STUDY PROTOCOL
AND
STATISTICAL ANALYSIS PLAN

PROJECT TITLE: Mobile Web-based Behavioral Intervention for Improving Caregiver Well-being

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PROJECT TITLE

Mobile web-based behavioral intervention for improving caregiver

PRINCIPAL INVESTIGATOR

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DURATION OF THE STUDY

5 years

LAY LANGUAGE SUMMARY OR SYNOPSIS

Caregivers of persons with dementia suffer great amounts of distress that significantly impacts their mental and physical well-being, and ability to care for the patient at home without resort to nursing home placement. Yet, caregivers' access to quality, evidence-based interventions to assist them is currently very limited. We propose to test the efficacy of a web-based Behavioral Activation intervention called the Pleasant Events Project (mPEP) that has potential to significantly improve caregiver well-being.

SPECIFIC AIMS

Aim 1: Test the efficacy of wBA for improving caregiver well-being.

H1: Caregivers receiving the mPEP intervention will report improved positive affect, reduced negative affect, and improved mental and physical well-being compared to caregivers receiving a web-based bibliotherapy intervention.

Aim 2: Assess mechanisms of the mPEP intervention that promote well-being.

H2: Via data collected in the web-based portal, greater engagement in pleasant activities (i.e., treatment adherence) will be associated with greater improvement of caregiver well-being outcomes.

Aim 3: Assess the influence of the mPEP intervention for promoting physical health.

H3: Caregivers assigned to the mPEP intervention will show greater reduction in blood pressure relative to those assigned to a web-based bibliotherapy intervention.

BACKGROUND AND SIGNIFICANCE

The primary aim of this study is to conduct a stage II randomized clinical trial to test the efficacy of a newly adapted web-based Behavioral Activation treatment called the mobile Pleasant Events Project (mPEP), that can be widely disseminated at low cost and in a convenient manner to caregivers of persons with Alzheimer's Disease and Related Dementias (ADRD). Our lab has demonstrated that a face-to-face version of this intervention is efficacious for promoting well-being in caregivers, and we also have preliminary evidence that the mechanisms associated with the intervention (i.e., greater engagement in pleasant activities) are associated with improved blood pressure in this population. Over 15 million men and women provide informal caregiving services to family members who have dementia. The literature is replete with evidence that caregiving results in high rates of distress, and potentially high rates of physical morbidity. Caregivers consistently report increased distress and reduced well-being relative to their non-caregiving peers, and increased distress is associated with physical health consequences (e.g., cardiovascular disease). Thus, efficacious interventions that are more easily accessible to caregivers are critical for improving mental and physical well-being in this population.

Although much research has been conducted evaluating the efficacy of psychosocial interventions for reducing

distress in this population, caregivers continue to have difficulty accessing these treatments. Currently, most caregiver intervention frameworks require caregivers to meet with a therapist in one of four formats: a) face-to-face meetings with a therapist outside the caregiver's home, b) face-to-face meetings with a therapist in the caregiver's home, c) in-person, group-based meetings (e.g., support groups, group therapy) where the caregiver receives treatment with other caregivers, or d) phone-based interventions in which caregivers call a therapist or support group. While possibly efficacious in reducing caregiver distress, these therapeutic formats are limited because: a) community agencies serving caregivers do not offer Evidence-Based Therapies (EBTs), b) the interventions are often not accessible to caregivers who reside outside the care network, c) they require caregivers to attend therapy sessions on specific days and at specific times that may not be convenient for them, or d) they may require caregivers to find alternate care for their care recipients while they attend the therapy. To address these limitations, we adapted our existing, evidence-based and brief face-to-face Behavioral Activation intervention, into a mobile web application. Our intervention was designed to help caregivers understand factors that contribute to and maintain their distress symptoms and to implement strategies designed to help them create positive, rewarding environments that promote mental and physical well-being. In the newly developed mPEP intervention, caregivers will learn and apply specific behavioral strategies to promote well-being, and be able to receive feedback, on their mobile phones, on how these behavioral strategies are working to promote their well-being. Of particular advantage to the mPEP intervention over other potential intervention adaptations are: a) The theoretical background of behavioral activation is intuitive to end-users, and implementation of the principles of the intervention are simple and straightforward, making it highly scalable and acceptable to both caregivers and community-based organization who may implement it, and b) The ability to capture real-time data allows caregivers and researchers to better understand the mechanisms by which the intervention reduces distress and improves well-being (i.e., behavioral activation). Overall, the current proposal seeks to increase caregivers' access to quality care by demonstrating that our adapted, scalable, evidence-based intervention (i.e., mPEP) is efficacious via delivery through a web-based portal, while simultaneously allowing for better scientific understand of intervention mechanisms.

