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The Design and Implementation of an Intervention Development Study: Retaining Cognition While Avoiding Late-Life Depression (ReCALL)

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Abstract

Objective—To discuss the design, rationale, and implementation of an intervention development study addressing indicated and selective prevention of depression and anxiety in individuals 60 years and older with Mild Cognitive Impairment (MCI), as well as in their caregivers.

Methods—In Phase I, now completed, we developed and standardized Problem Solving Therapy (PST) and the combined PST + moderate-intensity physical exercise (PE) intervention to be administered to participants with MCI and their caregivers together -- dyadically -- with both participants working with the same interventionist in the same therapy sessions. In Phase II, we have been testing the interventions against enhanced usual care (EUC), and we have addressed challenges to recruitment. Randomization was to one of three cells: PST + PE, PST, or EUC.

Results—Although we set out to intervene dyadically, many individuals with MCI lived alone or did not have a support person who could participate in the study with them. Consequently, we modified the study to include MCI participants with and without support persons. Ninety-four participants were enrolled: 20 with MCI together with their support persons (n=20 dyads), and 54

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MCI participants without accompanying support persons. The majority of participants have been satisfied with the usefulness of the interventions in managing stress and cognitive problems.

Conclusion—PST and moderate-intensity PE are acceptable interventions for depression and anxiety prevention in older adults with MCI and their available caregivers.

Keywords

Depression prevention; Aged; Mild Cognitive Impairment; Problem-Solving Therapy; Physical Exercise

INTRODUCTION

In this report, we describe the design and rationale of a depression and anxiety prevention pilot study focused on older adults with mild cognitive impairment (MCI) and their support persons, “Retaining Cognition while Avoiding Late-Life Depression (ReCALL).” We focus on individuals with MCI and their support persons because depressive and anxiety symptoms frequently co-occur with MCI (1-3), and unpaid caregivers of individuals with MCI are also at increased risk for depression and anxiety due to the stresses related to caregiving (1, 4). Further, MCI is often a transitional state between normal cognitive function and dementia -- roughly one-third of individuals with MCI later develop dementia (5) -- and neuropsychiatric symptoms (NPS), particularly depressive symptoms, may be modifiable risk factors to slow cognitive decline and prevent dementia(6).

Although the extant literature is not yet clear on how strong a risk factor is depressive symptomatology for dementia conversion, older adults with depressive symptoms, either major or subsyndromal depression, do have increased risk of progression to all cause dementia (7, 8). Further, targeting treatment of subsyndromal depression may also have an impact on disability in individuals with MCI (9, 10). Additionally, while stresses associated with dementia caregiving (e.g., dealing with changes in behavior and personality, dealing with functional and physical decline, needing to provide more supervision, anticipatory grief) are not present to the same extent in MCI caregiving, research by our group and others has shown that MCI support persons endorsed elevated levels of task-related responsibilities, subjective caregiver burden, and anticipatory grief (1, 4, 11).

Syndromal and subsyndromal depressive and anxiety symptoms in MCI likely have multiple etiologies. The underlying neuropathology that causes cognitive dysfunction may also disrupt the neural circuits involved in mood regulation (12). However, cognitive loss may also act as a psychosocial stressor, leading to increased depression risk. There appears to be a bi-directional relationship between NPS (depressive symptoms) and cognitive decline; having one condition enhances the risk of developing or worsening the other (3, 13-16). Mechanistically, depressive symptoms may increase the risk of further cognitive decline through multiple neurobiologic mechanisms (i.e., vascular, neurodegenerative, stress hormone toxicity), probably partially mediated by neuroinflammation (12).

For this pilot intervention development study, we chose to examine two interventions that might prevent major depression and anxiety disorders in older adults with MCI and their

support persons, Problem-Solving Therapy (PST) and moderate-intensity physical exercise (PE). Since both the individuals with MCI and their support persons are at increased risk for depression and anxiety disorders, we decided to take an innovative approach in developing an intervention that would be targeted at both members of a dyad at the same time, not previously examined in this population. The support person was to play a dual role: both as recipient of PST for depression/anxiety disorder prevention in him/herself and as a PST “coach” for their MCI partner. The rationale for PST is that older adults with MCI have heterogeneous cognitive deficits, but the most common -- slowed information processing, impaired memory, and executive dysfunction -- compromise problem-solving.

