PROTOCOL TITLE:
Life Enhancing Activities for Family Caregivers (LEAF) 2.0

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1.0 Purpose of the study:

The Life Enhancing Activities for Family Caregivers (LEAF) 2.0 Course is an intervention containing a series of positive emotion skills for the family caregivers of individuals with Alzheimer's Disease (AD) (1R01AG05613-01). LEAF 2.0 builds upon the LEAF 1.0 intervention (R01NR014435) in that it specifically targets positive emotion, focuses on the caregiver, is a multicomponent intervention that offers an array of skills, and offers online delivery (either facilitated or self-guided) which makes the intervention accessible and convenient.

We will conduct a 3-arm randomized controlled trial with 500 total caregivers of individuals with AD. 200 will be assigned to the web-based facilitated LEAF program (Condition 1), 200 assigned to the web-based self-guided LEAF program (Condition 2), and 100 will be assigned to the emotion reporting waitlist-control condition (Condition 3) with crossover to the either the facilitated version or to the self-guided version; 50 in each condition, respectively. The crossovers take place after approximately 7 months into the study. Participation in the study lasts about 14 months.

LEAF 2.0's three main aims are:

> **Aim 1:** To compare the effect of online self-guided and facilitator-guided delivery modes of LEAF to an emotion-reporting control condition on positive affect, depression, anxiety, and perceived stress.
>
> **Aim 2:** To explore the effects of LEAF on caregiving burden, self-efficacy, positive aspects of caregiving, quality of care, and AD patient quality of life and assess whether these effects on outcomes are mediated by improvements in positive emotion.
>
> **Aim 3:** To test whether caregiver age, gender, or baseline stress (dementia severity) moderate the effects of the intervention.

2.0 Background / Literature Review / Rationale for the study:

Currently there are 5.5 million people in the United States diagnosed with Alzheimer's disease (AD) and this number could rise as high as 16 million by 2050. The average life expectancy post diagnosis is 8 to 10 years, although some people live as long as 20 years, experiencing increased functional, psychological, and physical dependence as the disease progresses.[1] Family members provide the vast majority of informal care to people with dementia and report significant stress as a result. Caregiving-related stress contributes to mental and physical illness and increases the risk of caregiver death.[2-6] As the number of people diagnosed with AD increases, there is a growing need for interventions that can effectively buffer these deleterious psychological and physical consequences in informal caregivers. Currently, most caregiver interventions focus on reducing burden stress, and negative emotions. However, positive emotion is uniquely associated with beneficial health outcomes, independent of the effects of negative emotion,[7-11] and holds promise for countering the negative psychological and physical health effects of caregiving. We

developed an intervention that specifically targets positive emotion[12-14] for people experiencing various types of life stress, including the stress of dementia caregiving.[15] The theory and empirically-based program includes eight skills (noticing and capitalizing on positive events, gratitude, mindfulness, positive reappraisal, personal strengths, attainable goals, and acts of kindness), can be delivered by a trained facilitator in person or via the web, and also has a self-guided online format. Across delivery modes and type of participant stress, the intervention has shown good feasibility, acceptability, and efficacy.[12-17]

The intervention is based on revised Stress and Coping Theory[20] and the Broaden-and-Build Theory of positive emotion. The preliminary data for the proposed study consists of 1) A randomized trial of the online facilitator-delivered LEAF skills intervention (N = 86) compared to a waitlist-control (N=84); 2) Pilot data from the self-guided online positive emotion skills intervention in people coping with health related stress; and 3) Development work in which we are testing three "enhancements" to increase adherence and retention to the self-guided online positive emotion skills intervention and built-in structure to support continued practice of the skills.

The goal of the proposed intervention, called LEAF (Life Enhancing Activities for Family Caregivers) is to reduce burden and increase well-being in Alzheimer's Disease caregivers through the practice of positive emotion skills. We will evaluate two methods of online delivery of LEAF: facilitated and self-guided and compare them to an emotion-reporting waitlist control condition. If effective, the LEAF program can be disseminated to Alzheimer's caregivers nation-wide.

3.0 Inclusion and Exclusion Criteria:

Inclusion criteria:

- Age 18 and over
- Identifies as the primary family caregiver of a person with Alzheimer's Disease (AD)
- Speaks and reads English
- Has access to high speed internet connection at home or in a location where they can speak privately with a facilitator (e.g. a library)

4.0 Sample Size:

We will recruit a total of 500 participants nationwide into the LEAF 2.0 randomized controlled trial. Once participants complete the online consent and baseline questionnaire, they will be randomized 2:2:1 to Facilitated LEAF (N = 200), Self-guided LEAF (N = 200) or emotion reporting waitlist control (N = 100). The waitlist control group will crossover during the study to receive either the Facilitated LEAF (N = 50) or the Self-guided LEAF (N = 50).

5.0 Research Locations:

Research will be based at Northwestern University's (NU) Feinberg School of Medicine through the Department of Medical Social Sciences (MSS) as the lead research site. NU holds the IRB of record. The research will involve Bright Outcome (https://www.brightoutcome.com/), a company experienced in designing online platforms for patient reported outcomes research. Bright Outcome has a proven track record of collaboration and delivery of technology products/services to investigators at the Feinberg School of Medicine.

6.0 Multiple sites:

Northwestern University is the lead (primary) research site for the LEAF 2.0 Study. The University of California San Francisco (UCSF) is the secondary research site for the LEAF 2.0 Study. The Principal Investigator (Dr. Judith Moskowitz), co-Investigators (Dr. Elizabeth Addington and Dr. Elaine Cheung), the NU Project Director (Eva Shiu) are at NU, in addition to the several team members who are doctoral students mentored by Dr. Moskowitz, and other research assistants on the project. Only IRB-approved staff will have contact with participants.

The co-Investigator is at the UCSF School of Nursing (Dr. Glenna Dowling) and the Project Director (Karin "Kari" Snowberg) manages recruitment, phone screening, and the technology orientation at UCSF. Paul Cotten is also a study team member, LEAF 2.0 facilitator and is at UCSF.

Northwestern and UCSF will be working collaboratively on this project and we will rely on the Northwestern IRB as the IRB of record. The management of tablets (shipment, technology training, etc.) will take place at Northwestern. We have weekly all-team meetings that include everyone from both sites. Subs-groups also meeting weekly or every other week (e.g. content development or the measures team) to review and discuss relevant topics. The frequency and length of the all-team meeting and sub-group meetings will adapt as the study launches.

NU and UCSF are jointly working towards our recruitment goal of N = 500. There will not be a recruitment distinction between sites, since we are collectively recruiting caregivers nation-wide and there is no in-person contact with participants. All modifications will be jointly discussed between NU-UCSF, but first submitted and approved through the NU IRB (IRB of record). Once changes have been approved through the NU IRB, then we will send the Modification Approval Letter to UCSF for UCSF IRB approval.

7.0 Reliance Agreements/Single IRB:

LEAF 2.0 is a multi-site study with reliance on a single IRB through Northwestern's Social and Behavioral Research Panel. We will be pursuing a reliance agreement with UCSF through SMART IRB. No research activities at UCSF will take place until the submission to modify the study with the reliance agreement is approved by the IRB.

8.0 Procedures Involved:

This study has been registered with clinicaltrials.gov and the NCT number is: **NCT03610698.** The clinicaltrials.gov registration number (NCT) will be listed on the consent forms and recruitment materials and approved by the NU IRB prior to starting recruitment.

Online Pre-Screener Link

Interested individuals will click on an online link posted on our various recruitment outlets. The link leads to a REDCap pre-screener questionnaire that helps determine eligibility. **A copy of the pre-screener questionnaire has been attached with this submission**. These questions verify whether an individual has met the study criteria to participate. If an individual is eligible, they will see a message that says a member of the study team will reach out to schedule a phone call. If an individual does not meet the criteria, they will see a message after completing the pre-screener that thanks for them their time, but notifies them that unfortunately, they are ineligible to participate in the LEAF study. Ineligible individuals will, however, be asked if they would like to be contacted about a study that utilizes a similar positive emotion skills platform called SAGE LEAF (STU00215548) that is open to all dementia caregivers rather than just caregivers of those with Alzheimer's diseaseThe following question will be added to the screen failure message: "Would you like us to contact you about a similar study that teaches positive emotion skills and is open to all dementia caregivers?" Participant will indicate yes or no, with a written statement that specifies a response of "yes" gives the study team permission to maintain their pre-screener information in REDCap and reach out to them within 6 months.

