Caregiver Outcomes of Alzheimer's Disease Screening (COADS) Protocol

NCT03300180

5/12/2022

The Caregiver Outcomes of Alzheimer's Disease Screening (COADS)
Protocol
5.12.2022

BACKGROUND AND STUDY AIMS

The United States Preventive Services Task Force (USPSTF) stated, *"Although the evidence on routine screening is insufficient, there may be important reasons to identify early cognitive impairment. This information may also be useful to patients and* ***their caregivers and family members*** *in anticipating and planning for future problems that may develop as a result of progression of cognitive impairment."* Currently, half of Americans with Alzheimer's disease or a related dementia (AD) never receive a diagnosis. For those who do, the diagnosis often occurs two to five years after the onset of symptoms. A majority of people with AD receive care from their family. A delayed AD diagnosis may perpetuate family beliefs that changes in cognition are part of "normal aging" which have been shown to aggravate caregivers' stress, burden, and sense of isolation. Furthermore, family members may not notice their own changing role, leaving them vulnerable or unprepared to become a caregiver.

Early detection of AD from screening may enhance the family member's transition to a caregiver by providing an opportunity for them to learn about the syndrome, receive interventions, and prepare for their caregiving role. Alternatively, early detection might trigger a process of role transition for the family member to a caregiver that evokes negative emotions or incurs social costs that are too high given the lack of a cure. **The benefits and risks of AD screening for family members of older adults are unknown.**

We are proposing the first randomized controlled trial (RCT) to evaluate the benefits and harms of AD screening on family members of older adults. The proposed trial will randomize1,800 dyad (older adult and family member) into three groups; Screen Only, Screen Plus and Control group, and will have 1,800 completed dyad baselines.

Patients in the Screen Only and Screen Plus groups will be screened at baseline utilizing either the Mini-Cog (in-person recruitment) or MIS-T (phone recruitment). During COVID 19 in person restrictions, we will use the MIS-T for every phone screen and add the clock draw portion of the mini-cog as a pass/fail measure to capture visual/spatial and executive function not found in the MIS-T alone if the patient is able. Information, in plain language, about how the patient performed on the screening will be disclosed in separate letters to the patient and to the family member. For patients who fail the screen, the patient and family members will also receive an infographic that visually represents the information in the letter regarding the screening test and brain health.

- Patients and family members in the Screen Only group will also receive a resource guide with local clinical resources for memory specialists. The Screening Plus group will not receive the resource guide but the family members in this group will receive two phone calls following receipt of the letter and infographic. The first call will be from the COADS PI (or their designee thanking them for being in the study and letting them they will be

receiving a phone call from a staff member at the Aging Brain Program (ABC) to answer any questions they may have and schedule a follow-up for diagnostic assessment.

- This phone call will include an opportunity for the family to ask questions and have a conversation about the program and diagnostic evaluation and management. Follow-up diagnostic evaluation can occur at the Aging Brain Care Program or, if preferred in the patient's home with trained personnel in an attempt to replicate the clinic visit. Dyads will be offered transportation assistance if they chose the Aging Brain Care Program and are unable to get themselves there. If the visit occurs in the home, dyads will also be given the opportunity to have a post home visit meeting which can occur in the Aging Brain Care Program or at home. Dyads have the option to refuse the follow-up visit. The patient's PCP is also be notified of the screening results.

In both the Screen Only and Screen Plus groups, the patient's PCP will be notified, through the patient's EHR, that the patient is participating in this study and a statement, in plain language, about how they performed on the screening test.

The Control group patients will not be screened at baseline therefore patients and family members will not receive a letter or infographic. Control group patients will be observed through surveillance of their EHR for any screening or incident AD diagnoses that occur as part of routine care for 24 months. At the last follow-up assessment (24 months), we will screen patients in the control group and conduct an interview with the family member to detect possible cognitive impairment.

Specific Aim 1: Evaluate the impact of AD screening on family members' quality of life.
Hypothesis 1: In comparison to the control group, family members randomized to the Screen Only or the Screen Plus groups will express higher levels of health-related quality of life at 24 months as measured by the Short Form Health Survey (SF-36).

Specific Aim 2: Evaluate the impact of AD screening on family members' mood and anxiety.
Hypothesis 2: In comparison to the control group, family members randomized to the Screen Only or the Screen Plus groups will express lower rates of depressive symptoms and anxiety at 24 months as measured by the Patient Health Questionnaire (PHQ-9) and the Generalized Anxiety Disorder Scale (GAD-7).