RESEARCH DESIGN AND METHODS

SUBJECTS

Setting: Because some CG find it difficult to leave home and find alternate care arrangements for their spouse in order to participate in research, assessments will take place online using the online survey tool Qualtrics. This design increases participation and retention. Further, by bringing the research closer to the real-life circumstances of caregiving, we enhance the study's ecological validity.

Sample: The study will enroll 200 participants, with the following inclusion criteria: a) English-speaking; b) at least 40 years of age; c) have access to a web-based device (e.g., computer; smartphone); d) be in-home caregivers of a loved-one with probable Alzheimer's Disease or related dementia (ADRD), e) be living with their care recipients; and f) providing a minimum of 20 hours of care per week. Participants are required to speak English because a) our web-based materials are only available in English, b) we do not have staff or resources to conduct the intervention or assessments in Spanish; and c) assessment tools, surveys, questionnaires or psychological tests are only available in English. Participants will be excluded if: a) the caregiver or AD patient is diagnosed with a terminal illness with a life expectancy of less than 1 year, b) caregivers are cognitively impaired as measured by a brief screen for cognitive functioning; i.e., a Mini Mental State Exam (MMSE) score of <27, c) caregivers are enrolled in another intervention study or are already receiving psychotherapy to improve well-being or reduce distress. The sample will be recruited from: a) the UCSD Alzheimer's Disease Research Center, b) community-based organizations with whom our research team already has well-established relationships (e.g., the San Diego chapter of the Alzheimer's Association; the Southern Caregiver Resource Center); and c) community support groups. Participants will be of varied gender

and ethnicity.

Assessments: Outcomes will be collected at 4 times: a) Pre-intervention, b) mid-therapy (3-months), c) post-therapy (6-months), and 6-months post-intervention. Assessment will be completed online via UCSD's Qualtrics Survey software (https://ucsd.co1.qualtrics.com/ControlPanel/). Qualtrics offers a high level of security including 256-bit encryption and HIPAA Compliant Certification. The testing will be via the secured UCSD Qualtrics website and the participant will be given a random digit access code and password via e-mail which will not have any identifying information associated with it (including email address) when the survey is completed/returned. Again, to maintain confidentiality, no identifiable information will be included on the assessment survey.

Details of the survey provided to participants are as follows:

Measures

Blood Pressure: Blood pressure will be collected using an Omron HEM 907XL IntelliSense Professional Digital Blood Pressure Monitor sent to participants using US Mail or similar format. Blood pressure will be self-assessed by participants at baseline, 3-, 9-, and 15-months.

The following section details the information to be collected from caregivers via online administration. Further, we detail the specific time-points at which the information will be collected:

Depressive Symptoms (Primary Outcome): Symptoms of depression will be assessed using the Center for Epidemiological Studies Depression Scale—Revised (CESD-R). The CESD-R is a 20-item scale that asks patients to rate the degree to which they have experienced several symptoms of depression over the past week. Scores of ≥16 correlate highly with a diagnosis of depression. The scale was revised to better reflect the diagnostic criteria of the DSM-5, and the scale continues to good psychometric properties. This scale addresses RFA-AG-18-030, as depressive symptoms is a key well-being outcome in caregivers. This scale will be administered at baseline, 3-, 9-, and 15-months.