PST is based on the premise that problem-solving deficits lead to ineffective coping, worsening life stress, and ultimately depressive symptoms (syndromal or subsyndromal) in those at risk (17). PST teaches individuals to systematically approach and solve problems, exerting control over them. Once learned, the PST skills can be used to alleviate depressive symptoms and potentially mitigate depression risk (18). Alexopoulos, Arean and colleagues have reported that modified PST improved problem-solving skills that alleviated depressive symptoms and disability in individuals with late-life depression-executive dysfunction syndrome (19, 20). Recently, Kiosses and colleagues demonstrated that 12 weeks of Problem Adaptation Therapy -- based on PST, but focused on developing personalized strategies to regulate situations or problems that trigger negative emotions -- was more effective than comparable supportive therapy for cognitively impaired adults 65 years and older with major depression (21).

Physical exercise (PE) is efficacious in older adults for reducing depressive symptoms (22, 23) and may protect against new major depressive episodes (24, 25). Further, the majority of older adults do not engage in the recommended amount of PE. Modest increases in physical activity may not only prevent depressive symptoms in vulnerable elders, but also have substantial general health benefits, including slowing cognitive decline.(26, 27)

In this report, we discuss how we addressed difficulties in the implementation of the study, most of which were not anticipated when the study was designed. We share our experience with the research community to help others in designing future studies involving depression and anxiety prevention in a vulnerable population of older adults and their caregivers.

METHODS

Specific Aims and Overall Study Design

We conducted a pilot randomized clinical trial (RCT) to examine --

- The efficacy of PST for living with cognitive impairments (PST-cog) and subsyndromal depression in individuals with MCI and their support persons at preventing common mental disorders (major depression and anxiety disorders) and reducing depressive or anxiety symptoms over 12 months in probands with MCI and their support persons

- The effects of moderate-intensity PE added to PST-cog on preventing new episodes of major depression and anxiety disorders and reducing depressive or anxiety symptoms in individuals with MCI and their support persons.
- The effects of moderate PE added to PST-cog on improving or slowing deterioration of problem-solving and instrumental activities of daily living (IADL) skills in MCI probands.

This project has consisted of two phases. Phase I, now completed, focused on developing and standardizing PST to be delivered to the MCI participant and their support person together (dyadically), and implementing moderate-intensity PE. Phase II has focused on deploying the interventions in a RCT.

The study design is shown in Figure 1. In Phase II, after baseline assessment (T1), participants have been randomly assigned to one of three cells (1:1:1): PST + PE, PST, or EUC (enhanced usual care, that is, usual care enhanced by the provision of research assessment results to the usual care clinician). The interventions are described below. After the acute intervention, lasting up to 16 weeks (or 12 weeks for those in EUC), participants have post-intervention assessment (T2) and are assessed every three months (T3-T6) for 12 months.

Participants (inclusion/exclusion criteria)

To enter the study, probands (those with MCI) were 60 years or older, had a score on the Patient Health Questionnaire-9 (PHQ-9) (28) > 1 with at least a score of 1 on question 1 or 2 (depressed mood or anhedonia) and did not meet criteria for a major depressive episode or current anxiety disorder, except for specific phobia (DSM-IV TR) (29), had adequate physical and sensory function to undergo neuropsychological assessment, and ability to engage in moderate-intensity exercise (e.g., brisk walking 30 minutes 3 $\times$ per week).