Data collected from the pre-screener link will be stored on a secure, HIPAA-compliant, and password-protected server at the Feinberg School of Medicine. We will flag identifiers on the REDCap platform, so that these variables will be excluded from any data exports. For example, we will flag First Name, Last Name, phone number, and email address. Any data from the pre-screener will only be for purposes of gauging the reach of our national recruitment efforts such as zip code and assessing trends or characteristics among those who take the screener e.g. whether the pool of interested individuals are women mainly caring for their husbands with Alzheimer's Disease (relationship with the care recipient) or women who mostly found out about the study based on a referral from an in-person support group (method of recruitment). Outside of REDCap, identifying information will never be linked with the data from the pre-screener. Only de-identified data will be exported from REDCap and saved on the password-protected FSM server. Only IRB-approved individuals will be able to access the data on REDCap. This de-identified data will be aggregated and used only for the purposes of gauging recruitment trends.

Phone Screen (~30 minutes)

A copy of the phone screen script has been uploaded to the Supporting Documents section of the IRB application. The pre-screener information from eligible individuals will feed into the REDCap database and dashboard, where the Project Director (PD) can view eligible individuals to schedule phone calls. The PD or a member of the study team will then reach out to the individual to schedule a ~30 minute phone call to discuss what the LEAF 2.0 study entails, including time commitment, timing and number of assessments, overall summary of the LEAF 2.0 course, randomization, and the use of a tablet or computer to complete study activities. If participant does not have a tablet or

computer at home, study staff will take down mailing address to send a Samsung tablet via Fedex. This allows the individual to ask questions, discuss any concerns, and decide whether or not they want to be in the study.

Consent, Baseline Assessment (T1), Randomization
After the phone screen, and if the individual wants to continue, the PD or study staff member will email the individual a link to the online consent form through REDCap.

Consent scenarios:

- If a participant consents "Yes," they will automatically continue on to complete the online baseline assessment (T1).
- If an individual does not respond to the consent form, our study team will follow-up with a reminder up to 3 times by phone or email (based on information provided on the screener.
- If an individual responds "No" and declines to participate, they will see a message thanking them for their time, and answer a brief (optional) question about why they declined.

Consenting individuals will continue to take the baseline assessment (T1) which takes up to 1 hour. Once the baseline assessment is complete, participants will be randomized to either the Facilitated LEAF "Video Session" Group (N=200), Self-guided LEAF "Online Lessons" Group (N=200), or an emotion reporting waitlist control. Both the "Online Lessons" and "Video Sessions" consists of 6 modules for the intervention; one-module unlocked per week over 6 weeks, but participants will have an 8-week period to complete the 6-module intervention. The emotion reporting control group reports their daily emotions for 8-weeks (equivalent to the 8-week intervention period), and then crosses over to receive the intervention at time point 4 (T4) as either the "Video Sessions" (N=50) or "Online Lessons" (N=50), after a waiting period of 7 months. Home practice exercises and the daily emotion check-ins will be done over the internet on the Bright Outcome platform for all research arms (N=500). The intervention content, emotion reporting forms, and assessment questionnaires are all mobile-enabled so can be completed on desktop, laptop, tablet, or smartphone.

Randomization:
Condition 1: one-on-one video sessions with a facilitator
Condition 2: self-guided online lessons
Condition 3: emotion reporting condition that will get either the one-on-one video sessions or self-guided online lessons later

Mailing and Receiving a Tablet
During the screening call, study staff will assess whether participant has a device at home with which they can access study activities (computer, tablet, or smartphone). After a participant has been randomized, the PD will mail a tablet to participants who do not have a device they can use to access study activities, and arereceiving the LEAF 2.0 intervention right away e.g. those randomized to the "Videos Sessions" **Condition 1** or "Online Lessons" **Condition 2** (NOT in the emotional reporting control group). Emotion-reporting participants **(Condition 3)** who need a study tablet will receive the tablet at T4 when they

complete the waitlist portion of the study and just prior to the beginning of the intervention. The PD will mail and track the delivery of a tablet to the participants who opt in to receiving one.

6 Sessions over 8 Weeks: 60 min/session
Facilitator-Guided Intervention "Video Sessions"
Since the intervention is delivered online, caregivers will participate in a place of their choosing that offers privacy and comfort. Facilitators will participate in a private room in their work setting. The sessions will take place over approximately 8 weeks (6 weekly modules and online home practice with 2 weeks of "catch-up"). Sessions will be conducted on an encrypted internet connection and all sessions will be video-recorded on Zoom for both quality assurance and intervention evaluation. They will also complete daily stress and emotion questions included in the control condition. Between training sessions, participants in the facilitator-guided sessions will complete home exercises and write daily experiences on the Bright Outcome online platform. Bright Outcome data we are collecting also include number of log-ins, progress in the course, completed home exercises, number of audio plays on the meditation file, content page access, etc. These data will be securely stored on Northwestern servers, accessible only to IRB-approved study staff.

6 Sessions over 8 weeks: approx. 30 minutes/online module
Week Self-Guided Intervention "Online Lessons"
In the self-guided version of LEAF, the skills will be delivered within 8 weeks (6 weekly, hour-long sessions, scheduled with a facilitator within an 8-week period) via video-conference on a device of their choice. Caregivers can participate from their home computer, smartphone, or a study supplied tablet if they opt to receive one, from a location with wifi. A week will consist of 1-2 days of didactic material and 5-6 days of real-life skills practice and reporting. Participants cannot skip ahead, and can only progress to the next lesson if they have completed the current one, but they can return to old lessons or exercises if they wish to. As part of the daily home practice, intervention participants will be asked to complete the daily stress and emotion questions included in the control condition. Data from participants engaged in the self-guided LEAF skills condition collected from the Bright Outcome platform will be securely stored on Northwestern servers, accessible only to IRB-approved study staff. These data include number of log-ins, completed home exercises, number of skills completed, data from the daily emotion reporting surveys, number of awards earned, discussion posts, etc.

Waitlist/Emotion Reporting Control Condition
In past research we have established that emotion reporting is acceptable as a control condition and that participants perceive it as being beneficial. Participants will be asked to log on to the website daily for 8 weeks, comparable to the 8 week intervention period. They will be prompted to report on positive and negative emotions and stressful events experienced in the past day. Based on past studies, we expect that this reporting will be about 5 minutes per day. Note that participants in the LEAF intervention conditions will also be completing the daily reporting of emotions and stress as part of their home practice. Data from the emotion reporting will also be tracked/exported from the Bright

Outcome platform and securely stored on Northwestern servers, accessible only to IRB-approved staff.

Time Commitment
The estimated time commitment for participating in the LEAF Study is up to 30 hours over 14 months, depending on research condition. Conditions 1 and 2 (who receive the LEAF Skills right away) will spend up to 25.5 hours in the study. Condition 3 (who wait 7 months before receiving the LEAF Skills) will spend up to 30 hours in the study.

Conditions 1 and 2: <24.5 hours

Event	Time Commitment
7 surveys (up to 1 hour each)	7 hours
6 LEAF Sessions	<6 hours
Daily Home Practice + Daily Check-in During the LEAF Sessions	11.5 hours
Total Hours over 14 months	**<25.5 hours**

Condition 3: <30 hours

Event	Time Commitment
8 weeks of Daily Emotion Check-in	4.5 hours
7 surveys (up to 1 hour each)	7 hours
6 LEAF Sessions	<6 hours
Daily Home Practice + Daily Check-in During the LEAF Sessions	11.5 hours
Total Hours over 14 months	**<30 hours**

Bright Outcome Platform
Depending on the research arm the participant is assigned to, the participant will have access to different features on the platform. Below, the check-marks indicate the website features available on the platform based on the research arm assigned.