Positive and Negative Affect. We will utilize the Positive and Negative Affect Schedule (PANAS) to assess positive (PA) and negative affect (NA). The PANAS contains 20 items assessing PA and NA. Alpha reliability is excellent, ranging from .83-.90 for the PA scale and .85-.90 for NA.37 This scale addresses RFA-AG-18-030, which lists positive and negative affect as key outcomes to be assessed. This scale will be administered at baseline, 3-, 9-, and 15-months.

Mental and Physical Well-Being: Mental and physical well-being will be assessed using the SF-12 scale, which is a multi-purpose, short form health survey consisting of 12 questions. Test-retest and internal reliability exceed 0.70 in studies of this scale's psychometric properties. The SF-36 also has excellent content, criterion, and predictive validity. This scale will be administered at baseline, 3-, 9-, and 15-months.

Caregiver Stress: Stress will be assessed using the short form of the Zarit Burden Interview (ZBI), which consists of 12 items asking caregivers to rate stress specifically associated with being a caregiver. The has excellent reliability and validity in caregiver populations. Daily stress will be assessed using the Role Overload scale37 and will be administered via the mPEP program. The Role Overload scale consists of 4 items in which participants are asked to rate the extent to which they feel globally overloaded by life responsibilities. This scale will be administered at baseline, 3-, 9-, and 15-months.

Care Recipient Functioning. We will assess multiple aspects of care recipient (patient) functioning including

cognitive status, problem behaviors, and problems with daily functional tasks (i.e., ADLs and IADLs). To assess patient cognitive functioning, we will utilize the Clinical Dementia Rating (CDR) scale. This scale is administered to the caregiver only, and is a report of the caregivers experience regarding their loved one's cognitive functioning. The CDR will be administered at baseline and 15 months only. ADLs and IADLs will be assessed using the Activities of Daily Living Questionnaire (ADLQ). This scale consists of 28 items, administered to the caregiver, asking about their loved-one's functioning in 6 domains. This scale will be administered at baseline, 3-months, 9-months, and 15-months. Problem behaviors of patients will be assessed using the Revised Memory and Behavior Problem Checklist (RMBPC). This scale will be administered at baseline, 3-months, 9-months, and 15-months.

Randomization Procedures: Once the candidate is eligible, willing to participate, and signs our consent form, he/she will be randomly assigned to one of the two intervention groups via a randomization table.

Interventions: As described above, participants will be randomized to one of two intervention conditions. Below are descriptions of the two conditions.

a. Web-based Pleasant Events Project intervention (mPEP) – The mPEP intervention is designed to be primarily self-administered via mobile technology, with an initial phase-in period whereby caregivers receive phone coaching and check-ins every two weeks. The mPEP intervention is ideographic in nature; accounting for individual differences in the pleasantness of individual activities across caregivers and the impact of such activities on individual well-being states. The overarching theme of the mPEP intervention is that participants have weekly goals for experiencing positive activities and events which, in the parlance of our app, is characterized by "hearts." Similar to a Fitbit® sports watch, which sets daily goals for steps and helps individuals track progress toward these goals, our participants receive weekly goals for "obtaining hearts", whereby hearts are assigned to various activities they personally enjoy, and each time they participate in those activities, they achieve a certain number of hearts (i.e., 1-5 hearts/activity). The mPEP app then helps participants visually see their progress toward their weekly hearts goal, which provides motivation to seek out and participate in more activities if needed. The protocol is also programmed to be adaptable and idiographic to each caregiver. That is, if participants achieve a particular week's hearts goal, but do not see benefit to their moods, the app will use an algorithm to increase the hearts goal for the subsequent week. If individuals do not meet their hearts goal for a week, but achieve mood benefit, the app will adapt and set the next week heart goal slightly lower.

