mortem assessment

Attach any non-standard instruments at the end of the application.

15.3 Conduct of study procedures or tests off-site by non-UCSF personnel:

○ Yes ◉ No

If yes, explain:

No, all study procedures will be conducted by UCSF personnel. Study staff will communicate with patient's providers who may not be UCSF personnel, but these non-UCSF providers will not conduct study procedures.

15.4 Sharing of experimental research test results with subjects or their care providers:

○ Yes ◉ No

If yes, explain:

15.5 * Specimen collection for future research and/or specimen repository/bank administration:

○ Yes ◉ No

15.6 Time commitment (per visit and in total):

Pre-screening interview, consent and randomization: 45 minutes
Baseline and annual outcome measures: 2 hours (to be completed in 2 separate 1 hour phone calls or during an in-person visit)
Agile measures at 3 months (Navigated Care only): 20 minutes
Outcome measures at 6 months: 45 minutes
Monthly CTN-initiated contact: minimum 5 minutes and longer depending on subject answers, needs, or preferences

15.7 Locations:

Recruitment, pre-screening, and consenting will be performed at the recruitment sites: UCSF Memory and Aging Center Clinic, 1500 Owens St, #320, San Francisco or UCSF General Medicine Clinics, 400 Parnassus Ave, San Francisco, or San Francisco General Hospital Clinics, 1001 Potrero Avenue, San Francisco, or the Chinatown Memory Clinics located at: Chinatown Public Health, 1490 Mason Street and Chinese Hospital, 845 Jackson Street, San Francisco

15.8 Describe the resources in place to conduct this study in a way that assures protection of the rights and welfare of participants:

1. Patients seen in the recruitment sites that are determined to be eligible will be asked by their physician or project staff to participate. The purpose, procedures, risks and benefits will be explained to the patient and a family member and, if interested, they will consent. We believe the risks involved are minimal and most cognitively impaired subjects are able to understand the information we give them; and we ensure that they have familiar, trusted, and responsible individuals involved in their decision process. We will comply with HIPAA and UCSF Committee on Human Research (CHR) Human Subjects privacy and confidentiality standards. The MAC emphasizes staff training on matters of confidentiality and privacy standards. The MAC augments UCSF HIPAA training with additional training covering MAC-specific confidentiality procedures.

2. We will offer opportunities for breaks during the assessment periods. In the event the subject appears or reports undue strain, we will terminate the assessment session.

3. Comprehensive training and supervision of study staff will provide strong protection of patient rights. a. For patients and caregivers enrolled in Navigated Care, a primary focus of our research protections will concern the training and clinical oversight of the Care Team Navigator (CTN). Each CTN will have a caseload of 80-90 patient/caregiver dyads, whom he/she will contact monthly (with more frequent contact in the initial stages of enrollment). CTNs will play an important role in maintaining longitudinal contact with patients and caregivers, in directing patients and caregivers to appropriate community and educational resources, and in helping to coordinate patients' interactions with their own medical providers and with the Care Ecosystem Clinical Team. Prior to beginning work, CTNs will undergo two weeks of intensive training,

including the UCSF Medical Center Orientation and separate instruction on topics such as roles and responsibilities of the healthcare team, privacy/confidentiality, mandatory reporting, facilitating completion of benchmarks outlined in the modules, and communication and sensitivity in working with a vulnerable population. Training will include 9 days of didactics in addition to directly supervised contact with subjects. Because CTNs will not give medical advice, a particular focus of instruction is the routing of patient problems and issues to the supervising nurse, licensed social worker and pharmacist in the Clinical Core. Instruction will include extensive role-playing in different anticipated scenarios, such as suspicion of elder abuse and expressed suicidality in order to prepare CTNs for issues that can arise in telephone contact with patients who have dementia and their family caregivers. CTNs will be directly supervised by the Clinic Core Director and/or Nurse Coordinators; prior to each CTN-initiated patient/caregiver contact they will review overall objectives for the contact on the Dashboard Patient Management Tool. A sample of phone calls by the CTNs will be audio-recorded (with patient consent) and reviewed for quality and adherence to study protocol. CTNs will meet weekly with supervisors in the Clinical Core to discuss patient problems and receive clarification and further training from supervisors and one another as needed.

b. The Research Coordinators responsible for recruitment and enrollment will receive a shorter amount of training that focuses more on consenting, privacy, and study protocol concerns. In addition to 7 days of didactics, they will have 3 days of supervision in the field being observed with potential subjects. The RCs will meet weekly as a group with Dr. Merrilees and the Project Manager to review enrollment and any concerns that have arisen.

c. Nurse Coordinator(s) will undergo training on study protocol, the role of the CTNs and RCs. They will have 5 days of didactics along with direct supervision by Dr. Merrilees in their interactions with CTNs, RCs and clinical staff. They will meet weekly with Dr. Merrilees to discuss study protocol, clinical concerns, and problem-solving.

Please refer to the Training Table as an attachment for details regarding study personnel (CTN, RC, and Nurse Coordinator) training.