Research Arm:	Daily Emotion Check-In	Skills Review ("Review" on Dashboard = 1-2 sentences for skill summary)	Home Practice	Home Practice Review	Self-Guided: LEAF Skills	Discussion	Awards
Condition 1: Facilitated "Video Sessions"	☑ 8 weeks	☑	☑				
Condition 2: Self-Guided "Online Lessons"	☑ 8 weeks	☑	☑	☑	☑	☑	☑
Condition 3: Waitlist Control → "Video Sessions"	☑ 8 weeks	☑ Unlock at 7 months	☑ Unlock at 7 months				
Condition 3: Waitlist Control	☑	☑	☑	☑	☑	☑	☑

→ "Online Lessons"	8 weeks	Unlock at 7 months	Unlock at 7 months	Unlock at 7 months	Unlock at 7 months	Unlock at 7 months	Unlock at 7 months

Bright Outcome "Discussion" Feature
Participants accessing the "Online Lessons" on the platform will have a tab called "Discussion" where they can discuss topics related to the study. These topics will be based on the Skills. For example, there will be a discussion thread called "Gratitude" so that participants can post there about their comments/thoughts on practicing gratitude. The discussion threads will be moderated by a staff member on the research team. The moderator will post weekly prompts to generate discussion, moderate the discussions to stay on-topic, and address and respond to any signs of distress or suicidal ideation. All posts will be tied to a LEAF Study ID and an avatar. No identifiable information will be posted/shared. All participants in this arm will watch a video and receive instructions on how to use the Discussion feature on the website. Guidelines will include refraining posting personal/identifiable information such as names and contact information, and refraining from bullying or using harsh/offensive language online. We will develop, tailor, and prepare a data safety and monitoring plan for the Discussion posts (in addition to a plan for handling a range of distress revealed to us at any point in the study), based on our previous online studies with an online forum such as MARIGOLD and LARKSPUR. These will be internal team documents. (See Section **17.0 Data Monitoring Plan to Ensure Safety of Participants** for more details).

Bright Outcome "Awards" Feature
Participants accessing the "Online Lessons" on the platform will have a tab called "Awards" where they will receive virtual badges for reaching certain goals e.g. logging in daily for 7 days, completing home practice for 4 consecutive days, or completing an online module. This data will also be collected on Bright Outcome. Each participant will be able to see their earned badges as an incentive to proceed and engage with the study.

Self-Report Assessments (T1, T2, T3, T4, T5, T6, T7)
Self-report data will be collected via online assessments (administered through REDCap) at 7 time points, emailed to participants at baseline (Time point 1) each approximately 2 months apart from baseline (T1). These assessments take approximately 1 hour to complete each time. They will be emailed to the participant (default setting), but we will offer participants the option to receive the assessments via SMS text message. The participant can choose their preference. If a participant consents to receive SMS text messages for the study, we will send participants periodic text reminders about their assessments and other research-related reminders. All data used for analysis will be de-identified. No identifiable data will ever be stored locally on staff computers, and no data are ever stored locally on participants' devices (tablet, home computer, or mobile device). All measures will be completed from home via tablet, a home computer, or mobile device. Administration of most of these measures has been shown to be feasible and acceptable to caregivers of dementia patients in LEAF 1.0 with caregivers (R01NR014435). In addition to the self-report measures of psychological well-being, frequency of positive and negative emotion and various caregiving outcomes, we will also assess the following demographic variables: age, gender, urban/rural residence, race/ethnicity, education, household income,

caregiver relationship to patient (spouse, partner, family member), time since dementia diagnosis, and how long the caregiver has been providing care to the patient.

Participant Timeline & Time Commitment Based on Research Arm

Time Commitment	Name of event			
15 minutes	Pre-screener Link			
30 minutes	Phone Screen			
60 minutes	Consent & T1 (T1 = "Assessment at Timepoint 1")			
N/A	Randomization			
30-60 minutes	Technology Phone Call			
(duration 8 weeks; time commitment varies by arm)	**"Video Sessions" Condition 1** 6 Sessions (60 minutes each) conducted within 8 weeks; daily home practice & emotion check-in (10-30 min daily)	**"Online Lessons" Condition 2** 6 Sessions (30 min each) accessed over 8 weeks; daily home practice & emotion check-in (10-30 min daily)	**Emotion Reporting Control Condition 3** 8 weeks of daily emotion check-in (~5 min daily)	**Emotion Reporting Control Condition 3** 8 weeks of daily emotion check-in (~5 min daily)
60 minutes	T2*	T2	T2	T2
60 minutes	T3	T3	T3	T3
60 minutes	T4	T4	T4	T4
(duration 8 weeks; time commitment varies by arm)	N/A	N/A	Cross-over to **"Video Sessions"**	Cross-over to **"Online Lessons"**
60 minutes	T5	T5	T5	T5
60 minutes	T6	T6	T6	T6
60 minutes	T7	T7	T7	T7
	Closing Message and Thank you			

*Note: Each time point is approximately 8 weeks apart from T1 to T2, T2 to T3, etc.

****Please see the specific timelines for each condition, uploaded on supporting documents. We will be providing these timelines to participants, based on the condition to which they're assigned.**

LEAF 2.0 Positive Emotion Skills

Please see the table below for an overview of the intervention's skills, goals, and home practice exercises. The Bright Outcome online platform will be used for all research arms of the study: the self-guided, facilitator-guided, and emotion reporting control versions. The online platform will be tailored depending on the group to which the participant has been randomized. **The content (facilitator-guided and self-guided versions) have been uploaded to the IRB.**

The total time involved from the beginning to the end of the study is approximately 14 months. This includes the baseline assessment (T1), a few weeks for scheduling phone calls for the phone screen, mailing a study tablet if applicable, the 6-session intervention over 8 weeks (or emotion-reporting control condition), and the subsequent assessments at T2, T3, T4, T5, T6, T7.

Overview of Intervention sessions, Goals, and Home Practice.		
Skills	**Goals of session**	**Home Practice**
Session 1: Positive Events, Savoring, Gratitude	Recognize positive events and the associated positive emotion; practice ways to amplify the experience of positive events; and learning to practice gratitude.	Noting a positive event each day and writing about it (savoring); starting a daily

		gratitude journal and daily emotion reports. The gratitude list home practice continues through the rest of the intervention period.
Session 2: Everyday Mindfulness and Mindfulness Meditation	Learn and practice the awareness and nonjudgment components of mindfulness	Daily informal mindfulness activities, a 10-minute formal breath awareness activity, continuing the gratitude journal and daily emotion reports.
Session 3: Positive Reappraisal	Understanding positive reappraisal and the idea that different forms of positive reappraisal can all lead to increased positive emotion in the face of stress	Reporting a relatively minor stressor each day, then listing ways in which the event can be positively reappraised. The daily formal mindfulness practice, gratitude journal, and the emotion reports continue.
Session 4: Self-Compassion	Participant learns about how to show compassion for the self, especially in the context of a caregiver. Understanding how self-compassion relates to the skills throughout the rest of the LEAF 2.0 course.	Listing an act of self compassion for each day. The 10-minute mindful breathing, gratitude journal, and daily emotion reports continue.
Session 5: Personal Strengths, Attainable Goals	Participant lists his or her personal strengths and notes how they may have used these strengths recently; Understanding characteristics of attainable goals and setting some goals for the week.	Listing a strength each day and how it was "expressed" behaviorally, working toward one of the attainable goals, and noting progress each day. The 10-minute mindful breathing, the gratitude journal, and the daily emotion reports continue.
Session 6: Skills Summary	Participants will receive a summary of the LEAF 2.0 course as a whole. Participants will identify which skills they enjoyed or did not enjoy and why. They will make a plan to practice the positive emotion skills beyond the LEAF 2.0 course.	Course wrap-up. The 10-minute mindful breathing, the gratitude journal, and the daily emotion reports continue.
Catch-Up Week	No new skills introduced. Participants continue with daily emotion reports and catch up on any home practice exercises.**	Daily emotion reports continue.
Catch-Up Week	No new skills introduced. Participants continue with daily emotion reports and catch up on any home practice exercises.**	Daily emotion reports continue.