A key element to keep participants engaged in the program is the use of text reminders. Each night, at a time of the participant's choosing, a text is sent to participants with a hyperlink to their individualized web-portals. Along with the hyperlink is a message asking users to provide an update on their progress toward their goals for the week. In addition, for the first three months of using the mPEP intervention, participants will receive bi-monthly 10-minute "check-in" calls from a coach to answer questions on how to use the web site, problem-solve any barriers to participating in activities, and encourage participants to do their best to achieve their weekly goals. So as not to overburden caregivers, these check-in calls will be scheduled between the coach and caregiver at a time of the caregiver's choosing. Participants complete a total of three phases in the project, which are (sample screen shots presented in Figure 3):

Phase 1: This phase involves self-monitoring activities over the course of one week. This phase is designed to capture activities the participants already engages in (and when), to help increase awareness of how balanced their lives are with regard to self-care activities vs caregiving activities. At the end of each day, participants complete an activity detailing when they woke up, activities they completed throughout the course of the day, and ratings of how enjoyable/pleasant each activity was. Each activity is entered into a personalized calendar so

they can visually see how they spent their day, as well as how many hearts they received from each activity.

Phases 2 and 3: These phases involve the selection and engagement in activities designed to promote overall well-being for the caregiver. In Phase 2, the participant completes a mood questionnaire of their positive and negative affect over the previous week. This is designed to provide participants with a baseline assessment of their well-being, on which to track progress as they move through the stages of the application. Following completion of the questionnaire, the participant receives feedback on all activities during phase 1 that were rated
as at least moderately pleasurable (i.e., rated as 3 hearts). Then, the participant will be provided with a structured group of tasks to help identify treatment goals, including: a) select new activities from several life domains (e.g., hobbies) that may increase access to rewarding experiences, and b) create a weekly goal for "hearts" designed to help participants start with achievable activities that are most likely to produce successful attainment of goals. This helps maintain motivation by taking a stepwise goal-setting approach while helping reduce barriers to treatment compliance. During phase 3, participants track their daily engagement in activities , with each participated activity adding to their weekly hearts goal. At the completion of one week of activities, participants again complete their weekly mood questionnaire. Particpants then see their weekly accomplishments for hearts achieved and overall mood score. The mPEP algorithm then computes the following week's hearts goal based on hearts achieved and overall mood. Finally, participants repeat phases 2 and 3 until completion of the program.

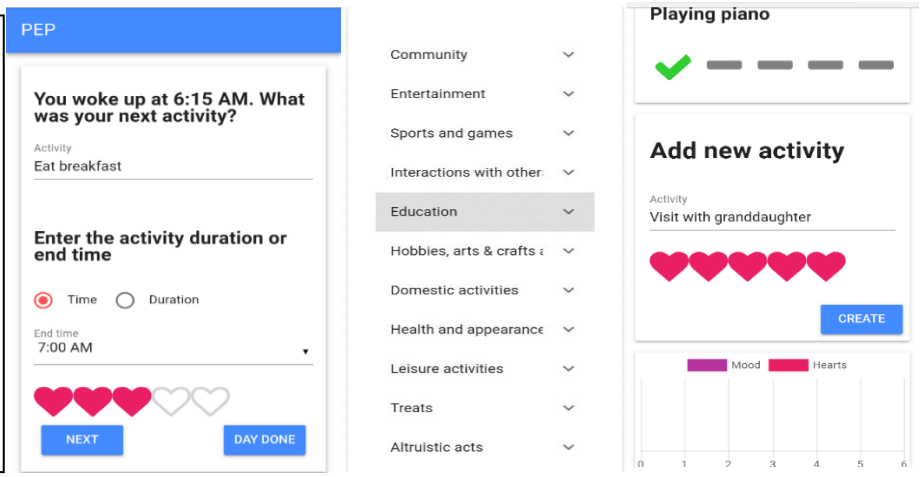

Figure 3. Screenshots from mPEP. Left = Phase 1 (self-monitoring), Middle = Phase 2 (activity selection; Right = Phase 3, activity tracking.