MCI diagnosis was conferred through a two-step process. First was an initial cognitive screening battery comprising the 3MS (30), Trail Making A & B (31), Digit Symbol Substitution (32), and the Quick Mild Cognitive Impairment Screen (Qmci) (33). Individuals testing in the normal range (< 1 SD below normed mean on all 3 tests and/or Qmci) or whose scores reflected dementia (either > 2 SD below normed means on all 3 tests or > 2 SD below normed means on Qmci) were screened out. Based on the most common psychometric definition of MCI, individuals who scored between < 1 and < 2 below the normed mean on any test moved on to the comprehensive assessment and diagnostic adjudication session to determine MCI status. We acknowledge that the first level of MCI screening may have inadvertently screened out a small number of individuals as demented or normal who had early MCI. For those who screened in (or were questionably demented or normal), the initial cognitive screen was followed by more comprehensive assessment involving the Wide Range Achievement Test-IV (WRAT-IV)-Reading Subtest (34), Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) (35) and Delis-Kaplan Executive Function System (DKEFS) Trail Making and Color-Word Tests (36), the IQCODE (37), the 3-item version of the Performance Assessment of Self-Care Skills (38) (medication and finance management, flashlight repair), the Clinical Dementia Rating Scale, and the Unified Parkinson's Disease Rating Scale (39). The comprehensive assessment was reviewed at a

diagnostic adjudication conference by a neuropsychologist, neurologist, and geriatric psychiatrist in which the NIA-AA criteria (40) were used to diagnose dementia or the National Alzheimer's Coordinating Center comprehensive criteria / Revised Petersen criteria (2004) to diagnose MCI (41). We did not require subjective cognitive complaints on the part of the MCI participant, but rather complaints from an informant, via the IQCODE. The information from the informant on the IQCODE was used in the consensus conference to determine whether there had been a change in cognitive function from a previously higher level. To determine whether an elderly person had declined we used a cutoff of 3.2 in addition to clinical interpretation of the IQCODE.

Exclusion criteria for the MCI proband included disorder affecting the central nervous system (CNS), e.g., multiple sclerosis; depression in the past year; substance use disorder in the past year; currently taking an antidepressant; or lifetime history of bipolar disorder or schizophrenia. The inclusion/exclusion criteria were designed to capture a heterogeneous group of older adults with MCI with subsyndromal depression, but who did not have other conditions that would require treatment outside the scope of the study.

Inclusion/exclusion criteria for the support person were more limited: age 18 and normal cognitive function, no CNS disorder, substance use disorder in the past year, or lifetime history of bipolar disorder or schizophrenia. Support persons underwent the same two-step cognitive screening procedures as for the MCI participant to ensure no cognitive disorder was present.

Recruitment

Recruitment was initially planned from primary care physician (PCP) offices and community agencies concentrated in low-income communities with whom our research has a history of collaborating. In addition, we collaborated with the University of Pittsburgh Alzheimer's Disease Research Center (ADRC), who referred appropriate participants (those diagnosed with MCI) to our study.

Schedule of Assessments

The primary outcome is time to onset of major depression or anxiety disorder. We emphasize that depression/anxiety prevention interventions may not decrease the frequency of developing a major depressive episode or anxiety disorder, but may delay their onset. We have determined onset of major depressive episodes (DSM-IV TR) and anxiety disorders with the PRIME-MD/MINI (42, 43). Symptom burden has been measured at all research assessments. Participants meeting diagnoses have been referred for treatment, but have continued with research follow-up assessments. Independent evaluators blind to randomized intervention assignment have assessed subjects by phone or in person. Participants have been assessed at six time points: pre-intervention (T1), post-intervention (T2), and subsequently at 3-month intervals (T3-T6) with an assessment battery that was shared and identical with other depression prevention studies conducted in our Center (see Table 1).

Interventions

PST-Cog—Our therapy was based on manuals for individuals with cognitive loss developed by co-investigator Dr. Linda Garand and consultants to our study, Drs. Patricia Arean and Dimitris Kiosses. Dr. Arean developed PST to treat older adults with depression and executive dysfunction (20), and Dr. Kiosses developed PST to target elders with major depression and cognitive impairment (21). As part of Dr. Kiosses' intervention, he developed and cataloged an array of tools to help with cognitive disabilities. Dr. Garand developed an intervention targeted at spouses of persons with MCI.(44) When needed, the Kiosses intervention engages the caregiver in treatment such as facilitating the problem-solving process, promoting pleasurable activities, and helping the cognitively impaired participant avoid negatively charged situations. However, none of the interventions was designed to be delivered to dyads exclusively. We thus integrated these therapies into a dyadic intervention – one that is delivered to both members of a dyad at the same time -- focused on preventing depression and enhancing cognitive function in individuals with MCI and depressive symptoms and preventing depression in support persons. Based on work by Rovner (45), participants in the treatment arm received booster sessions at 3 and 9 months following the end of the prevention intervention.