Participants in the "Video Sessions" group will have up to 8 weeks to schedule all 6 sessions. This timeline allows for some flexibility for the caregiver e.g. if they need to reschedule due to vacation, travel, doctors appointment, etc. Participants in the "Online

Lessons" group will have up to 8 weeks to complete the online course. The daily emotion reporting period will stop after Week 8 in both of these groups.

Measures

Caregivers will complete self-report questionnaires at 7 time points over approximately 15 months. The assessments will be named by their time point "T", e.g. T1 (baseline), T2, (approx. 2 months from baseline), T3 (approx. 2 months from T2), T4 (approx. 2 months from T3), T5 (approx. 2 months from T4), T6 (approx. 2 months from T5), T7 (approx.. 2 months from T6). All assessments will be completed from home via tablet, a home computer, or mobile device. All instruments will be uploaded to this application for NU IRB approval. Administration of most of these measures has been shown to be feasible and acceptable to caregivers of dementia patients in LEAF 1.0 with caregivers (R01NR014435). In addition to the self-report measures (listed below), we will also assess the following demographic variables: age, gender, urban/rural residence, race/ethnicity, education, household income, caregiver relationship to patient (spouse, partner, family member), time since dementia diagnosis, and how long the caregiver has been providing care to the patient. We will assess the following self-report measures in each assessment:

- ***Psychological Well-being***
  - *Psychological well-being* will assessed using measures drawn from NIH Toolbox[87,95] and the related PROMIS measurement system.[96,97] We will use the short-form measures of anxiety and depression from the PROMIS measurement system. In addition, we will assess the following additional indicators of psychological well-being from the NIH Toolbox: perceived stress, life satisfaction, self-efficacy, and meaning and purpose.
  - *Frequency of positive and negative emotion* will be assessed using a modified version of the *Differential Emotions Scale* (DES).[90,98] This version of the DES was modified by Fredrickson to include a wider range of positive emotions. The full scale assesses interest, enjoyment, surprise, sadness, anger, disgust, contempt, fear, guilt, shame, shyness, amusement, awe, contentment, gratitude, hope, love, pride, sympathy, and sexual feelings. Participants will be asked to respond to each item in terms of how frequently they felt that particular affect in the past week on a 4-point scale: 0 = never, 1 = hardly, 2 = some of the time, 3 = often, and 4 = most of the time.The scale can be scored for total positive and negative emotion, grouped according to where they would fall on the circumplex model of affect (e.g., high activation vs. lower activation), or individual emotions can be examined.

- ***Caregiving Outcomes***

  - *Problematic Patient Behaviors* will be our proxy for dementia severity and will be assessed using the Revised Memory and Behavior Problems Checklist.[99] The Revised Memory and Behavior Problems Checklist is a 24-item scale completed by caregivers that measures the frequency of problematic behaviors exhibited by patients with dementia and the caregiver's reactions to these behaviors.

- *Caregiving burden* will be measured using a brief version of the Zarit Burden Interview.[89] This is a 12-item inventory that assesses subjective feelings of the impact of caregiving on emotional and physical health function, social life, and financial status and performs as well as the full 22-item Zarit Burden scale.
- *Caregiving self-efficacy* will be measured using the Caregiving Mastery subscale, Short Form, by Lawton, et al.[100] The Caregiving Mastery subscale is a 6-item measure that assesses the caregiver's sense of efficacy with caregiving, such as their confidence in handling problems when caring for the patient and being able to figure out what the patient needs.
- *Positive aspects of caregiving* will be measured with the Positive Aspects of Caregiving Scale.[91] This is an 11-item scale that identifies positive consequences of caregiving such as feeling more useful, feeling appreciated, and strengthening relationships with others.
- *Quality of care provided* will be measured using the Satisfaction with One's Own Performance as a Caregiver subscale of the Sense of Competence Questionnaire.[101] The Satisfaction with One's Own Performance as a Caregiver subscale is a 12-item subscale that measures the caregiver's self-evaluations of their caregiving effectiveness, such as how useful they feel in their interactions with the patient and their capability in caring for the patient.
- *Quality of Life of Care Recipient* will be assessed with the Quality of Life in Alzheimer's Disease scale.[102] This 13-item scale, completed by the caregiver regarding the individual living with AD's QOL, assesses several domains on a scale from 1 (poor) to 4 (excellent): physical health, energy, mood, living situation, memory, family, marriage, friends, self, ability to do chores, ability to do things for fun, money, and life as a whole. Scores on the QOL-AD show reasonable correlations with activities of daily living and patient depression.[102]

Some of the instruments will only be administered based on branching. For example, if a participant reports that their care recipient has passed away (via the caregiving status question), subsequent questions regarding caring for their loved one will no longer be asked. In this case, questions related to caregiving will be hidden using branching.

For the Medical Outcomes Study (MOS) on general adherence, we have added a "Not applicable" response. For example, "In the past month, how often did you take your medications as the doctor prescribed?" We added a response that says "Not Applicable – or—my doctor has not told me that I should take any medications."

Table of Measures

	Full Name of Measure	**Abbrev. Name of Measure**	**Administered at:**	**In reference to:**
1	Demographics (see uploaded instruments)		Baseline (T1) only	
2	Technology Survey		Right before intervention content **Timing based on*	Technology/Usability

			*Research Arm***	
3	System Usability Scale	SUS	T2 (all research arms) and T5 (arms 3 and 4 only)	Technology/Usability
4	Differential Emotions Scale also called the "Daily Emotion Check-in"	DES	All timepoints** (T1, T2, T3, T4, T5, T6, T7); and daily during the 8-week intervention period	Psychological Adjustment
5	Daily Inventory of Stressful Events	DISE	All timepoints** (T1, T2, T3, T4, T5, T6, T7); daily during the 8-week intervention period; daily during the 8-week emotion reporting control period	Psychological Adjustment
6	Dementia Severity Rating Scale	DSRS	All timepoints	Quality of Life of Care Recipient
7	PROMIS SF v1.0-Depression 8a		All timepoints	Psychological Adjustment
8	PROMIS Anxiety v1.0 8a		All timepoints	Psychological Adjustment
9	Profile of Emotional Competence Scale	PEC	All timepoints	Psychological Adjustment
10	Emotional Complexity Scale	ECS	All timepoints	Psychological Adjustment
11	modified Perceived Partner Responsiveness	mPPR	T2 (all research arms) and T5 (arms 3 and 4 only)	Psychological Adjustment
12	Caregiving Status		All timepoints except T1	Caregiving Status
13	PROMIS SF v1.1 – Global Health		All timepoints	Psychological Adjustment
14	PROMIS SF v1.0 – Sleep Disturb 8b		All timepoints	Psychological Adjustment
15	PROMIS SF v1.0 – Meaning and Purpose 8a		All timepoints	Psychological Adjustment
16	Healthcare Utilization	HU	All timepoints	Health Behaviors
17	Oberst Caregiving Burden	OCBS-15	All timepoints	Caregiving Burden
18	Positive Aspects of Caregiving	PAC	All timepoints	Positive Aspects of Caregiving
19	Perceived Stress Scale	PSS-4	All timepoints	Psychological Adjustment
20	Satisfaction with Life Scale	SWLS	All timepoints	Psychological Adjustment
21	Satisfaction with one's own performance as a caregiver	SCQ	All timepoints	Quality of Care Provided
22	Self-Compassion (Neff), short form	SCS	All timepoints	Psychological Adjustment
23	Quality of life of Care Recipient	QOL-AD	All timepoints	Quality of Life of Care Recipient
24	Revised Memory and Behavior Checklist	RMBC	All timepoints	Problematic Patient Behaviors
25	COMBO Health Behavior Measures	COMBO	All timepoints	Health Behaviors
26	Five Facet Mindfulness Questionnaire	FFMQ-15	All timepoints	Psychological