b. Information and Support Intervention - Participants randomized to this condition will have personalized web access to a comprehensive resource guide containing materials on coping with specific CG stresses (e.g., developing problem-solving skills; managing care receiver problem behaviors; improving communication), and services available for caregivers in San Diego County (i.e., adult day care services; legal services for seniors; respite services). In this intervention, caregivers choose information most relevant to their current circumstances, accessible any time convenient to them. To ensure equivalent contact and support, for the first three months of using this intervention, participants will receive "check-in" calls every two weeks to answer questions on how to use the web site, problem-solve any barriers to participating in activities, and provide information and any referral to services. In addition, participants will receive a unique log-in key associated with their participant identification number, which will allow us to evaluate treatment compliance data and exposure to the treatment information (e.g., information accessed; time spent logged-in). Further, to ensure similarities in treatment delivery, participants will receive nightly text reminders to access and apply information learned at the web-site.

Screening Procedures: Screening will occur in person and will consist of a formal screening questionnaire assessing participant eligibility. In addition to the screening questionnaire, participants will be administered the mini-mental state exam (MMSE) to determine cognitive function and eligibility as per our eligibility criteria.

Participants scoring <27 on the MMSE will be informed they are not eligible to participate in the project.

Statistical Analyses: All hypotheses will be two-sided at the 0.05 level and intent-to-treat with data included for all subjects completing at least one post-baseline assessment. Data analyses will employ generalized additive mixed models (GAMMs) tailored for longitudinal data. GAMMs allow for potentially nonlinear effects of independent variables on outcomes; the nature of the nonlinearity and degree of smoothness is data-determined for each independent variable. Models will include as covariates variables that differ significantly by condition. We will use Akaike Information Criterion (AIC) to determine covariance structures and variable selection. To control for inflated Type I error rates from multiple testing within each hypothesis, we will use the Westfall-Young step down maxT randomization procedure, which adjusts p-values for significance in multiple comparisons while taking into account the correlation of the outcomes. In this way we can control for an overall family-wise error rate of .05 while achieving more power than Bonferroni adjustments. **Missing Data:** Follow-up data will be obtained on all participants, regardless of treatment completion. We will perform sensitivity analyses for impact of potentially informative missing data via pattern mixture models[47] extended to incorporate random effects. We anticipate 15% dropout between each time point, accounting for an overall (cumulative) dropout rate of 39%.

Hypothesis testing: Hypothesis 1: Caregivers receiving mPEP will report reduced depression, improved positive affect, reduced negative affect, and improved well-being compared to caregivers receiving a web-based bibliotherapy intervention. Dependent Variables: Depressive Symptoms, Positive and Negative Affect; SF-36 scores. Independent Variables: Condition and Time (Baseline, 3-, 9-, and 15-months). **Statistical Analysis:** This hypothesis will use GAMMs. Condition will be entered as a fixed-effect predictor along with time and their interaction. If the smoothed interaction of condition x time is significant at the .05 level (determined by an F test of relevant coefficients in the model) we will test for pairwise differences with Westfall-Young adjusted p values.
Power Analysis: Because the mPEP intervention is based upon our in-person version of PEP for caregivers, we anticipate effect sizes to be comparable to those seen in our previous trials. Accordingly, we powered our study based results showing an effect size of 0.4 (small to moderate) in favor of mPEP with an active comparator. Sample size estimates were based on the Hedeker, et al. method for various covariance structures for mixed effects models. For the proposed study, we assumed an autoregressive covariance structure, with a correlation between sequential assessments set at 0.5 based on our previous trial in caregivers. Using this methodology, assuming an alpha level of 0.05, we have a minimum 90% power to detect an effect size of 0.4 with 15% attrition between each time-point (39% cumulative drop-out rate), when there are 100 subjects per each condition.