16.0 Alternatives

16.1 Study drug or treatment is available off-study:

- ○ Yes
- ○ No
- ◉ Not applicable

16.2 * Is there a standard of care (SOC) or usual care that would be offered to prospective subjects at UCSF (or the study site) if they did not participate:

◉ Yes ○ No

If yes, describe the SOC or usual care that patients would receive if they choose not to participate:

All patient subjects will receive usual dementia care from their clinicians regardless of their decision to participate.

16.3 Describe other alternatives to study participation that are available to prospective subjects:

Patient subjects may choose not to participate, which will not influence whether they receive usual dementia care.

17.0 Risks and Benefits

17.1 * Risks and discomforts:

1. Patients and caregivers in both groups will complete study questionnaires; patients and caregivers randomized to Navigated Care will complete further questionnaires and will participate in educational

interventions. This may be fatiguing for elderly individuals with cognitive impairment, and may add to perceived burdens for caregivers.
2. In the Navigated Care group, interventions for advance care planning will include information about the clinical course of Alzheimer's disease and other, including the absence of effective medical therapies and likely outcomes such as institutionalization, dysphagia, loss of the ability to communicate with or recognize family, and death. This information will be distressing to some patients and caregivers.
3. CTNs and members of the Clinical Core team are mandatory reporters. If they discover evidence of elder abuse, they are obligated to report this evidence or their reasonable suspicion to Adult Protective Services. This may result in APS investigation and guardianship if suspicions are corroborated.
4. Patients who are still driving will be reported to the Department of Motor Vehicles in accordance with California state law. This may result in their driving privileges being revoked.
5. There is a potential risk that unlawful actions will result in the loss of privacy.

17.2 Steps taken to minimize risks to subjects:

1. All measurement tools will be scrutinized for redundancy and the length of measurement tools will be minimized to reduce burden. Routine breaks will be scheduled; furthermore, because dementia patients' cognitive status and energy level can fluctuate during the day, research coordinators and CTNs will be prepared to reschedule contact sessions for time periods during which patients are able to fully participate. Patients and caregivers will also be reminded that they can always request breaks or rescheduling as needed, and always retain the right to withdraw from research if measurement is too burdensome. (Of course, because the research team aims for complete participation and follow-up, this is a further incentive to minimize subject burden.)
2. Recent literature and professional guidelines emphasize that truth-telling is preferable to withholding details from patients and families about the diagnosis and course of dementia; this information facilitates important planning and decision-making, and if performed sensitively truth-telling both reduces anxiety and improves quality of life. The Care Ecosystem Dementia Curriculum and Decision-making Module will draw upon our team's multidisciplinary expertise in nursing, palliative care and neurology to design materials that are informative while appropriately sensitive to the potential psychological burdens of this information.
3. Information about mandatory reporting for driving and for suspicion of elder abuse will be included in all informed consent materials and discussions prior to program enrollment.
4. Rigorous protocols for maintaining the security of protected health information are described below, under Confidentiality and Privacy.
5. By requiring subjects to have a primary caregiver in order to participate in this study, we are helping to insure that they have familiar, trusted, and responsible individuals involved in their decision process.
6. Study visits and monthly contacts by CTNs are scheduled according to the subject's preference and can be broken into several shorter appointments as needed to prevent boredom or fatigue.

17.3 Benefits to subjects:

(●) Yes ( ) No

If yes, describe:

Subjects randomized to Survey of Care will receive no benefit or minimal benefit from study procedures. They may receive some minimal benefit because if a need is identified during outcome measurement that our team thinks could be addressed by a referral to community resources, we will make this referral. Subjects randomized to Navigated Care will receive a new care model (in addition to usual dementia care provided by their physicians) designed around the role of the CTN, which is designed to improve patient care coordination, reduce avoidable complications and hospitalizations, and improve patient satisfaction while reducing caregiver burden.

17.4 Benefits to society:

The primary impetus of this project is that our society, and societies around the world, are currently unprepared to meet the growing costs and burdens of dementia. Our study is designed to develop and evaluate a new care model that will improve care and reduce costs, which can be implemented on a broader scale to improve the care of patients with dementia everywhere.

17.5 Explain why the risks to subjects are reasonable:

The risks borne by subjects are relatively small compared to the benefits of this research, both for research participants and to society as a whole. Other than risks related to fatigue in questionnaires, other risks (such as mandatory reporting and psychological burdens of knowledge about dementia course) are also present in the course of routine dementia care. Our model is designed to improve care for individual patients (particularly in the Navigated Care arm), and eventually for dementia patients elsewhere.

18.0 Data and Safety Monitoring Plan

18.1 Describe the plan for monitoring data and safety (Help Text updated 9/13):

There will be a formal Data and Safety Monitoring Board, described in the next full section of the application.

DATA INTEGRITY
To maintain blinding for study assessments, all primary outcome measures will be assessed by a Research Coordinator who is blinded to treatment assignment (Survey of Care versus Navigated Care) and who is distinct from both the CTNs and the Clinical Core. Data will be maintained on cloud services provided by Salesforce.com on a server cluster distributed throughout North America. Salesforce.com's security, architecture, and privacy documentation are available at **https://help.salesforce.com/servlet/servlet.FileDownload?file=015300000035PzoAAE**

SAFETY
Subjects will receive three levels of safety evaluations. Participants randomized to Navigated Care will, as part of the Decision-making Module, be provided with detailed instruction regarding safety issues in dementia, and will be assisted in performing necessary home modifications by the CTN if need be. Second, Navigated Care subjects and their caregivers will have 24/7/365 access to contact the care team for any questions. CTNs will be trained to provide appropriate answers for a majority of questions regarding nonpharmacological interventions to calm dementia-related behavioral disturbances; if CTNs feel that the issue exceeds their training, they will in turn be able to contact our team nursing/SW 24/7/365. Finally, staff physicians at both sites will be available 24/7/365 for nursing consultation as necessary.