				Adjustment
27	Zarit Burden Interview	ZBI-6	All timepoints	Caregiving Burden
28	Co-morbidity check-list		All timepoints	Comorbidity
29	Medication Adherence, single-item from Heart and Soul Study (Sin et al 2015)	medadhere	All timepoints	Health Behaviors
30	6-item Caregiving Mastery Subscale, SF	CM	All timepoints	Caregiving Self-Efficacy
31	PROMIS Positive Affect 15a		All timepoints	Psychological Adjustment
32	Recommendations & Skill Use		T2 or T5 based on research arm	

Schedule of Measurements by Timepoint:ER

Screener	Phone Screen	Participant Notes		Baseline/(T1)			Post / (T2)	(T3)	(T4)		(T5)	(T6)	(T7)	
--	Script Uploaded to REDCap	ptpstatus		--			Care status (carestat)	"	"		"	"	"	
Participated in L1	phonescreen_primary cg	Withdraw		Dsrs (12 items)			"	"	"		"	"	"	
primarycare	phonescreen_wifi	Datewithdraw		qol_ad (13 items)			"	"	"		"	"	"	
careduty	phonescreen_techcomfort	withdrawinitials		Ocbs (15 items)			"	"	"		"	"	"	
relationship	phonescreen_techcomfort	withdrawreason		**25%** -"save and return"										
diagnosis & date	phonescreen_checkpt 1	Nickname		Rmbc (24 items)			"	"	"		"	"	"	
lengthascaregiver	If "Yes" proceed with call	Firstname		zbi-6			"	"	"		"	"	"	
patienthousing	availabilityonphone	Last Name		Satisfactionperfcaregiver (scq) (12-items)			"	"	"		"	"	"	
Facility (current)	shippingaddress	Email Confirm												
Carefacility (plan to move)	cityship	Availability		Caregivingmastery (cm) (6 items)			"	"	"		"	"	"	
Firstname	stateship	Notes												
Lastname	zipcode	Shipping address												
Nickname	notesship													
age	phonescreen_checkpt 2			Posaspectscaregiving (pac) – (11 items)			"	"	"		"	"	"	
gender	If "Yes" send **Consent** to participant via **REDCap**													
City (of residence)														
State (of residence)				**50%** -"save and return"										
techscreen				Promisglobalhealth (10)			"	"	"		"	"	"	
Phoneno_screen				Promisdepression (8a)			"	"	"		"	"	"	
email				Promisanxiety (8a)			"	"	"		"	"	"	
commit				Promissleepdisturb (8b)			"	"	"		"	"	"	
hearofstudy				posaffect15a			"	"	"		"	"	"	
internetconfirm				Meaningpurpose SF v1.0 (15 items)			"	"	"		"	"	"	
techcomfort				Satisfactionwithlife (swls) (5 items)			"	"	"		"	"	"	
websitecomfort				pss-4			"	"	"		"	"	"	
Technologyuse-SF (12 items)				Ffmq-15			"	"	"		"	"	"	
				75% -"save and return"										
				self-compassion (scs) (12-item)			"	"	"		"	"	"	
				Des (20-items)			"	"	"		"	"	"	
				DISE (7 items)			"	"	"		"	"	"	
				Profile of Emotional Competence Scale (PEC)			"	"	"		"	"	"	
				Emotional Complexity Scale (ECS)			"	"	"		"	"	"	
				Comorbidchecklist (3 items)			"	"	"		"	"	"	
				Healthutilization (hu) (4 items)			"	"	"		"	"	"	
				Medadhere (1 item)			"	"	"		"	"	"	
				COMBO			"	"	"		"	"	"	
				Demographics +dob +timezone +school (education) +residence (urban/rural) +ethnicity +race +income			(System Usability Scale) **SUS**** (modified Perceived Partner Responsiveness scale) **mPPR** ****all participants receive SUS and mPPR at POST (Arms 1, 2, 3, 4) -- **Recommfriend * Recommcaregiver‡ Skilluse*** the above 3 instruments branched by intervention arms only (Arms 1 & 2)				**SUS* mPPR* Recommfriend * Recommcaregiver* Skilluse*** *branched by control arms (Arm 3 & 4 only)			
Screener	Phone Screen	Ptp Notes	Send to ptp	T1	T1 done	skills	T2	T3	T4	skills	T5	T6	T7	
Automated Invites for Surveys Projected From Day 0:					Day 0		Day 84	Day 140	Day 196		Day 280	Day 336	Day 392	

Consent | Baseline Complete **Triggers T2 – T7** | 8-week intervention period | Cross-over to intervention | Closing Message

Power

Simple group comparisons for single time points or pre-post comparisons between the facilitated (n=200) and self-guided (n=200) groups will have 80% power to detect effect

sizes of *d*=.28 (R^2=.019), below the observed effect sizes for positive emotion, negative emotion, stress, depression, and anxiety in our previous LEAF trial. Comparisons between the wait-list control group (n=100) and the LEAF interventions individually (n=200) or taken together (n=400) will have 80% power to detect effect sizes of *d*=.34 (R^2=.029) and *d*=.31 (R^2=.024), respectively.

Our design of seven time points and 500 individuals exceed established minimums for detecting predictors of individual differences[108] and for detecting associations between parallel growth processes.[109] Power for these models was estimated by Monto Carlo simulation to account for our longitudinal experimental design. Effects of observed predictors (i.e., LEAF group, Aim 1) had 80% power for effects of *d*=.27 (R^2=.018). Parallel growth curves showed 80% power for slope correlations of r=.14 (R^2=.019), and comparable power for indirect effects of (r=.15, R^2=.021), consistent with previous work on mediational power.[110]

Missing Data
Although our previous test of LEAF showed high adherence rates and minimal dropout, all longitudinal analyses must plan for missing data. All proposed models will be fit with full information maximum likelihood, which yields unbiased parameter estimation under common missing data mechanisms. Multiple imputation will be used in any cases where covariates predict missingness but would otherwise not be included in proposed models.

9.0 Incomplete Disclosure or Deception:

N/A

10.0 Recruitment Methods:

We plan to recruit participants over the period of 42 months. Recruitment efforts will target the 2 major national organizations servicing patients with dementia and their caregivers: 1) the Alzheimer's Association and 2) the Family Caregiver Alliance: National Center on Caregiving.

We will also use print, radio, and websites at the national and local level of these organizations to access a geographically and age diverse cohort. Subjects will also be recruited from the Northwestern University Alzheimer's Center, the University of California San Francisco Memory and Aging Center, The New Normal, and the NUCATS recruitment tool. We will also recruit on Alzheimer's-related websites that give us permission to post.

We will create and maintain a study website and Facebook page. In addition, we recruit on Twitter and on Research Match (an online database of open research studies and individuals seeking to participate in research studies) and Reddit online discussion boards on caregiving, Alzheimer's, and dementia. Both Research Match and Reddit have been previously used to successfully recruit participants online for positive emotion intervention studies. All recruitment text will be uploaded to the NU IRB for approval prior to starting recruitment.

Update December 2020: Due to difficulty in hitting target recruitment numbers, likely impacted by the pandemic, we will be utilizing the expertise of Recruitment Partners, LLC, a firm that specializes in recruitment for research studies related to Alzheimer's disease. Recruitment Partners (RP) will be collaborating in a consultant capacity, and will not be involved in consenting participants. They will spend a month getting familiar with our study and building a campaign to engage appropriate partners within the RP Network of care, adult day centers, patient and advocacy organizations, providing preliminary information about the study to generate enthusiasm and gauge interest from our community partners. RP will provide information about the LEAF study team and instruct on caregiver enrollment. RP will educate key contacts in the RP Network on the study, provide marketing materials, and coordinate strategic recruitment outreach with the care communities and organizations.