Training of Interventionists—Interventionists were master's-level therapists with greater than 10 years' experience in mental health intervention. A PST master trainer (JQM) supervised the interventionists and reviewed audiotapes of sessions to assess fidelity to training and suggest therapeutic strategies over the course of the intervention.

PE—Moderate-intensity PE was defined as any activity, such as walking, bicycling, home aerobics etc., which would raise heart-rate and would make breathing harder (“You'll be able to talk, but not to sing a song”). Subjects were encouraged to pursue whatever form of PE they preferred, specifically increasing their baseline activity level by 30 minutes three times per week. As an attention-control for participants randomized to PST without PE, we instructed participants to use stretching bands three times weekly for 30 minutes for non-aerobic exercise (46). For participants engaged in PE or using stretching bands, these activities were monitored and encouraged by the PST therapist “outside the frame” of therapy (i.e., before or after the session devoted to PST). If the participant identified engaging in these activities as a problem to address in PST, then it was addressed “within the frame” of therapy. Participants were asked to complete activity logs of how often they exercised or used stretching bands.

Enhanced Usual Care (EUC)—Participants assigned to EUC received the same assessments as those participants assigned to PST or PST + PE, but did not receive PST or PE. The usual care control arm was considered “enhanced” because participants were assessed for mood and cognitive problems on a regular basis and those who met criteria for depression or anxiety disorders, cognitive decline, or who reported new medical symptoms, were referred for medical care, as in the intervention arm.

RESULTS

Phase I: Developing, Piloting, and Standardizing the Study Interventions

Roughly six months were spent in treatment development and standardization. The team held “brain-storming” sessions to design the scope of the therapy, number and length of sessions, frequency of meetings, and role for booster sessions. In adapting PST for our study, we decided to make the support person serve as the “auxiliary brain” and “coach” for the MCI proband. Specifically, the support person would help the MCI proband when s/he had cognitive difficulties, such as memory impairment or executive dysfunction, as well as provide encouragement to follow through the PST steps. While we did not expect the support person to serve as a therapist, we wanted her/him to be sufficiently skilled with PST, so that s/he could assist or coach the MCI subject to employ PST effectively as well as be able to apply PST for her/himself.

PST sessions were held with both members of the dyad present together, focusing on the MCI proband as the patient and working with the support person to serve as the coach. For MCI probands, we often used “pleasant events” both to support behavioral activation – targeting behaviors that are “anti-depressant” rather than internal factors such as cognitions -- and to provide a working example to teach the PST steps. While not prescriptive, we encouraged exploration of sleep disturbances as a problem in PST. We focused on sleep disturbances given the impact of disturbed sleep on mood and cognition (47). To help identify sleep problems, participants randomized to PST or PST and PE were asked to complete a sleep diary following baseline evaluation. Support persons were also taught basic PST steps, not just to help work with their partner (as a coach), but also to apply PST to for themselves for a self-identified problem that was the focus of one session, in which the MCI proband and the support person, separately, worked on solving a problem.

In Phase I, we identified potential problems with the use of PST that might occur with participants. For example, we noted that for some married couples, it was necessary to place limits on the scope of therapy, explicitly stating that *marital therapy* was beyond the scope of the intervention. However, some marital issues were appropriate for PST; for example, one dyad indicated they wanted to be “more social as a couple.” Other issues were related to coaching. Some MCI participants disliked being coached by their spouses. Additionally, some support persons were natural coaches, while others needed to develop their coaching skills. We identified when coaching was “going with” or “going against the grain” of the relationship.