Specific Aim 3: Assess the impact of AD screening on family members' caregiving preparedness and caregiving self-efficacy.
Hypothesis 3: In comparison to the control group, family members randomized to the Screen Only or the Screen Plus group, will be more prepared for caregiving and have higher self-efficacy at 24 months as measured by the Preparedness for Caregiving Scale and the Revised Scale for Caregiving Self-Efficacy.

Specific Aim 4: Compare the effectiveness of two strategies for diagnostic evaluation and management after AD screening.
Hypothesis 4: In comparison to the Screen Only group, family members randomized to the Screen Plus group will express higher levels of health-related quality of life, caregiver preparedness and caregiving self-efficacy and lower levels of depressive and anxiety symptoms

at 24 months, as measured by the SF-36, Preparedness for Caregiving Scale, the Revised Scale for Caregiving Self-Efficacy, PHQ-9, and GAD-7, respectively.

METHODS

Study Design

- Three arm, blinded, randomized controlled trial
- 1,900 patient-family member dyads from primary care clinics in central Indiana (n=3800)
- 1800 completed baselines; 600 dyads randomized to each of the three study arms
- **Screen Only group:** Patients will receive screening for AD (n=600). Patient and family members will receive a letter about how the patient performed on the screening. If they screen positive (e.g. ≤5 on the MIS-T or clock draw pass/fail with the MIS-T) the patient and family member will receive an infographic and some information about local clinical resources for them to peruse regarding follow-up care. The patient's PCP will also be notified of the screening results. Additionally, at the 24 month follow up, family members will be asked to complete the IQCODE to detect possible cognitive impairment in the participant
- **Screen Plus group**: Patients will receive screening for AD (n=600). Patient and family members will receive a letter about how the patient performed on the screening. If they screen positive (e.g. ≤5 on the MIS-T and clock draw pass/fail with the MIS-T), the patient and family member will receive an infographic. Also, the family member will receive two follow-up phone calls. One from the COADS Study PI (or their designee) and one from a staff member at the Aging Brain Care Program (ABC). This phone call will include an opportunity for the family to ask questions and have a conversation about the program and diagnostic evaluation and management. Follow-up diagnostic evaluation can occur at the Aging Brain Care Program or, if preferred in the patient's home with trained personnel in an attempt to replicate the clinic visit. Dyads will be offered transportation assistance if they chose the Aging Brain Care Program and are unable to get themselves there. If the visit occurs in the home, dyads will also be given the opportunity to have a post home visit meeting which can occur in the Aging Brain Care Program or at home. Dyads have the option to refuse the follow-up visit. The patient's PCP will also be notified of the screening results. Additionally, at the 24 month follow up, family members will be asked to complete the IQCODE to detect possible cognitive impairment in the participant
- **Control group:** Patients will receive no AD screening (n=600 dyads) at baseline. At the 24-month follow-up, patients will complete the Cognitive Change Index (CCI) and an interview with the family member will be completed to detect possible cognitive impairment.

Participants

- Patients will be adults 65 years or older;
- Have no prevalent diagnosis of Alzheimer's disease or related dementia and not previously screened for AD as part of a research study.
- Family members will be 21 years or older and identified by the patient as the person who would most likely assist with activities of daily living and/or medical decision making if the patient needed assistance.
- See Table 1 for patient and caregiver inclusion and exclusion criteria

Table 1. Inclusion and exclusion criteria for the proposed trial

Inclusion Criteria	
Patients	**Family Members**
65 years or older	21 years of older
At least one visit to primary care practice within past 24 months	Lives with the patient or lives within a 50 mile radius
Ability to provide informed consent	Ability to provide informed consent
Ability to communicate in English	Ability to communicate in English
	Identified by patient as the person most likely to provide them care if needed
Exclusion Criteria	
Patients	**Family Members**
Has a diagnosis of AD as determined by ICD-10 code	Is a non-family member who is not a legal Healthcare Power of Attorney
Evidence of a prescription for a cholinesterase inhibitors or memantine	
Has a serious mental illness such as bipolar or schizophrenia as determined by ICD-10 code	Has a serious mental illness such as bipolar or schizophrenia as determined by ICD-10 code
Permanent resident of a nursing facility	Has a diagnosis of AD as determined by ICD-10 code
Is already enrolled in HABC programs	

Recruitment Sites (as of 9/17/18):

- Indiana University Health Primary Care Practices
- Eskenazi Health Primary Care Practices

Primary outcome: Family member quality of life at 24 months.