Hypothesis 2: Greater treatment-associated change in behavioral activation will be associated with greater improvement of caregiver well-being outcomes.
Statistical Analysis: For this hypothesis, multilevel (mixed) models will be used. To test for mediation, we will utilize the analytic strategy described by Krull and MacKinnon. In this approach, four conditions are tested: a) the relationship between intervention condition and the dependent variables (e.g. Depressive symptoms), b) the relationship between intervention condition and mediatior (behavioral activation), c) the relationship between behavioral activation and the outcome, and d) the relationship between intervention condition and outcome after controlling for the proposed mediator. Mediation will be tested using the Monte Carlo Method for Assessing Mediation (MCMM). **Power Analysis:** The proposed study will be powered to detect if treatment-related change in behavioral activation mediates treatment-related change in depressive symptoms. Therefore, power is based upon the strength of both the 'a' path (i.e., mPEP significantly increases behavioral activation relative to our control condition) and 'b' path (i.e., change in behavioral activation is significantly associated with change in depressive symptoms). As per our pilot data, we conservatively estimate a small-to-medium effect (r=.20) between mPEP and behavioral activation (r=.20) between mPEP and

depressive symptoms, and a medium effect (r=.50) between change in behavioral activation and change in depressive symptoms. With N = 200 and alpha of 0.05, we have 81% power to detect a significant mediation effect. These power estimates are based on 15% attrition between time-points (39% overall project attrition).

Hypothesis 3: Caregivers assigned to the mPEP intervention will show greater reduction in blood pressure relative to those assigned to a web-based bibliotherapy intervention.
Dependent Variables: Systolic and Diastolic Blood Pressure. Independent Variables: Condition and Time (Baseline, 3-, 9-, and 15-months). Moderator: Age.
Statistical Analysis: This hypothesis will be tested using GAMMs. Condition will be entered into the model as a fixed-effect predictor along with time and their interaction. Because age is a known predictor of blood pressure we will enter age as a covariate and moderator of treatment efficacy in analyses. If the smoothed interaction of treatment condition and time is significant at the .05 level (determined by an F test of the relevant coefficients in the model) we will test all pairwise differences with Westfall-Young adjusted p values. **Power Analysis:** Power estimates were calculated using the Hedeker, et al. method for various covariance structures for mixed effects models. For the proposed study, we assumed an autoregressive covariance structure. An estimated correlation of 0.4 was assumed between sequential assessments based on our pilot data. Using this methodology, assuming an alpha level of 0.05 and 200 subjects (100 per treatment arm), and 15% attrition between time-points (39% cumulative dropout across time-points), we have 80% power to detect a small-to-medium effect size of 0.32.

HUMAN SUBJECTS

The study will enroll 200 participants, with the following inclusion criteria: a) at least 18 years of age; b) have access to a web-based device (e.g., computer; smartphone); c) be in-home caregivers of a loved-one with probable Alzheimer's Disease (AD) or related dementia, d) be living with their care recipients; and e) providing a minimum of 20 hours of care per week. Participants will be excluded if: a) the caregiver or ADRD patient is diagnosed with a terminal illness with a life expectancy of less than 1 year, b) caregivers are cognitively impaired as measured by a brief screen for cognitive functioning; i.e., a Mini Mental State Exam (MMSE) score of <27, c) caregivers are enrolled in another intervention study or are already receiving psychotherapy to improve well-being or reduce distress. The sample will be recruited from: a) the UCSD Alzheimer's Disease Research Center, b) community-based organizations with whom our research team already has well-established relationships (e.g., the San Diego chapter of the Alzheimer's Association; the Southern Caregiver Resource Center); and c) community support groups. Participants will be of varied gender and ethnicity.

RECRUITMENT AND PROCEDURES PREPARATORY TO RESEARCH

The primary referral source is the UCSD Alzheimer's Disease Research Center (ADRC). Added recruitments occur following informational meetings with various community based organizations serving the Alzheimer community and the elderly. At the ADRC caregivers will either be assessed by ADRC staff to determine if they are appropriate for inclusion in this study when they are enrolled into the ADRC, or by our staff. The ADRC has evaluated over 2,000 Alzheimer Disease patients to date, and these individuals are often brought by their caregivers to appointments. Thus, in this situation, ADRC staff will explain our study to the caregiver and, if the caregiver is appropriate for inclusion into the study, a staff member will describe the study to the potential participant.