Importantly, prior to initiating PST, we planned that all participants, including those assigned to EUC, would have a “Meet and Greet” session in which the overall study was reviewed including the overall study benefits. The cognitive test results would be discussed, and in particular, we would discuss in detail the MCI diagnosis and its implications. A goal of the session would be to enhance motivation for study participation. Further, if a dyad was participating, another goal of the meeting would be to gauge interpersonal style and assess the dynamics of the dyad to understand how they would work as a team in learning and applying PST. The format of the Meet and Greet was optimized in Phase I.

We also piloted the PE intervention and use of devices that served to monitor physical activity via accelerometry and physiological monitoring (e.g., heart fluctuation). In Phase I, both MCI probands and support persons were asked to record the amount of time they exercised and if they were able to increase their baseline activity level by 90 minutes per week. Interventionists asked about PE before or after PST sessions, addressing obstacles to increasing their activity level and motivating participants to engage in increased PE. Additionally, we used Sensewear™ accelerometers at study start and midway through the intervention to monitor PE as well as the first week of the follow-up phase of the study to examine the durability of increasing PE.

Phase II. Implementing the Study Interventions and Addressing Problems with Recruitment

Since this prevention intervention development project was being conducted in preparation for a confirmatory R01 grant, we expected that many changes to the protocol would be required during Phase II. Developmental and methodological changes are summarized in Table 2. The primary challenge with this phase was recruitment. Many of the modifications made to the study related to enhancing recruitment and ensuring that the participants who were recruited reflected the larger community of older adults as well as making the study findings generalizable. Table 3 presents the number of participants screened, eligible, and enrolled. The most important issue was that, by year 2 of the project, we determined that substantial numbers of interested and otherwise eligible participants were excluded because they did not have an eligible or willing support person. Further, given the high rate of older adults who live alone, including those with MCI, not including older adults who live alone would limit the generalizability of the study findings (48). We therefore opened up recruitment to individuals with MCI who did not have a caregiver (“singletons”).

We also identified other challenges to enrollment: 1) most people in the community living with MCI are undiagnosed, and therefore unaware of the disorder (i.e., may identify their difficulties as normal aging) and 2) screening and evaluating community dwelling older adults for MCI was much more labor-intensive than initially planned. While there was little that we could do regarding obstacle #1, regarding obstacle #2, we redirected and expanded resources to recruitment.

Recruitment strategies—There was no one particular recruitment method that was effective. Rather a multi-pronged approach was required. It involved scouring research registries, encouraging word of mouth by community champions and prior research subjects, mailings targeted to older adults, and most importantly faculty presentations discussing cognitive aging at senior centers and senior hi-rises immediately followed by cognitive screening of individuals interested in the study participation.

Adherence, uptake, fidelity—We have tracked the uptake of PST by MCI participants. In general, they were able to learn and apply problem-solving skills via PST. At the end of every PST session, the interventionist filled out a 3-point rating scale (1=lowest, 3=highest) aimed at assessing uptake. Among subjects who completed the study (n=37) versus those

who dropped out (n=3): participation was 2.90 vs. 3.00, understanding of material was 2.77 vs. 2.28, and homework effort and participation was 2.53 vs. 2.24.

We recruited 94 participants (see Table 4). We enrolled 20 MCI subjects with 20 support persons (i.e., 20 dyads); the remainder of the subjects (n=54), were all MCI singletons. Non-white participation (%) was significantly higher than the demographics of Allegheny County (18.7%).(49)

Patient Satisfaction—We have surveyed 20 MCI participants after study completion. Because the study team is still blinded, data are combined across intervention groups. For items on: flexibility of scheduling study appointments and helpfulness of the therapist, 100% were “Satisfied” or “Highly Satisfied”; frequency of appointments and usefulness of the interventions in managing stress, 95% were “Satisfied” or “Highly Satisfied”; on usefulness in managing cognitive problems, 89% were “Satisfied” or “Highly Satisfied.” In addition, 12 participants completed an additional questionnaire and 83% (10/12) were willing to participate in a future exercise intervention study, 80% (8/10) of those were very willing or somewhat willing to participate in a community site an average of 2.4 sessions per week. Of those, 63% (5/8) preferred a 6-month study duration.