Co-Primary outcomes: Family member depressive symptoms and family member anxiety at 24 months.

Co-Secondary outcomes: Family member caregiving preparedness and caregiving self-efficacy at 24 months.

Exploratory outcome: Comparison of all outcomes (noted above) between the family members in Screen Only vs. Screen Plus groups.

Table 2. Measures							
Outcomes	**Construct/Core Attributes**	**Outcome measure(s)**	**Name of Measure**	**Description**	**Scoring**	**When**	**Source**
Primary outcome	Family member Quality of Life	Quality of Life	Medical Outcomes Study Short Form Health Survey 36 (SF-36)	36-items that measure health-related quality of life, mental, physical, and social functioning	Scores range 0-100; Higher scores more QOL	Baseline 6 mos. 12 mos. 18 mos. 24 mos.	Family reported Patient reported
Secondary outcomes	Family member Mood	Depressive symptoms	The Patient Health Questionnaire -9 (PHQ-9)	9-item measures of depressive symptoms.	Depression Severity: 0-4 none, 5-9 mild, 10-14 moderate, 15-19 moderately severe, 20-27 severe.	B 6 12 18 24	Family reported Patient reported
		Anxiety	Generalized Anxiety Disorder Scale-7 (GAD-7)	7-item measure of anxiety	GAD-7 total score for the seven items ranges from 0 to 21. Scores of 5, 10, and 15 represent cut points for mild, moderate, and severe anxiety.	B 6 12 18 24	Family reported Patient reported
	Caregiver preparedness	Caregiver preparedness	Caregiver Preparedness Scale	8-item measure with 1 open-ended question. Self-rated instrument that consists of eight items that asks caregivers how well prepared they believe they are for multiple domains of caregiving. Responses are rated on a 5-point scale with scores ranging from 0 (not at all prepared) to 4 (very well prepared).	The scale is scored by calculating the mean of all items answered with a score range of 0 to 4. The higher the score the more prepared the caregiver feels for caregiving	B 6 12 18 24	Family reported
	Caregiving self-efficacy	Caregiving self-efficacy	The Revised Scale for Caregiver Self Efficacy	15 item measure with three domains of caregiving self-efficacy: Obtaining	Use of a total score reflecting the sum of all 15 items is contrary to	B 6 12 18 24	Family reported

				Respite, Responding to Disruptive Patient Behaviors, and Controlling Upsetting Thoughts	the view of self-efficacy as domain specific and can mask significant relationships between subscales and other constructs. For these reasons, we strongly advocate using scores for the three subscales rather than a total score.		
Other measures	Socio-demographics	Socio-demographics	COADS Created	Questionnaire to measure items such as relationship to the patient/family, frequency and type of contact with the patient, geographic distance from the patient, education level, annual income, self-reported health status, etc.	Co-variates	B	Family reported Patient reported
	Cognitive impairment	Cognitive impairment	Mini-Cog	For in-person recruitment we will use the Mini-Cog which is a 3 minute test of cognition including a clock draw and 3 word recall	Score ranges from 0-5. 0=impairment;1-2 abnormal clock draw then positive for cognitive impairment; 1-2 Normal clock draw then negative for cognitive impairment; 3 negative screen	B (patients randomized to screening only)	Patient reported
			MIS-T	The MIS-T is comprised of four-items with semantic cues to assess episodic memory performance; a cut-point of 5 or less was used to classify those with potential memory impairment	6+ not impaired <=5 impaired	B (patients randomized to screening only)	Patient reported