Subjects will also learn of the study via IRB-approved online advertisements, through our lab web site, or through web sites such as Research Match or ClinicalTrials.gov. In these cases, subjects will call our lab phone number and will be screened over the phone and, should they meet inclusion criteria and express interest in joining the study, they will be sent the consent form via mail, e-mail, or fax. A member of our research lab

witllwill go over the consent form verbally with the participant, and participants will then complete the consent form and return either by US Mail, e-mail (by scanning a copy of their consent and e-mailing), or by fax.

In all cases, fully informed consent will be obtained, and Dr. Mausbach and other co-investigators will be directly available to clarify questions should any be raised by the participant. Signed consent forms will be kept on file in a specially secured cabinet. All of the investigators have completed the required federal human subjects certification.

INFORMED CONSENT

If a subject is appropriate for inclusion into the study, a staff member describes the study, including questionnaires, assessments, and the glucose measurement. The consent will detail the purpose of the project and its minimal risks. Also, participants will be informed that participation in the project is voluntary and they will be afforded the opportunity to discontinue their participation without consequences at any time during the project. Signed consent forms will be printed and kept on file in a specially secured cabinet. Participants who call in to our lab from online recruitment advertisements, from our lab web site, Research Match, or Clinicaltrials.gov will be screened over the phone for eligibility, and a copy of our consent form will be mailed, e-mailed, or faxed to them. A member of our research team will go over the consent verbally by phone, and a signed copy of the consent will be mailed, e-mailed, or faxed back to our lab. Those participants who wish to discontinue the project will be provided referrals to other agencies that can provide them with services.

ALTERNATIVES TO STUDY PARTICIPATION

The alternative to participation is not to participate.

POTENTIAL RISKS

We anticipate the risks associated with this study will be minimal. However, participation in this study may involve some added risks or discomforts. These include the following:

1) *Boredom and fatigue* – Participation in the online assessments may require time and attention, and participants may become bored or fatigued. If this happens, participants will have the right to take a break to rest. They may also discontinue the interview and resume at a later date..

2) *Distress* – During the assessments, we will be asking questions about stress and mood experiences. Discussion of these experiences may be distressing. If this occurs, they have the right to take a break and rest, to not to answer questions that produce distress, or to discontinue the assessment. Again, staff will proactively inquire to participants every 20-30 minutes if they would like to take a break, discontinue, or postpone the assessment. Staff will also be trained by the PI to recognize non-verbal cues of discomfort and will be informed to discontinue assessments where clear distress is displayed by participants.

3) *Loss of Confidentiality* - There is a small potential for the loss of confidentiality but the following steps will be taken to minimize it: Assessment interviews will be conducted online and participants will receive a user-specific code allowing them to complete their personal set of questionnaires. Questionnaires completed online will be encrypted for added security and stored data will be behind a data firewall for added security. Access to data will be through password that only study personnel will have.
Privacy of data will be maintained by using a code identifier rather than participant name on any/all data and the codes will be unlinked with personal information. Only authorized personnel from the laboratory will have access to the data.. For the purposes of reports and publications, participant data and results will be presented only in pooled form, with no personal identifiers.
However, there are some circumstances under which information may not be kept confidential. Specifically, if

our team believes there is reasonable risk that participants will harm themselves (e.g., commit suicide) or others, or if our team believes there is reason to believe abuse or neglect is being conducted toward anyone being reported on in this study (e.g., either the caregiver or the care recipient), we are required by law to inform authorities so that steps can be taken to reduce this risk. Therefore, confidentiality cannot be maintained in these circumstances.

4) *Unknown Risks* - Because this is a research study, there may be some unknown risks that are currently unforeseeable.