Based on the demographics of AD caregivers nationally, we expect our sample to be approximately 66% White, 10% African American, and 8% Hispanic. We anticipate about 75% of the sample will be female.

11.0 Consent Process:

Online consent will be taken through a REDCap electronic consent form. Consent will be time-stamped and participants will be able to save, download, and/or print a copy of the consent form for their records. Participants will consent electronically by entering the date and by typing their full name into the form, which will represent their electronic signature. Participants will be considered "consented" only if they provide both items (date and electronic signature). Participants may also email the project director to request a copy of the consent form at any time.

If a participant chooses to withdraw during the study, their data will be retained up until their point of withdrawal. When a participant withdraws, they will no longer receive **future assessments** and they will no longer receive **daily reminders to log-in to the website.** If a participant indicated in the screening call that they would need a study tablet to be sent to them withdraws and has not yet received their computer tablet from the study, they will not be sent a computer tablet.

Participants can consent to be contacted for future studies. They can also consent to receive SMS text messages to receive their survey assessments. Please refer to the updated consent form.

12.0 Financial Compensation:

There is no financial compensation for completing this study. We hope that participants retain some benefit from learning thecoping skills that help reduce stress and increase positive mood.

13.0 Audio/Video Recording

The facilitator-guided LEAF sessions will be digitally video- and audio-recorded using a secure, encrypted internet connection on a password-protected platform such as Zoom. Each participant in the facilitator-guided intervention will have approximately 6 audio-recorded sessions (one for each intervention session, 6 total), recorded for quality assurance purposes and to evaluate the intervention. These recordings will be securely stored on Northwestern password-protected servers, accessible only to IRB-approved staff. The videos will be labeled by Study ID.

Fidelity will be assessed qualitatively with a checklist and comments for each component of a session as we have done in LEAF 1.0 and other face-to-face delivery of the intervention. Sessions will be reviewed by the project director to assess adherence to the protocol, delivery, facilitator/participant rapport, and session flow. All sessions of the first three participants (for each facilitator) will be reviewed immediately. This will be followed by regular (weekly, then monthly) reviews of selected sessions thereafter.

14.0 Potential Benefits to Participants:

There is no guaranteed benefit from participating in LEAF 2.0, however participants might enjoy the skills taught in LEAF and continue practicing them beyond the online course e.g. keeping a gratitude journal, completing everyday chores mindfully, or listening to a breath awareness meditation recording. Participants may gain mindfulness skills, regularly capitalize on positive events, or use positive reappraisal to reassess daily stressors. Even after completing the course, participants are encouraged to keep using their favorite skills, whether formally through the website and/or journaling about their experiences, or informally in their everyday lives.

On a broader scale, we predict that the skills taught in LEAF 2.0 may help family caregivers of dementia patients increase their positive affect and lower depression, anxiety, and perceived stress. We will explore the effects of this intervention on caregiving burden, caregiving efficacy, positive aspects of caregiving, quality of care, and AD patient quality of life. We will assess whether these effects on outcomes are mediated by improvements in positive emotion.

15.0 Risks to Participants:

Minimal Risk; Possible discomfort while interacting with the LEAF platform
LEAF is relatively easy to administer and is a low cost intervention compared to existing caregiver interventions. Many of the existing interventions require in-person interaction whereas LEAF can be delivered by a trained lay person via video conferencing. A potential risk of discomfort might arise with participants who do not have extensive experience using the internet, a tablet/computer, or mobile device. Participants might experience frustration or delayed onboarding if they are less familiar with using computer applications, browsing the internet, or connecting to wireless internet. We will provide any participant who does not have their own wifi compatible device and wants one with a tablet computer. All participants will receive clear instructions for website/technology use, and guidance on how to use the hardware/software required to participate in the study to ensure lack of

online experience is not a barrier to participation.

Minimal Risk; Possible discomfort when responding to questions

The risks of participating in LEAF 2.0 are minimal. In past research, we have not observed any participants experiencing serious or lasting distress in response to similar interventions or assessments. The intervention has been user-tested to remove any material/content that might be upsetting or insensitive, to reduce the chances of using those questions in future versions. Therefore, risk of discomfort is extremely low however, some might experience slight discomfort when asked about their emotions, coping, anxiety, and stressful events related to caregiving duties, or reflecting upon experienced negative emotions. Participants are notified that they may skip any questions they do not wish to answer. Declining to answer any questions, declining to participate in the study, or declining to continue with the study once enrolled, will not have any impact on a participant's medical care at Northwestern Hospital, Northwestern University Alzheimer's Center, the University of California San Francisco Memory and Aging Center or any affiliated specialty or primary clinics.

Potential loss of confidentiality in data

The risk of loss of confidentiality is extremely low. Identifiable information will be collected using REDCap which uses industry-standard encryption to protect participants' information while in transit from the moment data is entered to the moment it is stored on HIPAA compliant servers. Data is never fed back to participants or displayed on the participant website. Access to REDCap is granted to key personnel and all study staff handling personally identifiable information will have taken the CITI Human Subjects Training Course. Participants will be assigned and identified by a unique Study ID on the LEAF 2.0 platform, and their information will be stored in encrypted form on Northwestern computers. Any hard-copy documents will be stored in locked cabinets in the Department of Medical Social Sciences and all electronic copies of data, study emails, or records will be have double-protection through password-protected access for NU servers and to REDCap. Even if a participant's account is later compromised, submitted information on the website is protected and not released.

The REDCap instance at Northwestern supports the SMS text messages. We are using REDCap's new feature to integrate SMS text messaging with Twilio to send the assessments. Access to the phone numbers are password-protected and secure. The same data protections that exist for the REDCap PHI exists for the SMS messaging feature as well. Assessment data will not be stored locally on the phone or any device. If receiving an assessment via text, the message will include a link to a web-based survey (protected and hosted by NUCATS). If issues arise with the SMS feature, we will immediately contact the REDCap administrators at Northwestern University to resolve any issues.

The LEAF 2.0 online platform is hosted by Bright Outcome and is protected by end-to-end encryption and password measures. Participants will be able to access LEAF 2.0 intervention on their computer browser or on their mobile phones with an internet connection. Participants will submit their home practice through the website (i.e. gratitude journal) and submit their feedback for the lessons, since participants are encouraged to visit

the site every day. IRB-approved NU study staff will be able to access the data collected through the platform through direct export. No data will be stored locally on mobile phones nor participants' computers. All data will be collected directly through the website and stored on password-protected, secure NU servers. For participants who may receive a hard-copy version of the workbook, they will complete their home practice exercises directly on their workbook, mail their workbook back to Northwestern via self-addressed envelope for photo-copying, and then their workbook will be returned to them. Precautionary measures will be taken to track packages and ensure delivery arrives only for the persons intended to receive the study materials.

Potential loss of confidentiality in general
Once a participant is enrolled in the study, there is the chance someone might overhear the facilitator-guided sessions, or see a participant filling out assessments or reading the positive emotion skills on the platform. To protect participant privacy, we encourage all participants to find a private room with a closed door and to use headphones (if needed) when they have their scheduled facilitator-guided sessions. We will also encourage participants to be mindful and aware of their location (i.e. in a public or crowded space) when filling out their online assessments. Since the assessments are completed online, this allows for flexibility and participants can answer the questions from the comfort and privacy of their own home on their mobile device/tablet computer/laptop etc. All LEAF facilitators will be trained on the intervention content and will conduct the guided LEAF sessions in a private setting with the door closed and with headphones on.

"Pollyanna"
The risk of proclaiming the importance of positive affect in the stress and coping process is that it may appear to minimize the pain and serious individual and societal consequences associated with major stressful events. We are not advocating a simplistic "don't worry-be happy" approach nor do we believe that simply increasing positive emotion will prove to be a cure-all for the very real and complex issues facing AD caregivers. Such a Pollyanna-ish stance could easily degenerate into blaming the victim for not thinking the positive thoughts that may prevent depression or other negative consequence of enduring stress. However, we argue that an intervention to increase positive emotions in caregivers sets the stage for a cascade of adaptive consequences, including reduced burden and improved quality of care. Ultimately, given the high levels of stress and depression documented in dementia caregivers, we consider increasing positive emotion to be an inherently worthwhile intervention goal.