Of note, given the nature of this study, placement in nursing homes, ER evaluation, inpatient hospitalization, and changes in medical condition are not considered adverse events for this study, since these events constitute part of the natural history of neurodegenerative diseases and there are currently no validated agents to prevent this events.

A variety of internal process data will be monitored; these include IT parameters (system uptime, query response rate, needs for patching, etc.), study performance parameters (intervention deployment statistics), care team navigator statistics (caseload, documentation, etc.) and communications between study partners. This information will be analyzed by the UCSF team, and reports of their findings distributed to the group at large, the Data and Safety Monitoring Board and the study sponsor (CMS).

Quantifiable outcomes for each Module will be reviewed by the strategic leaders for each Module monthly. Data suggesting urgent or emergent problems (whether arising from any of the core activities or initiated by the subject's family) will be handled immediately. We will establish a chain of command to ensure that subjects will be able to contact a study CTN immediately during regular hours, with access to a member of the Clinical Core during night and weekend hours.

INTERIM ANALYSIS
We will conduct one planned interim analysis of efficacy at 2 years into the study period. This analysis will be conducted by the Data and Safety Monitoring Board, described below

WITHDRAWAL
Subjects will be withdrawn from the research for the following reasons:
1. Subject acquisition of hospice-eligible diagnosis,
2. Subject/caregiver/family desires to stop participation,
3. Subject relocates to new home outside of current coverage area,
4. Subject/family otherwise lost to follow-up (anticipated rare event)

18.2 This study requires a Data and Safety Monitoring Board:

- (•) Yes
- ( ) No or not sure

If **yes**, press **SAVE and CONTINUE** to move to the next section of the application.

18.3 If No, provide rationale:

- ○ Social/Behavioral research
- ○ Phase I trial
- ○ Treatment IND/Compassionate Use Trial
- ○ Other (explain below)

If **Other,** explain:

19.0 Data and Safety Monitoring Board

19.1 Provide details from the Data and Safety Monitoring Board's charter, including meeting frequency, and affiliations and qualifications of members:

The primary function of the DSMB for this study will be for data monitoring; in particular, to review interval progress toward enrollment goals, and to check that enrollment is sufficient to meet our study objectives. The DSMB will also review data from internal process monitoring as described above, and will be notified of any data breaches or threats to patient confidentiality.

The DSMB will be prepared to monitor safety; however, we do not expect safety monitoring to be a primary focus of the DSMB for several reasons. First, the primary interventions in this study are behavioral and of low risk. There is no biological intervention included in this trial; aside from the potential risks detailed under Risks and Discomforts above, there are no known side effects to monitor for Caregiver Education and Support or Decision-Making (such as advance care planning). For the Medications Module, any changes recommended will be implemented by the patient's primary physician. Second, given the nature of this study, placement in nursing homes, ER evaluation, inpatient hospitalization, and changes in medical condition are not considered adverse events for this study, since these events are part of the natural history of neurodegenerative diseases and there are currently no validated agents to prevent this events. Finally, we do not anticipate grounds for early termination of the study for efficacy. Our primary hard outcomes are long term such as time to nursing home placement, number of ER visits, number of hospital days, and Medicare dollars spent. Thus, we do not anticipate having sufficient information to determine overall project efficacy prior to completion of the trial. Still, we have planned an interim review of study efficacy at 2 years after initiation.

The DSMB will be composed of two members:

- Geoffrey Kerchner, MD PhD; Stanford University Department of Neurology
Dr. Kerchner provides expertise both in the conduct of clinical trials, and in the science and management of dementia.

- We will also recruit an independent statistician TBD.

The DSMB will convene for four scheduled meetings: at 12 months, 18 months, 24 months and 30 months after study initiation.

19.2 All of the members of the Data and Safety Monitoring Board are independent of the sponsor:

- ◉ Yes
- ○ No

20.0 Confidentiality and Privacy

20.1 Plans for maintaining privacy in the research setting:

Patient information will be handled as confidentially as possible. The Dashboard (the information hub of the Care Ecosystem) is being built using Salesforce.com; this platform allows institutions like ours to build

reliable and secure applications "in the cloud" (on servers and storage units located in secure data centers located in multiple locations in North America). As an institution, UCSF has selected Salesforce as a platform upon which to build critical applications for these same reasons (security, reliability, and the ability to be HIPAA compliant).

The Care Ecosystem team is partnering with UCSF's internal development team (the Information Services Unit, or ISU) to build the Dashboard: ISU's web site provides additional information about security and HIPAA compliance at **https://it.ucsf.edu/about/teams/salesforce-ucsf**.