RISK MANAGEMENT PROCEDURES AND ADEQUACY OF RESOURCES

1) *Boredom and fatigue* – Participation in the interviews may require time and attention, and participants may become bored or fatigued. If this happens, participants may may take a break in order to rest. They may also ask to discontinue theassessment and resume at a later date.

2) *Distress* – During the assessentsassessments, we will be asking questions about caregivers experiences, including some of the stresses they have faced while providing care to their loved ones. AnseringAnswering these questions may be distressing. If this occurs, they have the right to take a break and rest, to skipskip questions that produce distress, or to discontinue the assessmentassessment.

3) Suicidal Ideation - We have a standardized protocol for assessing and managing risk for suicidality. Our brief description of this protocol is as follows: During participant screening, participants will be assessed for suicidal ideation. Participants will be asked if they have recently (within the past month) had thoughts of (or considered) harming themselves or others. 'Yes' responses will be followed with clinical assessment of the nature of these thoughts, including whether the potential participant has the means of completing a suicide (e.g., access to a gun) or hurting others, and a plan (e.g., knows when and where he/she will act). Participants endorsing harm to self or to others will be managed clinically and will be referred to an appropriate mental health provider for further care. Participants endorsing clinically significant symptoms of depression (≥8 on the HADS) will be monitored throughout therapy via regular check-ins by phone to evaluate the potential for suicidal ideation or self-harm. Participants with active suicidal thoughts or intent will be managed clinically, referred for appropriate psychiatric care, and discontinued from participation in this study.

PRIVACY AND CONFIDENTIALITY CONSIDERATIONS INCLUDING DATA ACCESS AND MANAGEMENT

Loss of Confidentiality: Confidentiality will be maintained by keeping identifying information (such as names and phone numbers) in a separate location as the study results. Except for a contact form, research results will be identified by a subject number rather than by name. A number system will be used for identification of subjects; the key that links the number to the subject will be kept in a password protected Excel file, which will be stored on a removable medium so to not expose the file to potential attacks to networked computers. Study information will be stored in locked file cabinets inside a locked office as well as a password protected windows computer with a password protected file system. Qualtrics data will not contain any identifying information, including e-mail addresses. Only study personnel will have access to the identifying data, and only study personnel will have access to Qualtrics data. Subject identity will not be disclosed to any person, except in the event of a medical emergency or if required by law.

POTENTIAL BENEFITS

Participants may not receive direct benefit from participation in the project. The potential benefits of the research to the subjects themselves are a reduction in distress and improvement to overall mental and physical well-being. The benefits of the research to others might include an increased understanding of the effects of web-based behavior therapy on distress and well-being in ADRD caregivers.

RISK/BENEFIT RATIO

We judge the importance of knowledge resulting from this study and the potential for improving overall well-being among caregivers to be potentially significant. The risks are estimated to be minimal and therefore the risk to benefit ratio is low.

EXPENSE TO PARTICIPANT

N/A

COMPENSATION FOR PARTICIPATION

Participants will be paid $50 in cash for completing each of the 4 assessments (up to $200 total for full project participation). If a participant does not complete the full 2-hour assessment, partial compensation will be $25/hour completed, up to the maximum of $50.

CONFLICT OF INTEREST

None

PROCEDURES FOR SURROGATE CONSENT AND/OR DECISIONAL CAPACITY ASSESSMENT

To assess decisional capacity of each participant, we will administer the UCSD Brief Assessment of Capacity to Consent (UBACC). After participants go over the informed consent in detail, they will complete an online set of 7 items assessing his/her understanding and appreciation of the information concerning a research protocol. For each answer provided by the participant, the research assistant scores participants on a scale of 0 (clearly incapable) to 2 (clearly capable response). For the current study, only participants scoring '2' for each of the 7 items will be enrolled in the study. Participants who do not score a '2' on the first try will be provided a second opportunity to score a '2'. Total time to administer this assessment is approximately 5 minutes.