While our study focuses on positive emotion, we emphasize that LEAF 2.0 is not a replacement for therapy, nor is it considered a treatment for depression or anxiety. Participants are encouraged to follow the guidelines of their health care provider and advised that they should <u>not</u> put off starting therapy and/or medication or stop treatments recommended by their health care provider.

Withdrawal of participants
If a participant wishes to withdraw, he/she can communicate this on the phone or via email to the project director. A participant can also notify their LEAF facilitator during a LEAF session, email their facilitator, or send an email to the designated study email. Study staff

will also be monitoring communications and potentially withdrawal requests coming through on the study website, study email, or Facebook page. The participant will then be promptly withdrawn from the study, their data collected and eventually analyzed only up until the point of withdrawal. No further data will be collected after a participant has been withdrawn. We will document the reason for withdrawing. We do not foresee any circumstances under which participants will be withdrawn from the research without their consent.

16.0 Provisions to Protect the Privacy and Confidentiality of Participants and the Research Data:

The research team is committed to the protection of human participants. All study staff will participate in initial training, follow-up training, and ongoing monitoring and supervision to ensure understanding of ethical issues involved in this research. This includes, but is not limited to, the CITI Human Subjects course, training on HIPAA, and measures to protect confidentiality. The research team will also be trained on how to use the REDCap Database, which is encrypted, password-protected, and maintained by the Northwestern University Clinical and Translational Sciences Institute (NUCATS).

All data is stored and handled in a confidential manner and will only be stored on HIPAA compliant, password-protected servers accessible to IRB-approved study staff. Participants will not be identified by name on study documents or data shared with outside collaborators. Participants will be assigned and identified by their Study ID and all documents will be held to strict confidentiality and HIPAA compliant standards in double locked facilities. Confidentiality will be maintained through all phases, including data analysis and publication.

17.0 Data Monitoring Plan to Ensure the Safety of Participants:

We have developed the following data and safety monitoring plan. Our goal is to collect data on acceptability, adherence, and retention of the intervention through self-report measures and by tracking website usage and engagement. We aim to do so in a way that protects and ensures participants safety and confidentiality.

The assessments and intervention sessions pose no more than minimal risk to participants. The data and safety-monitoring plan identifies the PI as the primary monitor of risks to human subjects in the form of data and safety related risks. The study's biostatistician is the back-up data custodian to the PI, advising and providing support in data decisions. Prompt reporting of serious adverse events will be reported to the institution's IRB and project officer of the funding source by the study PI. Risks, monitoring procedures, and reporting and action plans are described below for both data and safety related risks.

Data Risks and Monitoring

Data related risks. Data related risks to participants could consist of circumstances where an insufficient amount of data was collected to answer the research questions, or a breach of confidentiality where the safety of identifiable data has been compromised.

Data monitoring procedures. The PI, Dr. Judith Moskowitz will be the primary data custodian for LEAF 2.0. Overall recruitment goals, missing data, and follow-up failures will be monitored by the project director in conjunction with the biostatistician, and the PI will receive regular updates and maintain constant communication with the biostatistician, the project director, and the rest of the team; at first bi-weekly, then monthly as needed. The biostatistician will also provide ongoing monitoring of study progress and advise with proposed changes and precautions, if necessary (i.e. updates to protocol to meet recruitment goals, etc.). Post-doctoral fellows and co-Investigators who will be assisting with data analysis will be added to the IRB.

Data risk reporting and action plan. The backup to the primary custodian (Dr. Elaine Cheung, the study's biostatistician) will oversee the data safety and monitoring plan, data management, and data security. She will work alongside the PI and the Project Director to compile the recruitment numbers during all phases of the study and responsible for assuring completion of required assessments, maintaining databases, and identifying missing data and missing follow-up assessments. Upon recognition of unacceptable recruitment, follow-up rates, or missing data, Dr. Moskowitz (PI) and Dr. Cheung (Biostatistician) will intervene with strategies to remedy the shortcomings or provide additional monitoring.

Safety Risks and Monitoring

Safety related risks. Safety related risks could consist of:

1) Emotional discomfort while using the LEAF platform
2) Emotional discomfort while completing assessments
3) Loss of confidentiality in data
4) Loss of confidentiality in general
5) "Pollyanna" effect and mistaking the intervention as therapy
6) Signs of distress or revealing identifying information on the "Discussion" forum

Safety monitoring procedures. All safety related risks will be monitored routinely throughout the study. (1-2) It will be made clear to participants that they are allowed to skip any exercises or questions that may cause them emotional distress. Participants are provided instructions on how to use the website, log-in, access the course, and are given the contact information of the Project Director, PI, and the designated study email. Guidelines and videos to use the website are provided. Participants can email or call study staff and the study is generally staffed Monday-Friday 9am-5pm except holidays, etc.

Study staff are monitoring the website weekly and will be trained to respond immediately to participant needs and/or questions on technology and the platform. There is also a FAQ page on the website for frequently asked questions. If a question is not listed/answered on the FAQ page, participants may call or email study staff. For the first version of this study LEAF 1.0, the PD developed a list of resources for the caregivers when they show signs of distress or if they are experiencing loss of their partner/dementia patient. We will be updating and tailoring these materials for LEAF 2.0. Based on our experience conducting LEAF 1.0 and prior trials of online self-guided delivery of positive affect skills (e.g.

MARIGOLD, LARKSPUR), the study team is well versed in handling/managing instances that might require providing caregivers with additional resources.

Dr. Elizabeth Addington is on the LEAF 2.0 study team and she is a clinical psychologist. She is also a Research Professor in the Department of Medical Social Sciences, Feinberg School of Medicine. She will be the main point of contact and the study advisor for questions regarding safety concerns. She will help the team make recommendations and take research precautions to ensure the safety of our participants.

(3) The security of confidential information will be monitored regularly. Participants will be informed that their responses will be kept confidential and not used against them in any legal, medical treatment, or any other manner. (4) Research facilitators are trained to deliver the intervention in a private setting with a closed door for participant confidentiality. Participants are encouraged to participate in the facilitator-guided session in a private space and to be mindfully of where they complete their online assessments, so as to limit the chance of someone overseeing their answers and to limit exposures of their responses from their computer/tablet/phone screen.

(5-6) In the event that a participant contacts the study directly to report severe distress or suicidality, or reveals this information online in an email or via the website's "Discussion" feature, the project director (Karin Snowberg at UCSF and Eva Shiu at NU) or study team member will immediately alert the clinical psychologist (Dr. Elizabeth Addington) so that PDs and Dr. Addington are immediately aware. Dr. Addington and the PDs will work together to assess the situation and take immediate, appropriate steps. If the situation is serious, we will inform the PI. Designated research staff will promptly respond to a distressed participant with appropriate information about how to seek help. In previous studies, we have developed monitoring plans for responding to signs of distress in an online forum. Study staff have the ability to archive/delete messages that are inappropriate to keep the discussion board related to discussing topics related to LEAF 2.0. Based on our past experience conducting online studies with a discussion feature (e.g. MARIGOLD, LARKSPUR), the risk of these occurrences are minimal and the study team is well versed in handling/managing these instances, if they happen.

Safety risk reporting and action plan. Any participant in need of treatment due to distress will be referred for appropriate services by the project director. In severe cases, the PI will be informed immediately. The project director will report breach of confidentiality risks incurred by participants to the PI. The PI will be responsible for informing the IRBs and the Project Officer immediately of any life threatening incidents (although this risk is very low and not expected to happen). The PI will take appropriate action to stop the study, release a participant from the study, or modify procedures to reduce and/or eliminate the occurrence of the abovementioned risks occurring at an unacceptable level.