All connections to and from the Dashboard, including both programmatic connections (server-to-server) as well as end-user connections (by Care Team Navigators, Research Coordinators, Patients and their Caregivers) will be conducted using secure HTTP (HTTP over a Secure Socket Layer, or HTTPS). This protocol encrypts all data while in transit between our Dashboard and the end-user's client (browser), creating a secure end-to-end tunnel.

Additional information about Salesforce.com's security, architecture, and privacy are available at **https://help.salesforce.com/servlet/servlet.FileDownload?file=015300000035PzoAAE**

To help protect privacy, we will apply for a Certificate of Confidentiality from the National Institutes of Health after receiving IRB approval for the study. With this Certificate, the researchers cannot be forced to disclose information that may identify research subjects, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceeding.

As detailed below, some information cannot be kept confidential such as information pertaining to mandatory reporting laws for abuse or driving safety. In addition, patient permission will be sought to share information with other medical providers to help coordinate patient care.

20.2 Possible consequences to subjects resulting from a loss of privacy:

The loss of privacy of study information could result in risks to subjects' reputation, as well as potential shame or embarrassment on the part of the patient, caregiver, or family. There also may be a risk to a patients' or family members' insurability if confidential details of the patient's condition were to be made known to unauthorized persons.

20.3 Study data are:

- ☐ Derived from the Integrated Data Repository (IDR) or The Health Record Data Service (THREDS) at SFGH
- ☑ Derived from a medical record (e.g. APeX, OnCore, etc. Identify source below)
- ☑ Added to the hospital or clinical medical record
- ☐ Created or collected as part of health care
- ☑ Used to make health care decisions
- ☑ Obtained from the subject, including interviews, questionnaires
- ☐ Obtained from a foreign country or countries only
- ☐ Obtained from records open to the public
- ☐ Obtained from existing research records
- ☐ None of the above

If **derived from a medical record**, identify source:

electronic medical records and/or paper medical records

20.4 Identifiers may be included in research records:

◉ Yes ○ No

If **yes**, check all the identifiers that may be included:

- ☑ Names

- [x] Dates
- [x] Postal addresses
- [x] Phone numbers
- [x] Fax numbers
- [x] Email addresses
- [x] Social Security Numbers*
- [x] Medical record numbers
- [x] Health plan numbers
- [ ] Account numbers
- [ ] License or certificate numbers
- [ ] Vehicle ID numbers
- [ ] Device identifiers or serial numbers
- [ ] Web URLs
- [x] IP address numbers
- [ ] Biometric identifiers
- [x] Facial photos or other identifiable images
- [ ] Any other unique identifier

* Required for studies conducted at the VAMC

20.5 Identifiable information might be disclosed as part of study activities:

(•) Yes ( ) No

If **yes**, indicate to whom identifiable information may be disclosed:

- [x] The subject's medical record
- [x] The study sponsor
- [x] Collaborators
- [ ] The US Food & Drug Administration (FDA)
- [x] Others (specify below)
- [ ] A Foreign Country or Countries (specify below)

If **Others**, specify:

20.6 Indicate how data are kept secure and protected from improper use and disclosure (check all that apply): NOTE: Whenever possible, do not store subject identifiers on laptops, PDAs, or other portable devices. If you collect subject identifiers on portable devices, you MUST encrypt the devices.

- [ ] Data are stored securely in My Research
- [ ] Data are coded; data key is destroyed at end of study
- [ ] Data are coded; data key is kept separately and securely
- [ ] Data are kept in a locked file cabinet
- [ ] Data are kept in a locked office or suite
- [x] Electronic data are protected with a password
- [x] Data are stored on a secure network
- [ ] Data are collected/stored using REDCap or REDCap Survey
- [ ] Data are securely stored in OnCore

20.7 Additional measures to assure confidentiality and protect identifiers from improper use and disclosure, if any:

Access to all study data will be controlled by requiring known users to log into our system for access, with unique and secure passwords. All user logon events are also logged. All user logon events are timestamped as specific events made within the system on a patient-by-patient basis.

Data "export" will be severely constrained -- end-users will be prevented from exporting data in machine-readable formats. Bulk data analysis will be performed using anonymized data to the extent possible, removing names and other external identifiers, and replacing those ID's with internal ID's that have no meaning "outside" the system. For example, this process would strip Patient Names and SSN's (as well as Medical Record Numbers) from records when exported, and insert an internal "CE-ID" field.

CMS (Medicare) will require that some reporting include Medicare ID's -- this data will be encrypted and transmitted securely, but these files must include these Medicare ID's to enable data processing by CMS.

20.8 This study may collect information that State or Federal law requires to be reported to other officials or ethically requires action:

(•) Yes ( ) No

Explain:

Suspicions of unsafe driving by a person with dementia and/or suspicion of abuse triggers mandatory reporting to state and local agencies.