			Cognitive Change Index (CCI-20-s)	The Cognitive Change Index (CCI) is a tool used to assess the perception of cognitive decline in memory, executive function, and language domains from both self and informant perspectives.		24 month	Patient Reported
			IQ CODE	16-item measure of the patient's changes in cognition and function as reported by the family	Sum each question and divide by the number of questions (16). The result is a score that ranges from 1 to 5. An average scor e of 3 means that the subject is rated as 'no change'. A score of 4 means 'a bit worse', and a score of 5 is 'much worse'.	24 months	Family reported
		Knowledge of patient being screened for AD	COADS Created	2-items to assess if family members are aware if the patient has been screened in the study and about their performance	Yes or no	6 12 18 24	Family reported
		Evidence of screening for AD or new diagnoses of AD	COADS Created	EHR diagnosis	Yes or no	B 6 12 18 24	EHR
		Caregiver burden	Oberst Caregiving Burden Scale	15-item questionnaire that rates 15 different types of caregiving tasks based on perceived time and difficulty (Each item is scored on a 5-point response scale.		B 12 24	Family reported
		COADS Loneliness Assessment for patient and caregiver	PROMIS NIH Toolbox Loneliness (Ages 18+)-Fixed Form	5-item questionnaire to assess loneliness on a scale from 1-5		B 6 12 18 24	Family reported Patient reported
		COADS COVID	NIH Toolbox	11-items to assess COVID-19		B 6	

				impact and experience (Asked after the PHQ-9 and GAD-7)		12 18 24	
		Economic Impact ?	Health Motivation Scale	8-item questionnaire to assess health motivation	All response are on a 7 point Likert Scale of (7) strongly agree, (1) strongly disagree	24	Family reported
		Economic Impact?	Motivation to Change Lifestyle and Health Behaviors for Dementia Risk Reduction (MCLHB-DRR) Scale	11-item assessment with 5 section about perceieved benefits, cues to action, general health motivation and self-efficacy	All response are on a 5 point Likert Scale of (5) strongly agree, (1) strongly disagree	24	Family reported
		Economic Impact	Resource Utilization in Dementia (RUD) Instrument			24	Family reported

Intervention Description and Timing of Measures

Participants will be recruited from primary care offices affiliated with Eskenazi Health and IU Health.

Step 1: Identification of Potential Participants

- Participants will be identified in a variety of ways and will be tailored based on the recruitment site. Patients will be identified via the Indiana Network for Patient Care, (INPC) which can access patient lists by doctor, clinic, and PC clinic schedules. Physicians will be notified first of their patients' potential eligibility and be asked if the COADS study personnel may approach the patient and their family member for participation. Physicians are routinely given 2 weeks to review the list of their potentially eligible patients (per IU PBRN). Physicians will be given the opportunity to opt-out of study participation at this time. Following either approval from the PCPs, or at the end of the two-week review period study personnel will mail out an introductory letter, email or post card to patients. Study personnel with then approach patients via telephone, email or in person in the-clinic to confirm eligibility and obtain informed consent.

- We will consider any man or woman 65 years or older who has not been diagnosed with AD or related dementia, and is considered an active patient (PCP visit in- person or virtual within 24 months including requests for prescription refills, or questions and is able to provide consent, and speaks English.

- We will approach the primary family member/caregiver/informant for each eligible participant. Family members will be eligible if they are patient-identified or self-identified as a person who is likely to provide care for the patient, is 21 years or older, lives within a 50-mile radius of the participant, is able to consent, and speaks English

- Rolling enrollment will take place over 36 months with an average monthly recruitment of 50 dyads

Step 2: Enrollment

- Following eligibility determination and the informed consent process (including HIPAA release), dyads will be randomly assigned to one of three groups, stratified by site (e.g. Eskenazi or IUH). Dyads are officially enrolled at this point.

- **Screen Only:** at baseline, the study personnel will administer the mini cog or clock draw and MIS-T to the patient. During COVID 19 restrictions, we are able to use phone recruitment only, if the participant is able, we will administer the clock draw aspect of the Mini-Cog or the mini-cog in person if applicable to capture the executive and visual spatial aspects of this test.

  Dyads will then receive a letter with information about the patient's AD screening results, provided in plain language. For patients who score ≥6 on the MIS-T and the clock draw as a pass/fail measure, the patient and family member will both receive a letter and infographic indicating the patient's screening outcome results do not indicate signs of cognitive impairment. In cases where the patient scored ≤5 on the MIS-T and pass/fail on the clock draw or positive mini-cog screen, the patient and family member will both receive a letter indicating the patient scored lower than expected. The letter will encourage the patient and family member to discuss the results with the patient's PCP at the earliest possible time. The dyad will also receive a resource guide with local clinical sources with memory specialists. At the 24 month assessment Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) will be administered to the family member. The patient's PCP is also notified of the screening results.