Adverse events. Due to the nature and scope of this study, we do not anticipate any adverse events. However, in the case that an adverse event arises, it will be tracked and the PI informed within 24 hours to assess the situation and follow-up. An adverse event form will be developed detailing the problem, actions taken, supervisor notes, and follow-up steps performed. The form, supplemented by regular session notes will be immediately sent to

appropriate agencies, including the IRB and NIH. Any action recommended by one of the IRBs will be conveyed to the NIH. The PI will be responsible for the monitoring and reporting of any adverse events. The co-investigators will be consulted as appropriate.

All problems having to do with subject safety will be reported by the Principal Investigator to the IRB within ten working days. Specifically, the following will be reported, in writing: 1) all serious adverse events associated with the study procedures, and/or 2) any incidents or problems involving the conduct of the study or participation, including problems with the recruitment and/or consent processes. The Principal Investigator will provide a discussion of any problems noticed during each year in the course of the study to the IRB and NIH on an annual basis.

If, during the course of communicating with study staff (e.g., synchronously on phone/video or asynchronously via email), a participant indicates severe elevation of distress or possible suicidal ideation, study staff will follow the attached Safety Protocol, which has been developed by Dr. Moskowitz (PI) and Dr. Addington (Co-I and licensed clinical psychologist), based on procedures used in their prior studies of positive emotion skills delivered online. Staff who are responsible for communicating directly with participants will be trained on the Safety Protocol by Dr. Moskowitz and/or Dr. Addington. Trainees will be responsible for reading the entire Safety Protocol prior to training. Then training will include: a discussion/review of all elements of the Safety Protocol; time for all trainees to discuss any relevant experience and ask questions; and the opportunity to role play using the telephone template responses.

18.0 Data, and if applicable, Specimen Banking:

- Pre-screener and consent data will be collected and housed via REDCap at Northwestern University.
- Assessment data at 7 time points (T1-T7) will be collected through REDCap hosted by Northwestern University and managed under the Northwestern University Clinical and Translational Sciences Institute (NUCATS). This secure server is password-protected, HIPAA-compliant, and protected by end-to-end encryption.
- Adherence data and daily emotions/stress reporting will be collected through the online platform hosted by Bright Outcome and overseen by LEAF 2.0 study staff at Northwestern University. The NU platform will be a tailored version of a course previously designed for an online intervention for people with depressive symptoms (MARIGOLD R34). Participants will be able to take the online intervention through the platform accessible via the website on their computer browser, or the website on their mobile phones. Participants will submit their home practice through the website (i.e. gratitude journal) and submit their feedback for the lessons, since participants are encouraged to visit the site every day. Study staff will then be able to access and export the data collected through the platform. No data will be stored on mobile phones. All data will be collected directly through the website and stored on secure NU servers. The online platform

is also HIPAA-compliant, password-protected, and secured by end-to-end encryption.

- All participants will be able to access the website on their mobile phone and web browsers, but data will not be stored locally on mobile phones nor on web browsers. All data will be collected directly through the website and stored on secure NU servers.
- Dr. Moskowitz, PI, is involved in the development of the online intervention, oversight of intervention sessions, analysis, data interpretation and manuscript write-up. She will have secure access to the data housed at NU. No other Northwestern personnel will have access to the data unless he/she is listed on the IRB as study personnel. Dr. Moskowitz and her NU collaborators will also use statistical programming on FSM desktops/computers and store analysis documents on FSM servers.
- Data, video recordings, manuscript drafts, forms and other study-related documents will be stored on secure FSM servers through the Department of Medical Social Sciences (MSS). For the information that must be identifiable for the purposes of the study (i.e. name, phone number, email address for facilitator/participant contact), this information will have added layers of protection (via password access to the file). Participants will be coded and identified by a unique participant ID.
- Data input, processing, tracking and storage will happen at Northwestern University. Dr. Moskowitz has oversight over each part of the process.
- Path to storage: Bright Outcome platform REDCap platform, and audio/video recordings (input/collection) → Northwestern HIPAA-compliant server (storage and analysis) on the FSMFILES MSS Departmental Server.
- Path to storage for recorded video sessions (for quality control/quality assurance): Zoom → FSMFILES MSS Departmental Servers. Only IRB-approved research study team members will have access to FSMFILES MSS Departmental Servers.

19.0 Data Sharing:

Identifiable data will only be shared internally amongst researchers listed on the IRB. Only IRB-approved individuals will have access to data through encrypted networks like the FSMFILES network or have permission to download datasets directly from REDCap (i.e. the PI, the biostatistician, the project director, IRB-approved study staff). De-identified data might be shared with collaborators for the purposes of data analysis, secondary data analysis, manuscript-writing, using Northwestern Box. We will take precautionary measures to protect the confidentiality of our participants.

20.0 Qualifications to Conduct Research and Resources Available:

Northwestern University (NU), whose component schools and clinical affiliates form the foundation of this proposal, supports and promotes a vibrant and ever-growing community

of clinical and translational scientists that is passionately committed to improving human health. Northwestern is one of the premier undergraduate and graduate universities in the world. It is ranked 12th among US national universities by *US News &World Report*, and is ranked in the top 30 world-wide. NU has notable strengths in medicine, public health, chemistry, nanotechnology, life sciences, engineering, communications, law and business/management. Northwestern's sponsored research awards grew to $620 million in fiscal year 2015, the largest amount in the University's history and a 4 percent increase over 2014's $593.9 million. NU is located in Evanston and Chicago, Illinois. The University has a long history of leadership in interdisciplinary research programs and centers. More than 90 school-based centers and 26 University centers support interdisciplinary research that spans a wide spectrum of areas. Investigators with a Northwestern affiliation have access to the Galter Health Sciences Library at Northwestern University's Feinberg School of Medicine and all other Northwestern University libraries, including the Pritzker Research Library at Children's Memorial Hospital.

The proposed project will be based in FSM's **Department of Medical Social Sciences (MSS)**. MSS was established in 2009, with Dr. David Cella as founding and current chair, and provides a unique scientific home for applied researchers, integrating biomedical and social science approaches to improvement of health and health care delivery in diverse populations across the lifespan. Research themes include health measurement, quality of life measures, developmental mechanisms of health and disease and statistical tools to support clinical research with strength in application to specific disease processes such as cancer, neurologic disease, and early onset psychopathology. MSS is a catalyst for scientific integration across biomedical and social / life sciences campuses. MSS research cuts across traditional disciplinary boundaries, with collaborative ties with a broad range of research institutes and clinical departments across the University.

Within MSS, there is adequate office space and computer work stations for all planned staff and secure data storage (paper and electronic) designated for the proposed study. MSS has its own internal Information Technology group that manages all hardware, software, and support needs for the department. Department computers are generally on a three year replacement cycle and use whatever technology is current at the time of replacement. The computers use either Windows or MacOS operating systems and run individual firewalls, antivirus, backups, and disk encryption that are centrally managed. Servers, while managed by the department IT group, are hosted at the University Data Centers that are shared by all departments. Servers provide web services, database services, file storage, and print services. These are secured behind Data Center firewalls with specific ports open for each specific service. Network access is limited to authorized University IDs. Physical access is limited to specific IT personnel using three factor authentication including biometrics. Files are backed up daily and databases are backed up every two hours. The department currently utilizes 24 servers in a combination of physical machine and virtual machine configurations. Protected health information and personally identifiable information that are stored on MSS database servers and on MSS file servers are layered with various physical and electronic access protections and policies to ensure HIPAA compliance. There are approximately 120 laptop and desktop computers utilized by department faculty and staff for day to day computing needs, along with over 50 laptops dedicated to specific studies.

In addition, we will be working with **Bright Outcome,** a healthcare technology company led by DerShung Yang, PhD (President), who has built successful collaborations with other investigators at MSS. Dr. Yang has been head of Bright Outcome since 2003 and has worked with other clients such as the Centers for Disease Control and Prevention, the National Institute of Mental Health, the National Institute of Nursing Research, and the National Cancer Institute.