20.9 This study will be issued a Certificate of Confidentiality:

(•) Yes ( ) No

21.0 Subjects

21.1 Check all types of subjects that may be enrolled:

- [x] Inpatients
- [x] Outpatients
- [ ] Healthy volunteers
- [ ] Staff of UCSF or affiliated institutions

21.2 Additional vulnerable populations:

- [ ] Children
- [x] Subjects unable to consent for themselves
- [ ] Subjects unable to consent for themselves (emergency setting)
- [x] Subjects with diminished capacity to consent
- [x] Subjects unable to read, speak or understand English
- [ ] Pregnant women
- [ ] Fetuses
- [ ] Neonates
- [ ] Prisoners
- [ ] Economically or educationally disadvantaged persons
- [ ] Investigators' staff
- [ ] Students

Explain why it is appropriate to include the types of subjects checked above in this particular study:

This study will develop and test a new care model for patients with dementia, who presently are poorly served by current models of care that are fragmented, reactive, and poorly responsive to the needs of patients and families. Many patients will be unable to consent or have diminished capacity to consent, due to their dementia diagnosis. Some patients who previously were English-speaking will no longer be able to communicate because of their dementia diagnosis; in addition, to improve the generalizability of our study we will recruit Spanish-speaking, Cantonese-speaking and Mandarin-speaking subjects with dementia.

Describe the additional safeguards that have been included in the study to protect the rights and welfare of these subjects and minimize coercion or undue influence:

At the time of study enrollment, patients will be interviewed in person along with their study caregiver, and also (if this person is different from their study caregiver) by a family member legally authorized to consent to participation in research if the patient cannot (according to the priority given in California Health & Safety Code §24178). The study's purpose, procedures, benefits and risks will be explained to the patient, caregiver, and legally authorized decision-maker. The study caregiver participant (and, if necessary, legally authorized decision-maker) will be physically present with the patient throughout the study enrollment and consent process.

Most subject contact will occur by telephone with a CTN or research coordinator. In rare cases when patients are evaluated in person for any study purpose, they will not be left unattended at any time.

In addition, patients and caregivers randomized to Navigated Care will, as part of the Decision-making Module, receive further information and education on legal issues in dementia relevant to health and financial decisions. Patients with legal needs will be referred to outside, independent legal counsel.

22.0 Inclusion of Non-English Speaking Subjects

22.1 Indicate which method(s) you will use to consent non-English speaking subjects:

- [x] Preferred Method—Consent form and other study documents will be available in the subject's primary language Personnel able to discuss participation in the patient's language will be present for the consent process.
- [ ] Short-Form—A qualified interpreter will translate the consent form verbally, and subjects will be given the Experimental Subject's Bill of Rights in their primary language, following instructions in Those Who do not Read, Speak or Understand English for required witnessing and signatures

22.2 Explain how you will maintain the ability to communicate with non-English speakers throughout their participation in the study:

We plan to hire several CTNs and Research Coordinators who are bilingual thus ensuring that personnel able to communicate in the participant's language will be available for the consent process and throughout their participation in the study. This will increase access for patients who might typically be ineligible to participate in research. We will also use the UCSF Interpreter service as needed.

To address Bay Area demographics, the Memory and Aging Center focused outreach efforts within the Chinese-American community and have built relationships and successful clinical and research partnerships. For this reason, we will focus on Cantonese and Mandarin-speaking research staff. We also plan to recruit several CTNs and Research coordinators who speak Spanish to facilitate recruitment, participation, and care among patients at UCSF and SFGH. We will have our consent documents professionally translated from English into Spanish, Cantonese and Mandarin. The Alzheimer's Association and the Family Caregiver Alliance are national organizations devoted to dementia care. Many of their educational materials have been professionally translated and whenever possible, we will use their educational materials in the subjects preferred language.

23.0 Recruitment

23.1 * Methods (check all that apply):

- [x] Study investigators (and/or affiliated nurses or staff) recruit their own patients directly in person or by phone.
- [ ] Study investigators recruit their own patients by letter. Attach the letter for review.
- [x] Study investigators send a "Dear Doctor" letter to colleagues asking for referrals of eligible patients. If interested, the patient will contact the PI or the PI may directly recruit the patients (with documented permission from the patient). Investigators may give the referring physicians a study information

sheet for the patients.

- ☐ Study investigators provide their colleagues with a "Dear Patient" letter describing the study. This letter can be signed by the treating physicians and would inform the patients how to contact the study investigators. The study investigators may not have access to patient names and addresses for mailing
- ☑ Advertisements, notices, and/or media used to recruit subjects. Interested subjects initiate contact with study investigators. Attach ads, notices, or media text for review. In section below, please explain where ads will be posted.
- ☑ Study investigators identify prospective subjects through chart review. (Study investigators request a Waiver of Authorization for recruitment purposes.)
- ☐ Large-scale epidemiological studies and/or population-based studies: Prospective subjects are identified through a registry or medical records and contacted by someone other than their personal physician. (Study investigators request a Waiver of Authorization for recruitment purposes.)
- ☑ Direct contact of potential subjects who have previously given consent to be contacted for participation in research. Clinic or program develops a CHR-approved recruitment protocol that asks patients if they agree to be contacted for research (a recruitment database) or consent for future contact was documented using the consent form for another CHR-approved study.
- ☐ Study investigators list the study on the School of Medicine list of UCSF Clinical Trials website or a similarly managed site. Interested subjects initiate contact with investigators.
- ☐ Study investigators recruit potential subjects who are unknown to them through methods such as snowball sampling, direct approach, use of social networks, and random digit dialing.
- ☑ Other

If **Other**, explain:

Providers at our recruitment sites may provide names and contact information of patients that they believe would be interested/eligible to participate in this study. Patients will be mailed a letter stating that their provider suggested them for the study. The letter will provide a number to call if they would not be interested in being contacted and that study staff will contact them in 2 weeks of receipt of the letter if not instructed otherwise. At any time, patients or caregivers may decline to discuss or participate in the study.