DISCUSSION

We have presented the key aspects of the implementation and challenges we encountered to help the community of researchers learn from our efforts. The study findings will be reported after study completion in January 2016. In the coming years, depression and anxiety prevention studies will be increasingly important with the aging population of high-, middle-, and low-income countries, United States and developed world. Our “take home” points to our fellow researchers in geriatric mental health for maximizing feasibility and acceptability of depression and anxiety prevention research in MCI probands and their support persons are the following: first, prevention work is feasible with adequate resources directed for recruitment. Second, when recruiting individuals at risk for depression and anxiety, it is important to avoid making inclusion/exclusion criteria too restrictive, such that individuals who are most symptomatic, but do not meet diagnostic criteria for depression, are excluded because these are the individuals who are most likely to benefit from depression prevention interventions (i.e. indicated prevention). Third, individuals with cognitive impairment are often unaware of their cognitive diagnosis and may not “self-identify” for research studies of cognitive dysfunction. To address this “self-identification” problem, it is critical to combine research recruitment efforts with simultaneous screening for cognitive dysfunction. Fourth, support persons can be trained as PST coaches to promote positive aspects of their relationship. However, individuals with MCI often have limited or no supports, so PST depression/anxiety prevention needs to be flexibly designed to include or not include support persons. By publishing our methods, design, and issues with implementations, we expect that other researchers will benefit from our experience with our intervention development study ReCALL.

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Figure 1.
Study design

Table 1

Study assessments

Domain	Measure
Depression ⁺ (every 3 months)	Prime-MD/Mini ^{43, 50} Patient Health Questionnaire-9 (PHQ-9) ³⁰
Anxiety (every 3 months)	Prime-MD/Mini ^{43, 50} Generalized Anxiety Disorder-7 (GAD-7) ³¹
Medical burden/Medication Check List	Cumulative Illness Rating Scale (CIRS-G) ³²
Disability	Late-Life Functional Disability Inventory (LL-FDI) ³³
Functional status, physical performance	Short Physical Performance Battery (SPPB) ³⁴ Physical Activity Scale for Elderly (PASE)(49) Accelerometer Activity Log
Insomnia	Pittsburgh Sleep Quality Index (PSQI) ³⁵
Pain	Numeric Rating Scale for Pain (NRS-20) ³⁶
Cognitive Status	Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) ³⁷ Delis-Kaplan Executive Function System (DKEFS) ³⁸ Modified Mini-Mental Status (3MS) ³⁹ 3-item Performance Assessment of Self-Care Skills (PASS) (35)
Social Isolation/Support	Interpersonal Support Evaluation List (ISEL) ⁴⁰
Caregiving Burden	Zarit Burden Index (ZBI) ⁴¹ Dyadic Adjustment Scale (DAS) 1-item(48)
Personal Mastery and Self-Efficacy	Pearlin Sense of Mastery Scale (PSE) ⁴²
Problem Solving Skills	Problem Solving Skills Inventory (PSSI) ⁴³
Biosignatures	Inflammatory Cytokines (IL6, TNF alpha) + mRNA Transcription (blood draw)
Problem-Solving Therapy, intervention engagement	Participation Rating Scale