- **Screen Plus:** As described above, research assistants will screen patients with the MIS-T. and pass/fail on the clock draw or the mini-cog if possible. Patients, who score ≥6 on the MIS-T and pass/fail on the clock draw) or mini-cog if possible, will receive a letter and infographic. If the patient scores ≤5 on the MIS-T or ≤2 and a pass/fail on the clock draw or the mini-cog if possible , the phone call and letter to the dyad will indicate that they will be receiving a follow-up call from the ABC Program (letter includes ABC contact name who will be calling and phone information). At the 24 month assessment, the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) will be administered to the family member. The patient's PCP is also notified of the screening results.

- **Control Group (No screen, surveillance group)** Patients will not be screened for cognitive function at baseline. Similar to the design of cancer screening trials, this group

will undergo active surveillance throughout the study via EHR to monitor any AD screening, new diagnoses of AD, and/or new prescriptions for anti-dementia medications. At the 24-month outcome assessment, study personnel will administer the Short Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) to the family member and the patient will complete the Cognitive Change Index (CCI).

- Rolling enrollment will take place over 36 months with an average monthly enrollment of 50 dyads. The proposed trial will reduce loss to follow-up for longitudinal assessments by engaging the dyads every 6 months throughout the study (6, 12, 18, and 24 months). This includes keeping the assignment of research staff and participants consistent at each outcome assessment, sending reminder letters before each assessment, and sending birthday cards signed by the study team. This strategy has produced a <1% loss to follow-up in the pilot study.

Statistical Plan

Overview

Our study is a three-arm RCT to determine the impact of AD screening on older adults' family members. By design, it will also test the congruence of outcomes between the patient and family member. The 1:1:1 randomization creates three randomized groups.

- For analysis, we will first examine univariate distributions of continuous variables in order to detect any potential violations of assumptions to our planned parametric methods of analyses.

- Variables will be transformed as needed to ensure normal distribution assumptions are met.

- We will use nonparametric methods if transformations are inadequate.

- Demographic characteristics will be compared among the groups in order to evaluate whether the randomization effectively balance the dyads.

- We will use Chi-squared tests or Fisher's exact tests to compare the frequencies of categorical variables. Analysis of variance (ANOVA) or its nonparametric alternative, the Wilcoxon rank sum test, will be used to compare the distribution of continuous variables among the groups.

- All analyses will be conducted using SAS 9.4 (SAS Institute, Carey, North Carolina).

Primary Aim

- **Multi-level mixed effects models** will be used to examine differences in SF-36 scores for both patients and family members using dyadic analytic approaches. For this aim, we will compare family members in the two screening groups (Screen Only and Screen Plus) to those in the no screening (Control) group. Repeated SF-36 scores from both patients and family members will be included as the outcome variables with participant type (patient or family member), group (Screening Only and Screening Plus versus Control), time, and interaction between groups and time as independent variables. We will use a multi-level variance-covariance matrix in the mixed effects models to account for two sources of potential correlations. Correlations from measures obtained from the same individual over time, an autoregressive correlation will be used. Correlations within a dyad between a patient and his/her family member. A compound symmetry structure will be used for the within-dyad correlation. Parameter estimation and hypothesis tests for the mixed-effects models will be conducted using the maximum likelihood approach that provides robust estimation under the missing at random mechanisms.

- A significant interaction between group and time would indicate differences in changes of SF-36 over time between the two screening groups compared to the no screening group. Absence of significant interactions, significant main group effects will suggest differences in SF-36 between groups' at all follow-up times. For Hypothesis 1 we will use a linear contrast for SF-36 from family members in the combined screening groups (Screen Only and Screen Plus) versus the no screening (Control) group at 24 months. We will also include additional covariates in the mixed effects models to determine whether family member characteristics (relationship to patient, frequency or types of contact, etc.) and knowledge of screening are associated with the outcome measures.

- The multi-level mixed effects models provide a powerful modeling framework for analyzing dyadic outcomes. An alternative model using family member outcomes as the dependent variable and patient outcomes as an independent variable would underestimate variances in outcome measures by ignoring the randomness in the patients' outcomes by treating patient outcomes as fixed covariates. In our proposed models, correlations between patients and their family members on outcome measures (congruence) are explicitly included in the mixed effects models and estimated using maximum likelihood approach. The inclusion of the additional covariance structure due to repeated measures and within dyad correlation also makes it possible to estimate potential differences in patient-family member congruence over time. Comparisons on patient-family member congruence among the groups will be conducted using the likelihood ratio test (LRT) derived from a mixed effects model using group specific correlation structure versus a model using the same correlation in all groups. Changes in congruence can also be conducted using LRT comparing a mixed effects model with time specific correlation structure versus a model using equal correlations across time. By re-aligning data from the family member at specific lag time behind measures from patients, we will also be able to detect a lag effect in family member outcomes using this modeling framework.