23.2 * How, when, and by whom eligibility will be determined:

Patients will be referred by their provider familiar with our eligibility criteria. A Research Coordinator (RC) who has been oriented and trained for this project will confirm with the referring provider and/or conduct a chart review to ensure that the following criteria are met: patient has a diagnosis of dementia (a progressive neurodegenerative illness), has someone identified as a primary caregiver and who is willing to participate, has undergone a medical evaluation that has ruled out reversible causes for dementia, is on Medicare or Medi-caid or is Medicare/Medi-caid-pending, does not reside in a nursing home, death is not considered to be imminent, does not have an unstable mental illness that precedes the dementia, patient and caregiver speak either English, Cantonese, Mandarin, or Spanish, is 18 years or older, and lives in California, Nebraska or Iowa.

If there are laboratory tests that were not performed as part of a dementia work-up, the RC will ask the provider if those tests could be completed, but this does not preclude the patient from enrolling in the study.

23.3 * How, when, where and by whom potential subjects will be approached:

The RC will approach the patient and their caregiver either in-person or by telephone. S/he will explain that the patients physician suggested they might be interested in participating in this study. If they express interest, the RC will schedule a time to meet in-person to complete the screening and consent process.

23.4 * Protected health information (PHI) will be accessed prior to obtaining consent:

◉ Yes ○ No

24.0 Waiver of Consent/Authorization for Recruitment Purposes

This section is required when study investigators (and/or affiliated nurses or staff) recruit their own patients directly.

24.1 * Study personnel need to access protected health information (PHI) during the recruitment process and it is not practicable to obtain informed consent until potential subjects have been identified:

(•) Yes

If **no**, a waiver of consent/authorization is NOT needed.

24.2 * A waiver for screening of health records to identify potential subjects poses no more than minimal risk to privacy for participants:

(•) Yes

If **no**, a waiver of authorization can NOT be granted.

24.3 * Screening health records prior to obtaining consent will not adversely affect subjects' rights and welfare:

(•) Yes

If **no**, a waiver of authorization can NOT be granted.

24.4 * Check all the identifiers that will be collected prior to obtaining informed consent:

- [x] Names
- [x] Dates
- [ ] Postal addresses
- [x] Phone numbers
- [ ] Fax numbers
- [ ] Email addresses
- [ ] Social Security Numbers*
- [ ] Medical record numbers
- [ ] Health plan numbers
- [ ] Account numbers
- [ ] License or certificate numbers
- [ ] Vehicle ID numbers
- [ ] Device identifiers or serial numbers
- [ ] Web URLs
- [ ] IP address numbers
- [ ] Biometric identifiers
- [ ] Facial photos or other identifiable images
- [ ] Any other unique identifier
- [ ] None

Note: HIPAA rules require that you collect the minimum necessary.

24.5 * Describe any health information that will be collected prior to obtaining informed consent:

A chart review will be conducted by the RC to determine if the patient meets eligibility criteria (see 21.2 above).

Note: HIPAA requires that you collect the minimum necessary.

24.6 * Describe your plan to destroy the identifiers at the earliest opportunity consistent with the research or provide a health or research justification for retaining the identifiers, or indicate and explain that retention is required by law:

Data for whom informed consent is not obtained will be securely destroyed (shredded).

25.0 Informed Consent

25.1 * Methods (check all that apply):

- [x] Signed consent will be obtained from subjects and/or parents (if subjects are minors)
- [ ] Verbal consent will be obtained from subjects using an information sheet or script
- [ ] Electronic consent will be obtained from subjects via the web or email
- [ ] Implied consent will be obtained via mail, the web or email
- [x] Signed consent will be obtained from surrogates
- [ ] Emergency waiver of consent is being requested for subjects unable to provide consent
- [ ] Informed consent will not be obtained

25.2 * Process for obtaining informed consent:

At the time of study enrollment, patients will be interviewed in person along with their study caregiver, and also (if this person is different from their study caregiver) by a family member legally authorized to consent to participation in research if the patient cannot (according to the priority given in California Health & Safety Code §24178). The study's purpose, procedures, benefits and risks will be explained to the patient, caregiver, and legally authorized decision-maker. The study caregiver (and, if necessary, legally authorized decision-maker) will be physically present with the patient throughout the study enrollment and consent process. The patients and their caregivers will both consent to participating in the study.

25.3 * How investigators will make sure subjects understand the information provided to them:

Even when there is a dementia diagnosis or other indication of diminished capacity, persons who have reached the age of majority are presumed to have capacity to give informed consent to research. The policy of the UCSF Memory and Aging Center, described in greater detail in "Plans for assessing the decision-making capacity of prospective subjects" below, utilizes four different standards to assess capacity. Understanding falls under the second standard, requiring memory for ideas and sequences of information, and comprehension of the fundamental meaning of information about treatment. In particular, in cases of doubt the subject should express comprehension a) that participation is voluntary, b) the major procedures c) main risks and d) benefits.