Table 2

Developmental and Methodological challenges and changes

Challenges	Solutions
We anticipated that PST steps would be challenging for MCI participants to learn	We used Alexopoulos & Arean's modifications for executive impairment which included modifications for affect regulation, perseveration and initiation deficits. We further modified PST by building in additional repetition of material to accommodate memory impairment
PST is self-oriented and we were using it dyadically, so that the support person could coach the MCI proband to carry out the steps after the intervention period concluded.	Modified PST to first teach steps to the support person and then teach coaching skill to aid the MCI participant
A substantial number of potential participants were screened out because they did not endorse dysphoria or anhedonia, on the PHQ-2.	We requested permission to re-contact these potential participants 3 months later to re-screen them with the PHQ-2.
A substantial number of interested and otherwise eligible participants were excluded because they did not have a caregiver or the caregiver was ineligible or uninterested in research participation.	We opened up recruitment to individuals with MCI who did not have a caregiver ("singletons").
Inability of individuals with MCI to identify having MCI hampered recruitment.	Arranged and delivered presentations on cognitive aging in residences and community centers followed by on-site study screening of interested potential participants.
Early recruitment was skewed to individuals who were minimally symptomatic because of the inclusion/exclusion criteria, excluding participants with PHQ-9 > 9.	Adjusted study inclusion criteria by removing the ceiling on PHQ-9 scores as long as participants had not experienced a major depressive episode within the previous 12 months.
Early attempts by study staff to obtain blood for biomarker measurement resulted in low yield.	Hired a phlebotomist to travel to participants' homes to draw blood.

Table 3

Recruitment -- screened, eligible, and enrolled participants

Table 4

Baseline Characteristics (n = 94)

Variable	Descriptive Statistic	
	Participant (n=74)	Support Person (n=20)
Age (years)	75.0 (8.6)	66.6 (13.0)
% Female	63.5 (n=47)	80.0 (n=16)
% European American	77.0 (n=57)	95.0 (n=19)
Education (years)	15.2 (2.5)	15.5 (2.0)
Body Mass Index (BMI)	28.3 (4.4) [n=69]	28.6 (6.6) [n=19]
Cumulative Illness Rating Scale: Total (range = 0-52, higher = worse)	9.4 (3.6) [n=72]	7.6 (3.9) [n=19]
Cumulative Illness Rating Scale: Count (range = 0-13, higher = worse)	5.8 (2.0) [n=72]	5.0 (2.3) [n=19]
RAND12 Mental Health Component (t score: mean = 50; SD = 10, higher is better)	46.8 (7.8) [n=71]	47.4 (8.6)
RAND12 Physical Health Component (t score: mean = 50, SD = 10; higher = better)	39.6 (8.5) [n=71]	42.8 (8.2)
Short Physical Performance Battery (range 0-12; higher = better)	8.2 (3.5) [n=69]	9.9 (2.7) [n=19]
Patient Health Questionnaire (PHQ-9) (range 0-27, higher = more depression)	6.2 (2.9)	4.5 (3.0)
Generalized Anxiety Questionnaire (GAD7) (range 0-21; higher = more anxiety)	3.4 (2.7)	3.3 (2.9)
Interpersonal Support Evaluation List – modified 12 item (range 0-48; higher = more supports)	40.7 (5.9)	38.9 (6.5)
DKEFS: Trail Making Test: Set Shifting Scaled score. (range 0-19; mean=10, std=3; higher better) **	9.4 (3.6)	12.5 (2.1) [n=19]
DKEFS: Trail Making Test: Set Shifting vs. Motor Speed Scaled score (range 0-19; mean=10, std=3; higher better) **	9.3 (3.3)	10.6 (1.7) [n=19]
DKEFS: Color Word: Inhibition-Switching Scaled Score (range 0-19; mean=10, std=3; higher better) **	9.1 (3.6) [n=72]	12.5 (2.7)
RBANS: Language Index Score (mean=100, std=15; higher better) **	98.7 (9.9)	101.0 (7.5)
RBANS: Immediate Memory Index Score (mean=100, std=15; higher better) ***	95.5 (13.32)	108.0 (12.8)
RBANS: Delayed Memory Index Score (mean=100, std=15; higher better) ***	92.51 (12.7)	104.6 (12.8)
RBANS: Attention Index Score (mean=100, std=15; higher better) ***	98.6 (15.7)	106.2 (13.2)
RBANS: Visuospatial Index Score (mean=100, std=15; higher better) ***	94.4 (15.3)	104.0 (17.0)
RBANS: Total score Index Score (mean=100, std=15; higher better) ***	94.2 (10.9)	106.2 (10.5)

** Delis-Kaplan Executive Function System (DKEFS) - scores are scaled range=1-19, mean=10, SD=3.

*** Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) - scores are scaled: mean=100, SD=15