Secondary Aim

- **Separate mixed effects models** with PHQ-9 or GAD-7 scores collected at baseline, 6, 12, 18 and 24 months from both patients and family members will be used as the outcome variables for Specific Aim 2. Participant type, randomized group (Screen Only and Screen Plus versus no screening), time and interaction between group and time will be used as independent variables, similarly to the modeling procedures described in details for Aim 1 above. Linear contrasts will be used to compare PHQ-9 and GAD-7 scores from family members in the combined screening groups versus the no screening group at 24 months. Dyad congruence in PHQ-9 and GAD-9 will be examined using LRT from the mixed effects models following the procedure described for Aim 1.

Secondary Aim

- **Mixed effects models with Caregiver Preparedness Scale or the Revised Scale for Caregiver Self-Efficacy scores** collected at baseline, 6, 12, 18 and 24 months will be used as the outcome variables, group (Screen Only and Screen Plus versus Control), time and interaction between group and time as independent variables. Linear contrasts will be used to compare preparedness and caregiver self-efficacy scores in the combined screening groups versus the no screening group at 24 months. We will also evaluate potential interactions between patient's/family member characteristics and variables associated with increased level of caregiver preparedness and self-efficacy over time.

Secondary Aim

- **To measure the impact and compare strategies for evaluation and treatment post screening, we will compare quality of life measures, caregiver preparedness, caregiving self-efficacy, depression and anxiety symptoms from family members** in the Screen Only (notify dyad and PCP of results only) group to the Screen Plus (notify dyad and PCP and a referral to ABC Program if screen positive) group using multi-level mixed effects models, similarly to the approach described in details for Aim 1. Separate mixed effects models with SF-36, Caregiver Preparedness Scale, Revised Scale for Caregiver Self-Efficacy, PHQ-9 or GAD-7 scores collected at baseline, 6, 12, 18, and 24 months from family members will be used as the outcome variables. Screening group (Screening Only versus Screening Plus), time and interaction between group and time will be used as independent variables. Linear contrasts will be used to compare all scale scores between the two screening groups at 24 months.

Sensitivity analyses for the impact of refusals and other sources of missing data

- We will compare patient and family member characteristics between those who complete at least one or more follow-up assessment(s) after baseline and those who did not complete any assessment beyond baseline due to refusal or other reasons. Significant variables detected from these comparisons will be included in the mixed effects models for the primary and secondary outcomes as covariates to control for potential bias from those missing follow-up outcomes. Under the missing at random

assumption, results from the mixed effects models will remain unbiased if the variables contributing to the missing data are included as covariates in the models. We will also perform additional sensitivity analyses to examine whether the missing at random assumption using the selection model approach under an informative missing mechanism impacts our analyses.

Statistical Power

Sample Size and Power Considerations for COADS

For the models in Aims 1, 2 and 3, we assume a base correlation of 0.2 and a decay rate of 0.8 in a linear exponent autoregressive correlation structure for repeated measures and a continuous time response, we will need to have 540 dyads per group to have complete data at 24 month in order to achieve 82.6% power to detect a group by time interaction with an effect size of 0.24 SD with higher SF-36, lower PHQ-9, GAD-7, higher caregiver preparedness and self-efficacy scores at 24 months in the combined screening groups (Screen Only and Screen Plus) compared to family members in the no screening (Control) group. Our previous screening studies and studies in primary care had a 5% loss to follow-up (death or withdraw) within a 12-month period. Therefore, allowing a loss to follow-up rate of 10% over the 24 months, we plan to enroll 600 dyads per group into this study. For Aim 4, using similar assumptions on the correlation structure for repeated measures and also 10% attrition rate, we will have 83.4% power to detect a significant group and time interaction with an effect size of 0.28 SD comparing family members randomized to the screening plus group to those in the screening only group at 24 months. Power estimation was conducted using the GLM Power procedure in SAS.

Timeline

Table 3. Study Timeline

	Year 1	Year 2	Year 3	Year 4	Year 5
Hire/ train staff					
Revise protocol manual and database					
IRB modification and approval					
Subject recruitment and consent					
Data collection					
Data analysis					
Prepare abstracts and manuscripts					
Disseminate results					