26.0 Surrogate Consent

26.1 Subjects are inpatients on a psychiatric ward or mental health facility, or on psychiatric hold:

- (•) No

If **yes**, use of surrogate consent for research is NOT allowed in California.

26.2 This study is related to the cognitive impairment, lack of capacity, or serious or life-threatening diseases and conditions of the research subjects:

- (•) Yes

If **no**, use of surrogate consent for research is NOT allowed in California.

26.3 Explain why use of surrogates is necessary for completion of this study:

This study will develop and test a new care model for patients with dementia; many patients will be unable to consent or have diminished capacity to consent, due to their dementia diagnosis.

26.4 Plans for assessing the decision-making capacity of prospective subjects:

There are four different standards that might be used to assess capacity. They are listed a rough order of ascendancy. It is the policy of the UCSF Memory and Aging Center to accept a subject as competent to consent to research only when the person is judged capable with regard to all 4 standards.

There are four different standards that might be used to assess capacity. They are listed a rough order of ascendancy. It is the policy of the UCSF Memory and Aging Center to accept a subject as competent to consent to research only when the person is judged capable with regard to all 4 standards.

- **Standard 1. Did the research candidate "make a choice"?** *"This standard focuses on the presence or absence of a decision, and not on the quality of the decision"*

This is simply a question as to whether the subject can evidence a choice. If the subject offers a consistent choice about participating in the study this standard is met. If the subject's choice is ambiguous, either because it is inconsistent or unclearly demonstrated, then the standard is failed.

- **Standard 2. Did the research candidate show "understanding"?** *"This standard requires memory for words, phrases, ideas, and sequences of information, and also comprehension of the fundamental meaning of information about treatment."*

A subject need not demonstrate complete or comprehensive understanding of the study in order to meet this standard. However, verbatim recitation of fact without evidence of comprehension is not sufficient either. Consider whether or not the potential subject grasps sufficient information to form the basis for a reasoned decision. If the subject comprehends and remembers (even with assistance) a) that participation is voluntary, b) the major procedures c) main risks and d) benefits, then this standard is met. Failure on any element (a-d) means this standard is failed.

- **Standard 3. Did the research candidate show "reasoning/rational reasons"?** *"This standard tests the capacity to use logical processes to compare the benefits and risks of various treatment options and weigh this information to reach a decision. "*

The core of this standard is the ability to logically compare risks and benefits in order to reach a rational decision regarding participation. To meet this standard the subject needs to demonstrate the ability to consider both risk and benefit in relation to each other and use the information in a logical manner to come to a decision.

- **Standard 4. Did the research candidate show an "appreciation" of the personal risks /benefits of the study?** *"This standard emphasizes the patients' awareness of the consequences of a treatment decision: its emotional impact, rational requirements and future consequences"*

Appreciation seems to imply something more than an intellectual understanding, and incorporates an affective judgment of the impact of study participation in the context of the particular individual in his or her particular situation. Meeting standard 3 would seem to generally suffice for meeting this standard as long as the subject has a realistic understanding of his or her circumstances.

The routine assessment of capacity should begin with the examiner reviewing the informed consent form with the subject in the normal manner used to obtain consent. When the examiner has reviewed the study with the research candidate, he or she should ask the research candidate to explain the major elements of the study. Those elements are a) this is a research study (not routine treatment), b) participation is voluntary, c) study procedures, d) risks, e) benefits. In addition, as described in the standards above, the research candidate needs to make a rational choice based on an appreciation of the facts.

The consent process and capacity assessment should be recorded using the Capacity Assessment Record (CAR, attached). Although the CAR requires that the evaluator make a decision with regard to each standard, there is no need to methodically evaluate each standard in every case. The evaluator may focus on any or all of them, as seems appropriate given what is known about the potential subject. Thus, it may quickly be clear that a severely demented patient cannot meet standard 2. The evaluator may then move

directly to the issue of assent. Or, it may be clear that a subject with mild AD meets standards 1-3, and it is only 4 that is at issue. The reasons for your decision on each item should be documented, however briefly, using the CAR.

26.5 Plans for obtaining consent from subjects who regain ability to consent after a surrogate has given initial consent:

Given the progressive, rather than fluctuating overall course of dementia, we do not anticipate that patients who lose capacity to consent will routinely regain the capacity to give consent. Note that at all times, patient subjects who are not capable of consent to research still must assent to research in order to take part. Assent implies willingness or, minimally, lack of objection to taking part. It does not imply understanding. An interpretable statement from the subject regarding assent must be taken as valid regardless of the subject's level of confusion or dementia. Thus, a statement such as "whatever my daughter says is OK with me" is fine. The demonstration of assent need not be verbal. Passive lack of objection is acceptable in an alert patient. Indications of distress such as crying or attempts to escape the situation should be taken as refusals to assent to the study.

26.6 Requirements for any study involving surrogates for obtaining informed consent. Check to acknowledge:

- [x] Research takes place in California. All surrogates will complete the "Self-Certification of Surrogate Decision Makers for Participation in Research" form.
- [x] Conscious subjects will be notified of the decision to contact a surrogate. If subjects object to study participation, they will be excluded even if their surrogate has given consent.
- [x] Surrogates will not receive any financial compensation for providing consent.
- [x] If a higher-ranking surrogate is identified at any time, the investigators will defer to the higher-ranking surrogate's decision regarding the subject's participation in the research.

For research taking place outside of California, explain how investigators will confirm that surrogates are legally authorized representatives:

26.7 VA Studies Only
Provide any additional information to explain comply with the additional VAMC requirements for use of surrogates in research:

27.0 Financial Considerations

27.1 Subjects payment or compensation method (check all that apply):

Payments will be (check all that apply):

- [ ] Subjects will not be paid
- [ ] Cash
- [ ] Check
- [ ] Debit card
- [ ] Gift card
- [ ] Reimbursement for parking and other expenses
- [ ] Other:

Specify **Other**:

27.2 Describe the schedule and amounts of payments, including the total subjects can receive for completing the study. If deviating from recommendations in Subject Payment Guidelines, include specific justification below.

27.3 Costs to Subjects: Will subjects or their insurance be charged for any study procedures?

○ Yes ◉ No

If **yes,** describe those costs below, and compare subjects' costs to the costs associated with alternative care off-study. Finally, explain why it is appropriate to charge those costs to the subjects.

28.0 CTSI Screening Questions

28.1 * This study will be carried out at one of the UCSF Clinical Research Services (CRS) centers or will utilize CRS services. CRS centers are at the following sites:

- **SFGH Clinical Research Center**
- **Moffitt Adult Clinical Research Center**
- **Moffitt Hospital Pediatrics & NCRC**
- **Mount Zion Hospital Clinical Research Center**
- **Tenderloin Center**
- **CHORI Children's Hospital Pediatrics & Adult Clinical Research Center**
- **Kaiser Oakland Research Unit**
- **SF VA Medical Center Clinical Research Unit**

Please note: Effective 3/1/14, the CRS form will no longer be completed and submitted in iRIS. The CRS budget request form can be found at: https://accelerate.ucsf.edu/files/crs/BudgetRequest2015.docx. Follow the instructions on the form to submit. Even if you click 'Yes' to this question, the form will no longer proceed to the Clinical Research Services (CRS) Application Form section.

○ Yes ◉ No

28.2 This project involves community-based research:

○ Yes ◉ No

28.3 This project involves practice-based research:

○ Yes ◉ No

29.0 End of Study Application

29.1 End of Study Application Form **To continue working on the Study Application: Click on the section you need to edit in the left-hand menu. Remember to save through the entire Study Application after making changes. If you are done working on the Study Application: Click Save and Continue. If this is a new study, you will automatically enter the Initial Review Submission Packet form, where you can attach consent forms or other study documents. Review the Initial Review Submission Checklist for a list of required attachments. Answer all questions and attach all required documents to speed up your approval.**

Amendments

Trial Protocol Amendments

1. The screening visit, consents, and all outcome measurement were conducted via phone.
2. A $25 gift card was provided for completion of all 6-month and 12-month surveys.
3. The original trial protocol stated that QoL-AD would be collected with the caregiver only if the person with dementia was unable to complete it. Prior to study initiation, however, we decided to always collect all primary and secondary study outcomes with the caregiver for consistency.
4. The Agile Survey was administered to 132 participants in the intervention group 3-4 months following enrollment. It was then discontinued to minimize participant burden. The results from this survey were previously published (Possin et al., 2017).
5. The intervention was provided during normal business hours.
6. Several changes to the outcome measures and statistical analysis plan were made between submission of the trial protocol (10/31/2014) and enrollment of the first participant (3/20/2015). The final outcome measurement and statistical analysis plan is described in the Statistical Analysis Plan.

Statistical Analysis Plan Amendments

1. Initially, the FAST was used as the measure of dementia severity. The Quick Dementia Rating Scale (QDRS; Galvin 2015) was published shortly after study initiation and was felt to be a more appropriate measure for the study, and so a shift was made at that time.
2. The Statistical Analysis Plan indicated that we would not include 6-month data in the patient outcome treatment effect analyses because of the timeline of care that first addresses caregiver needs before taking actions to address patient needs. Because of this timeline of care, caregiver outcomes are expected to be impacted by 6-months, and PWD outcomes by 12-months. Guided by reviewer feedback that this may be confusing to include 6-month caregiver data but not 6-month patient data, we added the 6-month data to the models for the patient outcomes. The results were nearly identical to when these data were excluded from the analyses. The same patient outcomes (emergency department visits and quality of life) were significant using each method. In sum, we made this change for clarity and completeness but it did not impact the study findings.

Galvin JE. The Quick Dementia Rating System (QDRS): A Rapid Dementia Staging Tool. *Alzheimer's & dementia (Amsterdam, Netherlands).* 2015;1(2):249-259.

Possin KL, Merrilees J, Bonasera SJ, et al. Development of an adaptive, personalized, and scalable dementia care program: Early findings from the Care Ecosystem. *PLOS Medicine.* 2017;14(3):e1002260.